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MICROWAVE ASSISTED FRIEDLÄNDER CONDENSATION CATALYZED BY CLAY

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Abstract: Clay catalyzed Friedländer condensation of 2-amino arylaldehyde or ketone with carbonyl compounds containing α-methylene group has been achieved in solvent free condition under microwave irradiation to give polycyclic quinoline derivatives.

Friedländer synthesis[1-4] is an acid or base catalyzed condensation followed by a cyclodehydration between an aromatic 2-aminoaldehyde or ketone with the carbonyl compound containing a reactive α-methylene group. 2-Aminobenzaldehyde and 2-aminoacetophenones condense readily with active methylene compounds in the presence of base catalysts.[5] However, 2-aminobenzophenone fails to undergo base catalyzed Friedländer condensation with many active methylene compounds. This problem can often be overcome by the use of acidic catalysts. In many cases acid catalyzed[6-7] Friedländer condensations have been found to be more effective than those, by bases, especially one of the reactants being 2-aminoarylketone. Therefore, it is important to develop a simple and environmentally safe solvent free method to synthesize polycyclic quinoline derivatives.

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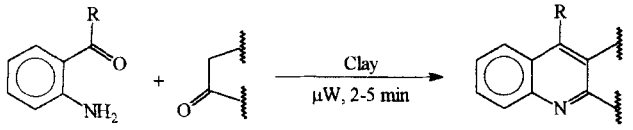
Microwave assisted reactions are advantageous in many ways over conventional approaches because of short reaction time,[8] cleaner reactions with easy workup. Recently use of inorganic solid supports[9] as catalysts have been developed for solvent free reactions resulting higher selectivity, milder conditions and easy to handle. Clay catalyzed organic reactions are gaining importance owing to their inexpensive nature and special catalytic attributes in heterogeneous reactions.[10] Our ongoing program to develop environmentally benign protocols[11] herein, we wish to report a montmorillonite KSF clay catalyzed Friedländer condensation under microwave irradiation in solvent free conditions.

Thus, 2-aminobenzaldehyde or 2-aminoarylketones were mixed with active methylene compounds such as 4-chromanone,[12] pyrazolone,[13] N-carbethoxy-3-pyrrolidone[14] etc., adsorbed on Montmorillonite KSF clay and irradiated in a microwave oven to give several polycyclic quinoline derivatives in good yields (Scheme-1). When the reaction mixtures were irradiated for longer time, the yields were reduced, may be due to thermal decomposition.

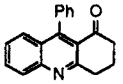
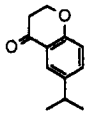
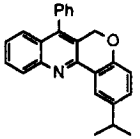
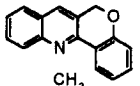
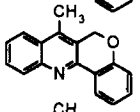
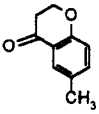
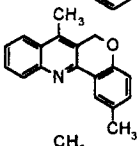
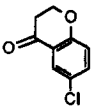
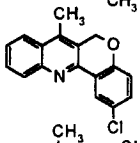
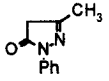
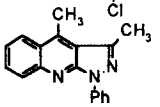
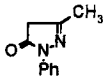
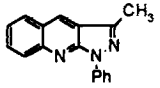
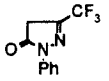
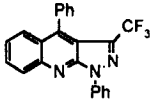
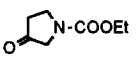
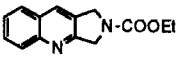


Scheme-1

This methodology can be explored to prepare quinolines with a wide range of substituents because the 2-aminocarbonyl and active methylene reactants may carry a variety of substituents. In order to know the role of microwave in rate enhancement for the Friedländer condensation, similar reactions were carried out in an oil bath at ~110 °C, where the reactions took longer time and low yields were observed. When the reactions were carried out for longer time we have isolated self condensed products.

In conclusion, we have demonstrated an easy and efficient procedure involving simple workup for the preparation of polycyclic quinoline derivatives under dry conditions using

Table 1. Preparation of polycyclic quinoline derivatives[a]

Entry	R	Active methylene	Product[a]	Irradiation Time[b] (min)	Yield[c] found/lit. (%)	M. P. found/lit. (°C)
1	Ph			5	62/80(thermal)	156/156[15]
2	Ph			4	82	148
3	H			2	66/73(base)	119/120[16]
4	CH_3			2	72/77(thermal)	111/112[16]
5	CH_3			2	68/75(thermal)	167/169[16]
6	CH_3			3	72/75(thermal)	156/159[16]
7	CH_3			4	62/80(thermal)	176/178[17]
8	H			2	62/80(thermal)	156/156[18]
9	Ph			4	72	125
10	H			4	45/90(acidic)	133/134[14b]

a) Products were identified by 1H NMR and Mass Spectra and by comparing the m.p. with authentic samples.[14-18]
b) Pulsed irradiation of one minute (20 seconds interval for each pulse)
c) Recrystallized from methanol.

microwave irradiation. The present method has an additional advantage like the use of non corrosive, inexpensive and environmentally friendly catalyst.

General procedure : 2-Aminoaldehyde or ketone (15 mmol) and active methylene compound (15 mmol) were mixed with KSF clay (1 g) subjected to microwave irradiation in a pyrex test tube at output of about 600 Watts. for a given time. The progress of the reaction was monitored by TLC at an each minute of intervals. Ethyl acetate was added to the reaction mixture and the clay is filtered off, after removing the solvent under reduced pressure, the crude product was recrystallised from hot methanol to give polycyclic quinoline derivatives (for time and yield see table 1). This method was successfully applied for 5-10g scale and gave moderate to good yields.

2-Isopropyl-7-phenyl-6*H*-benzopyrano[4,3-b] quinoline (2):

^{1}H NMR ($CDCl_3$) : δ 1.35 (d, 6H, CH_3, J=7.15 Hz), 2.95 (m, 1H, CH), 5.05 (s, 2H, OCH_2), 6.87 (d, 1H, ArH, J=9.06), 7.18-7.35 (m, 4H, ArH), 7.42-7.69 (m. 5H, ArH), 8.15 (d, 1H, ArH, J=9.5 Hz), 8.32 (s, 1H, ArH).

MS : m/z 351

1,4-Diphenyl-3-trifluoromethyl-1*H*-pyrazolo[3,4-b]quinoline (9):

^{1}H NMR ($CDCl_3$) : δ 7.25-7.48 (m, 5H, ArH), 7.52-7.60 (m. 5H, ArH), 7.62-7.85 (m, 2H, ArH), 8.21 (d, 1H, ArH, J=7.6 Hz), 8.51 (d, 1H, ArH, J=7.65 Hz).

MS : m/z 387

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