SHORT PAPER

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Zeolite-induced heterocyclization: a superior method of synthesis of condensed imidazoles†

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A superior method of synthesis of condensed imidazoles by the catalytic action of H–Y zeolite on the reaction of 1,2-diaminoaromatics with orthoesters is described.

Because of the increasing importance of benzimidazoles[1] and imidazopyridines[2] in the chemical literature we felt that an approach to the synthesis of these heterocyclic systems simpler than those hitherto described would be of great value.

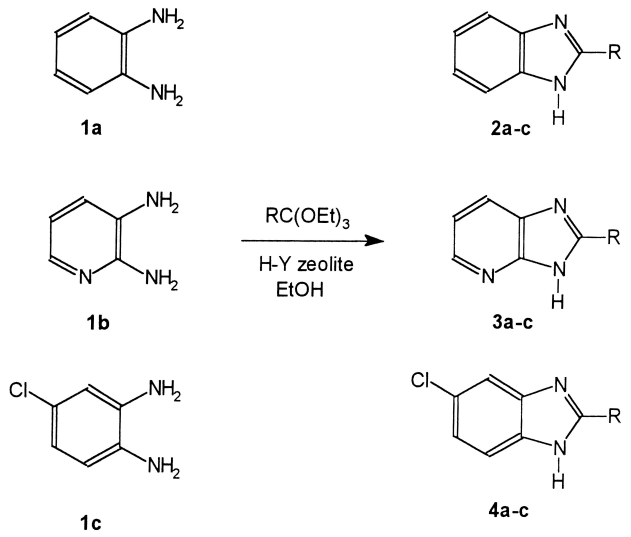
The synthesis of fine chemicals under environmentally friendly conditions represents a challenging goal in the field of synthetic organic chemistry.[3] In the last decade this approach has had a tremendous development, mainly due to the use of solid acids such as clays and zeolites.[4]

Zeolites and clays are strong Brønsted acids and have been used as catalysts for various organic reactions.[5] They are not only useful in terms of yield and selectivity but also concerning the work-up and effluent pollution. In spite of these advantages however their application in heterocyclization reactions has not fully been explored.

In continuation of our attempts to develop selective and preparatively useful methodology, based on the use of solid acids as promoters for the synthesis of fine chemicals,[6] herein we report a 'one pot' synthesis of benzimidazoles and imidazo-pyridines by the catalytic action of H–Y zeolite on the reaction of 1,2-diamino-aromatics with orthoesters. Reaction of *o*-phenylenediamine with orthoesters has been reported to take ten days without catalyst in good yields.[7] The reactions of substituted *o*-phenylenediamines and 2,3-diaminopyridine have not been reported so far.

All our attempts involving the reaction of 1,2-diaminoaromatics **1a–c** with orthoesters in refluxing EtOH or high boiling solvents such as DMSO and DMF in the absence of catalyst failed. When the same reactions were carried out in refluxing EtOH and catalytic amount of H–Y zeolite (acid type zeolite, average pore size 20Å surface area 200 ± 10 m^2/g) high yields of the corresponding fused imidazole compounds were obtained. (Scheme 1 and Table 1).

The use of HZSM-5 zeolite, montmorillonite K-10, KSF and silica gel gave products in lower yield, indicating that the activity of catalyst is likely a key factor in the activation of these reactions. In conclusion, we have developed mild, efficient and heterogeneous conditions for the synthesis of benzimidazoles and imidazopyridines using an inexpensive and eco-friendly catalyst. A further advantage of this methodology is the easy work-up procedure.



Scheme 1

Table 1

Substrate	Orthoester	Time	Product	Yield
	R	h		%
1a	H	4	**2a**	80
	Me	2	**2b**	81
	Et	2	**2c**	84
1b	H	10	**3a**	81
	Me	10	**3b**	66
	Et	10	**3c**	70
1c	H	10	**4a**	71
	Me	10	**4b**	74
	Et	10	**4c**	73

Experimental

The melting points were obtained using a Koffler Reichert hot plate melting point apparatus type 7841. The IR spectra recorded on Shimadzu spectrometer, ^{1}HNMR spectra on a Bruker AC 100 and mass spectra on a Varian 7 CH Massspectormeter at 70 eV.

General procedure for the preparation of condensed imidazoles **2a–c**, **3a–c** *and* **4a–c**: A solution of the appropriate 1,2-diaminoaromatic (**1a**, **1b** or **1c**) (10 mmole) and orthoester (10 mmole) was refluxed with H–Y-zeolite (1g in EtOH 20 ml) for the indicated time (see Table 1). The reaction mixture was monitored by TLC. The catalyst was filtered off and washed with EtOH. The solvent was evaporated to dryness under reduced pressure. The crude product was crystallized from a suitable solvent to afford the pure material (Table 1).

Benzimidazole **(2a)***:* ^{1}HNMR (d_6-DMSO) δ 7.2 and 7.6 (m, 4H, C_6H_4), 9.25 (s, 1H, CH), 10.2 (s, br, 1H, NH). IR (KBr disc) 2800, 1600, 1480, 1410, 1280, 750 cm^{-1}, MS, *m/z* 118. m.p.: 172–173 °C (lit.[1g]: 173–174 °C, AcOEt–hexane).

2-Methylbenzimidazole **(2b)***:* ^{1}HNMR ($CDCl_3$) δ 2.75 (s, 1H, Me), 7.25 and 7.45 (m, 4H, C_6H_4), 10.25 (s, br, 1H, NH), IR (KBr disc) 2750, 1550, 1450, 1430, 1280, 730 cm^{-1}. MS, *m/z* 132, m.p. 175–176 °C (Lit.[1a]: 176 °C, AcOEt–hexane).

2-Ethylbenzimidazole **(2c)***:* ^{1}HNMR ($CDCl_3$) δ 1.45 (t, 3H, Me), 3.0 (q, 2H, CH_2), 7.25 and 7.45 (m, 4H, C_6H_4), IR (KBr disc) 3750,

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1540, 1450, 1320, 1280, 750 cm^{-1}. MS, *m/z* 146, m.p.: 170–172 °C (lit.[1a]: 172 °C, AcOEt–hexane).

Imidazo[4,5-b*]pyridine* **(3a)***:* ^{1}HNMR ($CDCl_3$) δ 7.3 (m, 2H, pyridine hydrogen), 8.2 (m, 1H, pyridine hydrogen), 8.35 (s, 1H, hydrogen of imidazole), 8.5 (m, 1H, pyridine hydrogen), 13.7 (s, br, 1H, NH), IR (KBr disc) 3010, 1390, 1310, 780 cm^{-1}. MS, *m/z* 119, m.p.: 149–150 °C (lit.[1f]: 150–152 °C, AcOEt–hexane).

2-Methylimidazo[4,5-b*]pyridine* **(3b)**: ^{1}HNMR ($CDCl_3$) δ 2.75 (s, 3H, Me), 7.25 (m, 1H, pyridine hydrogen), 8.1 (m, 1H, pyridine hydrogen), 8.4 (m, 1H, pyridine hydrogen), 13.7 (s, br, 1H, NH), MS, *m/z* 133, m.p.: 189–190 °C (lit.[9]: 189.5–190.5°C, AcOEt–hexane).

2-Ethylimidazo[4,5-b*]pyridine* **(3c)***:* ^{1}HNMR ($CDCl_3$) δ 1.75 (t, 3H, Me), 3.2 (q, 2H, CH_2), 7.25 (m, 1H, pyridine hydrogen), 8.1 (m, 1H, pyridine hydrogen), 8.4 (m, 1H, pyridine hydrogen), 13.7 (s, br, 1H, NH), MS, *m/z* 147, m.p.: 138–139 °C (AcOEt–hexane).

5-Chlorobenzimidazole **(4a)***:* ^{1}HNMR ($CDCl_3$) δ 7.3, 7.4, 7.5 (m, 3H,C_6H_3), 8.15 (s, 1H, imidazole ring), 10.2 (s, br, 1H, NH), IR (KBr disc) 2750, 1410, 1290, 800 cm^{-1}. MS, *m/z* 166, m.p.: 123–126 °C (lit.[8]: 120–125 °C, AcOEt–hexane).

5-Chloro-2-methylbenzimidazole **(4b)***:* ^{1}HNMR ($CDCl_3$) δ 2.55 (s, 3H, Me), 7.1, 7.2, 7.4 (m, 3H, C_6H_3), IR (KBr disc) 2700, 1605, 1550, 1400, 1380, 950, 800 cm^{-1}. MS, *m/z* 166, m.p.: 199–200 °C (lit.[8]: 199 °C, AcOEt–hexane).

5-Chloro-2-ethylbenzimidazole **(4c)***:* ^{1}HNMR ($CDCl_3$) δ 1.5 (t, 3H, Me), 3.0 (q, 2H, CH_2), 7.1–7.6 (m, 3H, C_6H_3), 10.1 (s, br, 1H, NH), IR (KBr disc) 2750, 1620, 1550, 1480, 1320, 800 cm^{-1}. MS, *m/z* 180, m.p.: 170–171 °C (AcOEt–hexane).

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