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Note

Ecofriendly solvent free microwave enhanced alkyl migration in *N*-alkyl anilines in dry media conditions

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A rapid, cleaner, cost effective and ecofriendly synthesis of exclusive *para* alkyl anilines in solvent free conditions using solid supports under microwave irradiation is achieved.

Keywords: Mineral solid supports, solid state reactions, *N*-alkyl anilines, rearrangement, ring alkylated anilines, microwave enhancement

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Developing chemical compounds with the desired properties is time-consuming and expensive. Consequently, increasing interest is being directed towards technology that allows more rapid synthesis and screening of chemical substances to identify compounds with functional qualities. Microwave induced Organic Reaction Enhancement (MORE) chemistry offers a simple, non-conventional technique for the synthesis of a wide variety of compounds having medicinal, pharmaceutical and commercial importance[1,2]. Highly accelerated reaction rate is a main advantage, which enables to carry out a synthesis in much lesser time and with reasonable good yields[3]. Currently available classical methods require elaborate apparatus setup, longer heating time, large volume of organic solvents and there is virtually no control over the energy input. Recent simplification of MORE technique has increased safety and practical utility of the microwave ovens for their use in organic laboratories without any modifications[4]. In recent years the use of solid supports as well as microwaves[5,6] has been well established as a pollution free technique which allows reaction to occur on a preparative scale in open vessels under solvent free conditions which avoids the risk of high pressures and explosions[7,8]. Microwave activation rather than conventional heating is preferred, as solid supports are rather poor thermal conductors but strong microwave absorbents, which results in lesser evaporation of solvents preventing pollution[9]. Further the reactions are generally faster and the products obtained are of high purity[10].

Ring alkylated anilines find considerable application as antioxidants in rubber industry, dyes and pigment industries. They also find uses in the field of epoxy-resin hardeners, fungicides, accelerators and colour developers. The Hoffmann-Martius[11] rearrangement of hydrohalides of *N*-alkylanilines and Reilly-Hickinbottom[12] rearrangement of *N*-alkylanilines in the presence of catalysts to ring alkylated anilines were reported. However, these methods have many limitations like long reaction time, high reaction temperature, etc. Moreover these conventional methods usually gives both *ortho* and *para* products apart from small quantity of aniline. Also these reactions were carried out in organic solvents that are generally toxic to living beings.

It has been reported that amino aryl ketones and amino aryl amides could be prepared by thermal Fries rearrangement of anilides and phenyl ureas respectively in the presence of Lewis acids such as $TiCl_4$, $ZrOCl_2$, $BiCl_3$, etc[13].The same reactions under microwave irradiation on a mineral solid support produced exclusive *para* product in excellent yields[14]. (**Figure 1**)

In continuation of earlier work, a very clean, rapid and very high yielding method for the preparation of exclusive *para* alkyl anilines under solvent free conditions is reported. Rearrangement of *N*-alkylanilines in the presence of different Lewis acids like $AlCl_3$ adsorbed on an inert solid support such as neutral alumina under microwave irradiation afforded the exclusive products **(Scheme I)**. The reactions were completed within 3-5 minutes at 100% power (800 W) and complete conversion of reactants into single *para* product was noted even in the presence of

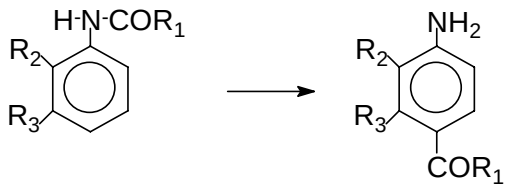
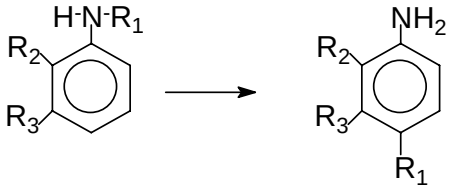


Figure 1

Table I — Results of rearrangement of *N*-Alkylanilines

Starting material	Product	Reaction Period (min)	Yield (%)	m.p.°C (lit)
N-Methyl aniline	*p*-Toluidine	3.0	94	44 (44-46, ref. 16)
N-Ethyl aniline	4-Ethyl aniline	3.0	86	214 (216*, ref. 16)
N-Isopropyl aniline	Cumidine	3.5	87	220 (226*, ref. 16)
2-Methyl- *N*-methyl aniline	2,4-Xylidine	4.0	92	215 (218*, ref. 17)
3-Methyl- *N*-methyl aniline	3,4-Xylidine	4.0	96	49 (49-51, ref. 17)
2-Bromo-*N*-methylaniline	2- Bromo- *p*-Toluidine	5.0	92	237 (240*, ref. 17)
3-Amino-*N*-methylaniline	Tolune-2,4-Diamine	4.5	90	97 (99, ref. 17)
3-Chloro-*N*-methylaniline	3-Chloro- *p*-Toluidine	5.0	91	235 (238*, ref. 17)

* Boiling points (°C)



Compd	R_1	R_2	R_3
1	CH_3	H	H
2	C_2H_5	H	H
3	$CH(CH_3)_2$	H	H
4	CH_3	CH_3	–
5	CH_3	H	CH_3
6	CH_3	Br	H
7	CH_3	H	NH_2
8	CH_3	H	Cl

Scheme I

a deactivating group in the ring **(Table I)**. The reaction is of general applicability and various substituted anilines were synthesized. It is noteworthy that these reactions did not proceed at all if the *para* position of aniline is blocked.

In conclusion, a solvent free, rapid, cleaner, cost effective and ecofriendly synthesis of *para* alkyl anilines under microwave irradiation is reported with excellent yields.

Experimental Section

Melting points were recorded on sulphuric acid-bath and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1600 spectrophotometer using KBr pellet. ^{1}H NMR spectra were recorded on a Brucker WH 400 instrument using TMS as internal standard. The reactions were carried out in a domestic microwave oven (LG 800W) operating at 2450 MHz frequency. The best yields were obtained under the combinations of catalyst ($AlCl_3$) and solid absorbent (Al_2O_3) (**Table I**).

General procedure. 1 mmole of the reactant **1**, 1 mmole of fused catalyst ($AlCl_3$) were ground well with 10 g of dry solid support neutral alumina. Alternatively, to a solution of reactant (1 mmole) in 20 mL of appropriate solvent taken in a 400 mL beaker, fused catalyst (1 mmole) and dried solid support (10 g) were mixed well and the solvent was evaporated in vacuo. This dry mixture was transferred to a 100 mL standard flask, which was kept inside a microwave oven operating at high power level, and irradiated for about 3-5 minutes with intermittent cooling at every 0.5 minutes interval. The cooling was necessary to avoid loss of product by evaporation from the solid support as the temperature attained was very high. The completion of the reaction was confirmed by TLC and products were recovered by following two methods. 1. The products were extracted by appropriate solvents (5 times, 10 mL), filtered, dried over anhydrous sodium sulphate and evaporated. To the mixture, 1:1 HCl was added (thrice, 10 mL), shaken thoroughly, filtered and the filtrates were neutralized by potassium hydroxide solution. The products formed were filtered, washed with water and dried. All products obtained were characterized by ^{1}H NMR spectra, and by comparison of their IR spectra, melting points and TLC spots with authentic samples.

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