Zeolite-induced Heterocyclization: a Superior Method of Synthesis of Imidazolidinones†

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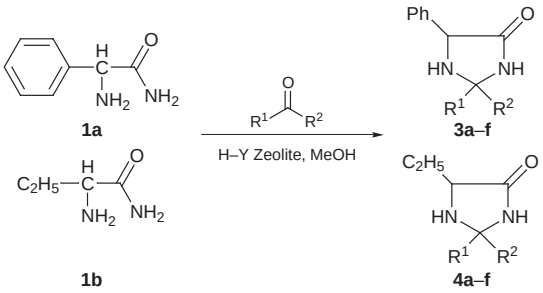
A superior method for synthesis of imidazolidinones by catalytic action of H-Y zeolite from the reaction of α-aminocarboxamides with carbonyl compounds is described.

Structure–activity relationships of antiepileptic agents show that synthesis of imidazolidinones could be of interest from the biological and synthetic points of view.[1] Imidazolidinones can be prepared by the interaction of β-aminonitriles with aldehydes and ketones in the presence of sodium alkoxide,[2] or by the reaction of *o*-carbobenzoxyamino acid amides with carbonyl compounds in the presence of a catalytic amount of a sulfonic acid, followed by removal of the carbobenzoxy group by catalytic hydrogenation.[3] Recently the preparation of these heterocyclic systems by the reaction of α-aminocarboxamides with carbonyl compounds using *p*-toluenesulfonic acid as catalyst has been reported.[1]

The preparation of fine chemicals following environmentally benign strategies represents a great challenge in organic synthesis today.[4–6] The use of environmentally friendly solid acid catalysts is now the best way for the synthesis of specific target compounds with minimum production of pollutants as well as reduction of the cost.[7]

Zeolites and other solid acids as catalysts for various organic reactions received considerable attention in the last decade, not only in terms of yield and selectivity, but also concerning the work-up and effluent pollution.[8] In spite of this, however, their application in heterocyclization reactions has not fully been explored.

In continuation of our studies to develop selective and preparatively useful methodology, based on the use of solid acids as promoters for the synthesis of fine chemicals,[9] we report a "one pot" synthesis of imidazolidinones by the catalytic action of H-Y zeolite on the reaction of carboxamides with carbonyl compounds.



Scheme 1

Attempts involving the reaction of α-amino-α-phenylacetamide[10] **1a** with acetone **2a** in refluxing MeOH in the absence of catalyst failed. When the same reaction was carried out in refluxing MeOH and a catalytic amount of H-Y zeolite (acid type zeolite, average pore size 20 Å, surface area 200 ± $m^2 g^{-1}$) high yields of the corresponding imidazolidinones **3a** were obtained. Most probably the reactants pass through the pore openings where the reaction takes place. To establish the generality of the method, **1a** and α-amino-α-ethylacetamide **1b**[11] were treated with various carbonyl compounds **2a–f** in the presence of H-Y zeolite in refluxing MeOH, giving good to high yields of the corresponding imidazolidinones **3a–f** and **4a–f** (Scheme 1, Table 1). The use of HZSM-5 zeolite and montmorillonite K-10 gave products with lower yields, showing that the acidity of catalyst is likely to play an important role in the activation of **2**.

It is also noteworthy that in these reactions, which could give two diastereomeric products, both diastereomers were obtained.

In summary, in comparison with other methods which have drawbacks from the standpoint of yield, price of catalyst (sodium methoxide) or corrosiveness, the advantages of the present method are apparent from the availability of inexpensive H-Y zeolite, heterogeneous conditions and easy work-up. The simplicity of method make it a convenient route to imidazolidinones.

Experimental

The melting points are uncorrected and were obtained by a Kofler Richart type 7841 melting point apparatus. The IR spectra were recorded on a Perkin–Elmer 781 spectrometer, ^{1}H NMR spectra on a Brucker Ac 80 spectrometer and the Mass spectra on a Fisson 800 Trio instrument at 70 eV.

General Procedure for the Preparation of Imidazolidinones **3a–f**, **4a–f**.—A solution of an appropriate α-aminocarboxamide (**1a** or **1b**) (0.67 mmol), carbonyl compound (0.67 mmol and H-Y zeolite (0.2 g) in MeOH (10 ml) was refluxed for the indicated time. The reaction was monitored by TLC. The catalyst was filtered off and the solvent evaporated to dryness under reduced pressure. The crude product was crystallized from EtOH to afford the corresponding imidazolidinones (Table 1).

Compound **3a**: ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 6 H, $2CH_3$), 2.1 (s, br, 1 H, NH), 4.6 (s, 1 H, CH), 7.3 (s, 5 H, Ph) and 7.6 (s, br, 1 H, NH); IR, (KBr disc) *j* 3170, 3078, 2977, 1714, 1442 and 751 cm^{-1}; MS *m/z* (relative intensity), 190 (71, M^+) 175 (9), 148 (11), 147 (100), 146 (42), 100 (69), 104 (20), 91 (21), 79 (22), 77 (25) and 58 (23).

Table 1

Substrate		Carbonyl compound R^1	R^2	*t*/h	Product	Yield (%)
1a	**2a**	CH_3	CH_3	12	**3a**	63
	2b	$[CH_2]_4$		6	**3b**	75
	2c	$[CH_2]_5$		4	**3c**	65
	2d	CH_3	C_2H_5	15	**3d**	70
	2e	Ph	H	5	**3e**	55
	2f	Ph	CH_3	48	**3f**	None
1b	**2a**			4	**4a**	80
	2b			4	**4b**	85
	2c			5	**4c**	79
	2d			6	**4d**	91
	2e			4	**4e**	83
	2f			48	**4f**	20

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Compound **3b**: ^{1}H NMR ($CDCl_3$) δ 1.8 (s, 8 H), 2.4 (s, br, 1 H, NH), 4.5 (s, 1 H, CH), 7.3 (s, 5 H, Ph) and 8.1 (s, br, 1 H, NH); IR, (KBr disc) ν 3153, 1704, 1449 and 669 cm^{-1}; MS *m/z* (relative intensity), 216 (31, M^+), 187 (85), 173 (31), 172 (62), 106 (100), 104 (38), 79 (8) and 77 (11).

Compound **3c**: ^{1}H NMR ($CDCl_3$) δ 1.6 (s, 10 H), 2.15 (s, br, 1 H, NH), 4.6 (s, 1 H, CH), 7.5 (m, 5 H, Ph) and 8.2 (s, br, 1 H, NH); IR, (KBr disc) ν MS *m/z* (relative intensity), 230 (25, M^+), 188 (12), 187 (100), 106 (88), 704 (19), 79 (38), 79 (29), 77 (25) and 54 (22).

Compound **4a**: ^{1}H NMR ($CDCl_3$) δ 1.1 (t, 3 H, CH_3), 1.45 (s, 6 H, $2CH_3$), 1.75 (q, 2 H, CH_2), 2.15 (br, 1 H, NH), 3.5 (m, 1 H, CH) and 8.1 (s, br, 1 H, NH); IR, (KBr disc) ν 3100, 1700 and 1420 cm^{-1}; MS *m/z* (relative intensity), 142 (2, M^+), 99 (52), 85 (48), 84 (100), 82 (8) and 69 (69).

Compound **4b**: ^{1}H NMR ($CDCl_3$) δ 0.99 (t, 3 H, CH_3), 1.7 (q, 3 H, CH_3), 1.8 (s, 8 H, $4CH_2$), 1.95 (s, br, 1 H, NH), 3.4 (m, 1 H, CH) and 8.1 (s, br, 1 H, NH); IR, (KBr disc) ν 3150, 2900, 1700 and 1410 cm^{-1}; MS *m/z* (relative intensity), 168 (24, M^+), 140 (28), 139 (100), 111 (71) and 58 (78).

Compound **4c**: ^{1}H NMR ($CDCl_3$) δ 0.98 (t, 3 H, CH_3), 1.4 (m, 10, $4CH_2$), 1.7 (q, 2 H, CH_2), 1.8 (br, 1 H, NH), 3.4 (m, 1 H, CH) and 6.9 (s, br, 1 H, NH); IR, (KBr disc) ν 3150, 2920, 1690 and 1425; MS *m/z* (relative intensity), 184 (5, M^+), 183 (11), 182 (30), 153 (15), 139 (100), 120 (28), 111 (18) and 97 (20).

Compound **4f**: ^{1}H NMR ($CDCl_3$) δ 0.99 (t, 3 H, CH_3), 1.5 (s, 3 H, CH_3), 1.7 (q, 2 H, CH_2), 2.0 (s, br, 1 H, NH), 3.5 (m, 1 H, CH), 7.4 (m, 5 H, Ph) and 8.1 (s, br, 1 H, NH); IR, (KBr disc) ν 3200, 2805, 1690 and 1450 cm^{-1}; MS *m/z* (relative intensity), 190 (11, M^+), 189 (99), 161 (51), 160 (72), 78 (25) and 77 (65).

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