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Natural Kaolinitic Clay Catalyzed Conversion of Nitriles to 2-Oxazolines

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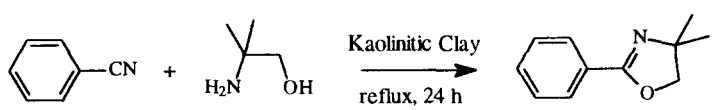
Abstract: Natural Kaolinitic clay has been found effective as catalyst in the conversion of aromatic and aliphatic nitriles with 1,2-aminoalcohol to 2-oxazolines (56 - 96 % yield).

Racemic and non-racemic oxazolines continue to be an important functionality in synthetic organic chemistry. Oxazoline has been used extensively as protecting group[1] while its optically active analogue has gained importance as valuable auxiliary in asymmetric synthesis.[2] Several chiral oxazolinyl ligand systems developed in the last few years include semicorrin,[3] aryl mono-oxazoline as well as C_2-symmetric bis-oxazoline[3,4] and pybox[5] have proved extremely efficient for a whole range of transition metal catalyzed enantioselective transformations. Numerous methods have been developed for the preparation of 2-substituted oxazolines from carboxylic acid,[6] carboxylic ester,[4a,7] nitrile,[8] aldehyde[9] and amido alcohol.[10] Most of the methods utilize complex reagents, strongly acidic conditions and stringent reaction parameters with occasionally low yields of the reaction products.

The applications of inorganic solids such as natural clays as efficient catalysts in organic transformations have been studied recently.[11] The natural clays have several advantages as they are inexpensive, environment friendly, non-toxic, recoverable, reusable and, also, mild catalysts. The acidic properties[12] of natural Kaolinitic clay have been exploited recently for a few synthetic applications.[13] In this communication we wish to present a new application of Kaolinitic clay as an efficient and mild catalyst for the conversion of aromatic and aliphatic nitriles to 2-substituted oxazolines. A mixture of benzonitrile, and Kaolinitic clay[14] (20 % w/w) was refluxed in 2-amino-2-methylpropanol (8 eq.) for 24 h (method A) to afford 2-phenyl-4,4-dimethyl-2-oxazoline, **1**, in good chemical yield after careful chromatography (scheme-1).



Scheme-1

1

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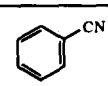
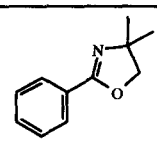
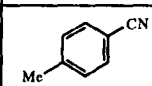
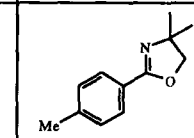
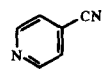
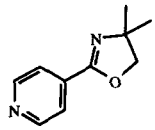
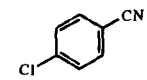
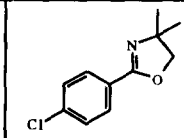
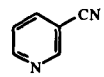
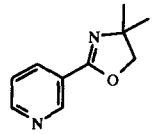
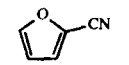
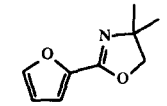
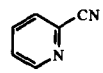
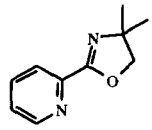
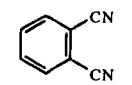
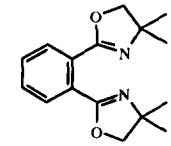
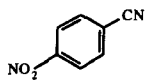
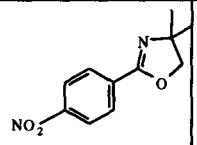
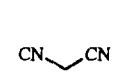
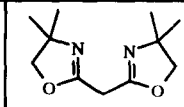
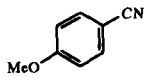
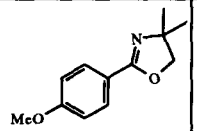
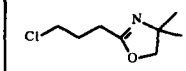
However, when the reaction was performed with 1.5 equivalent of aminoalcohol in refluxing *o*-dichlorobenzene the product was isolated in slightly lower yield (Table-1, entry 1, method B). Several different aromatic and aliphatic nitriles were converted to oxazolines under the same reaction conditions and the results are summarized in Table-1.

***Table-1**: Conversion of Nitriles to 4,4-Dimethyl 2-oxazolines with 2-amino-2-methylpropanol catalyzed by Koalinitic clay.*[a]

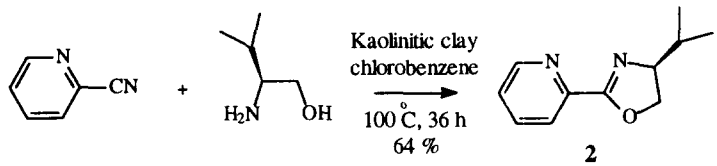
Entry	Nitrile	Oxazoline	Method[15] (% Yield[b])	Entry	Nitrile	Oxazoline	Method[15] (% Yield[b])
1			A (86) B (71)	7			A (82)
2			A (96) B (80)	8			A (75) B (66)
3			A (95)	9			A (90)
4			A (95)	10			A (85)
5			A (93)	11			A (90)
6			A (87) B (70)	12			A (56)

[a]All the oxazolines show satisfactory spectral data. [b]Isolated yield.

The nitriles attached to electron rich pyridyl nucleus were converted to oxazolines in excellent yields (entry 2-4). Moreover, aromatic nitriles with electron withdrawing or electron releasing functional group were converted to oxazolines with same efficacy (entry 5-7) with an exception of *p*-chlorobenzonitrile which gave

the oxazoline in lower yield (entry 8). The other examples include 2-cyanofuran and 1,2-dicyanobenzene furnished the corresponding oxazolines with 90 and 85% isolated yield respectively (entry 9 & 10). Different functional groups could tolerate this mild reaction condition and no cleavage of methoxy group (entry 6) was observed as reported by Clark and Wood[8b] under $ZnCl_2$ catalyzed microwave irradiation. Aliphatic nitriles were also converted to oxazolines in good yield as demonstrated for malononitrile (entry 11) and 4-chlorobutyronitrile (entry 12). The reusability of the catalyst was studied for the reaction of benzonitrile. The catalyst from the reaction of benzonitrile in *o*-dichlorobenzene (Table-1, entry-1) was separated by filtration, reactivated by treatment of 1 M HCl and was found to be equally efficient in the next cycle of the same reaction giving the oxazoline in 69% yield.

The reaction of 2-cyanopyridine with L-valinol gave (S)-(-)-4-isopropyl-2-(2-pyridinyl)oxazoline, **2**, with >98% optical purity as determined by comparison of optical rotation with literature value[8a] (scheme-2). Chiral pyridinyloxazolines of this type are used as efficient ligands in several asymmetric transformations.[16]



2

Scheme-2

This method of Kaolinitic clay catalyzed conversion of aromatic and aliphatic nitriles to 2-oxazolines offer several advantages over the reported procedures.[8] This transformation is generally very clean, involves simple work-up and the oxazolines are isolated in higher yields compared to other known methods. The environment friendly clay catalyst can be separated by simple filtration and efficiently reused for other reactions.

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14. The Kaolinitic clay was procured from the Padappakara mine of Quilon District, Kerala, India and was subsequently purified and characterised (ref. 13a).

15. **Method A**: A solution of benzonitrile (0.5 g; 4.85 mmol), 2-amino-2-methylpropanol (3.45 g; 38.8 mmol; 8 eq.) and Kaolinitic clay (0.1 g, 20% w/w) was stirred at 165 °C for 24 h. The reaction mixture was diluted with dichoromethane (40 mL), the catalyst was filtered, washed with the same solvent (3 X 20 mL) and the combined organic extract was washed with water, brine, dried on Na_2SO_4 and concentrated. The residue was purified by column chromatography on nutral alumina to afford the oxazoline, **1**, as oil (0.73 g; 86% yield) which was characterised by usual spectral methods.

Method B: A solution of benzonitrile, 2-amino-2-methylpropanol (1.5 eq.), catalyst (20 % w/w) was refluxed in *o*-dichlorobenzene (180 °C) for 24 h and the product was isolated by direct chromatography to afford the oxazoline **1** (71 % yield).

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