March 2010 ISSN: 0974 - 7516 Volume 6 Issue 1

Trade Science Inc.

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 6(1), 2010 [52-55]

Microwave assisted one pot synthesis of N-alkyl aromatic amines from benzanilide in presence of phase transfer catalyst

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Received: 16th January, 2010 ; Accepted: 26th January, 2010

ABSTRACT

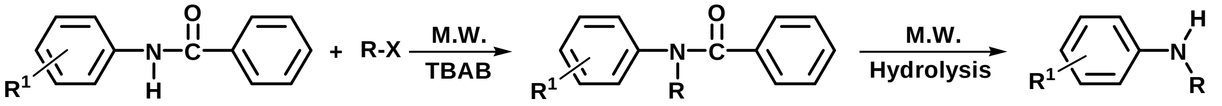
Number of substituted benzanilide reacts fast with alkyl halide, base, alcohol and phase transfer catalyst, under microwave irradiation to obtain the corresponding N-alkyl benzanilides, which were hydrolyzed by using sulphuric acid to obtain pure N-alkyl aromatic amines. Microwave assisted organic synthesis has attracted attention due to enhanced reaction rates, high yields, improved purity, ease of work up after the reaction and eco-friendly reaction conditions compared to the conventional methods.

KEYWORDS

Benzanilide;
Alkyl halides;
Base;
Alcohol;
Sulphuric acid;
Aromatic amine.

INTRODUCTION

Use of microwave oven as tool for synthetic chemistry is a fast growing area[1,2]. since the first reports of microwave assisted synthesis in 1986[3,4] The technique has been accepted as a method for reducing reaction times often by orders of magnitude and for increasing yields of product compared to conventional methods[5,6]. As a result, this has opened up the possibility of optimizing new reactions in a very short time. A key advantage of modern scientific microwave apparatus is the ability to control reaction conditions very specifically, monitoring temperature, pressure and reaction times. Several methods have been developed for performing reactions using microwaves including solvent free conditions or adsorbing reactants into inorganic supports such as silicas or clays. If the reactions need to be carried out in a solvent, the medium needs to have a high dielectric constant (ε) in order to take advantage of the microwave heating effect. To this end, solvents such as ethanol ($\varepsilon = 24.3$) were used althrough they are excellent solvent for performing the reaction[7]. Solution phase reactions performed in the presence of solvent can be either homogeneous or heterogeneous. Homogeneous reactions include standard organic reactions in which all reagents are dissolved in the solvent. Microwave irradiation has been used extensively and successfully with homogeneous solution-phase reactions[8]. Phase transfer catalysis (PTC) is now a commercially mature discipline with over 600 applications covering a wide spectrum of industries such as pharmaceuticals, agrochemicals, perfumes, flavours, dyes, specialty polymer and



Scheme 1

pollution control etc.[9-12]. N-monoalkyl aromatic amines are important intermediates and they find applications in almost every important sector of chemical industry such as polymers, pharmaceuticals, dyes and agrochemicals. These compounds are useful in the manufacture of fire resistant plastics[13] and other polymers made up of urea formaldehyde[14] or urethane[15]. They were also used as catalyst for the cross linking of polyester[16,17] and as the stabilizer for phenolic resins[18]. The pharmaceutical applications of N-alkyl aromatic amines include the synthesis of anxiolytics such as diazepam[19]. Recently, N-alkyl 2,6-disubstituted aromatic amines are reported to be useful for the preparation of anti-hypartensive[20], anti-ulcer[21] and anti-arrythmic agents[22].

N-alkyl aromatic amines such as N-ethyl aniline and N-ethyl m-toludine are useful as intermediates in the manufacture of disperse dyes[23], whereas N-benzyl aniline is used for the preparation of triphenyl methane dyes. Victoria blue BO an important blue dye required for ball pen inks, is prepared from N-ethyl 1-naphthyl amine. N-monoalkyl anilines are vital intermediates for agrochemicals. These compounds were used as intermediates for the manufacture of herbicides, insecticides and acaricides. They are also used as intermediates for the preparation of agents controlling ticks and fleas[24]. Some other applications of N-alkyl aromatic amines are in the field of preparation of eletrophotographic photoconductors[25], coagulants[26] and milling dyes[27]. They were also widely used as antiknock additives for gasoline and diesel fuel[28]. These compounds have been exploited for the extraction and separation of rare earths and noble metals such as uranium and platinum[29].

The present paper, reports the remarkable fast synthesis method of N-alkyl aniline via alkylation of benzanilide in presence of solvent under microwave irradiation. The synthesis were carried out by simple mixing of benzanilide with 25% excess of an alkyl halide, base, alcohol and a catalyst amount of tetrabutylammonium bromide (TBAB). These mixtures were irradiated in an open beaker in a microwave oven. The results were summarized in TABLE 1.

EXPERIMENTAL

Melting points were determined in open capillaries in Paraffin bath and is uncorrected. IR spectra were recorded in KBr disc on a Perkin Elmer spectrometer for all products ^{1}H-NMR spectra were recorded on NMR spectrometer in $CDCl_3$ using chloroform an internal standard. The mass spectra were recorded on GCMS-QP 2010 mass spectrometer. All the reagents used were of AR grade and were used without further purification. The reactions were carried out in microwave oven (CE2977 Samsung).

All compounds were characterized by modern spectral and elemental techniques.

Ic: ^{1}H NMR ($CDCl_3$): δ 3.895 (t, 2H, N-CH_2-), 1.667 (2H, -CH_2-), 0.939 (t, 3H, - H_3), 7.014- 8.118 (M, 10H, Aromatic). Mass (ES/MS): m/z 239 (M-H).

Id: ^{1}H NMR ($CDCl_3$): δ 0.911 (t, 3H, -CH_3), 1.377(M, 2H, -CH_2-), 1.612 (M, 2H, -CH_2-), 3.920 (t, 2H, -CH_2-N), 7.008-7.285 (M, 10H, Aromatic). Mass (ES/MS): m/z 253 (M-H).

Hd: ^{1}H NMR ($CDCl_3$): δ 0.939 (t, 3H, -CH_3), 1.398 (M, 2H, -CH_2-), 1.550 (M, 2H,-CH_2-), 3.073 (t, 2H, -CH_2-N), 3.910 (S, 1H, -N-H), 6.566-7.256 (M, 5H, Aromatic). Mass (ES/MS): m/z 149 (M-H).

RESULTS AND DISCUSSION

Under microwave synthesis, number of substituted benzanilide reacts fast with alkyl halide, base, alcohol and phase transfer catalyst to give corresponding N-alkyl benzanilides, which were hydrolyzed by using sulphuric acid to obtain pure N-alkyl aromatic amines. The results are summarized in TABLE 1 and 2.

Since the shape and size of the reaction vessel are important factors for the heating of dielectrics in a microwave oven, preferred reaction vessel is a tall beaker of much larger capacity than the volume of the reaction mixture. Superheating of liquids is common under microwave irradiation, thus the strategy of the reactions is to keep the reaction temperature substantially below the boiling point of each compound used for the reaction. Since it is difficult to measure in a household microwave oven, one of the best solution is to repeat an experiment several times increasing slowly power so that vapours do not escape outside of the beaker after the reaction, The work-up procedure is reduced to a treatment with an appropriate solvent (e.g. ethanol) and recrystallization.

TABLE 1 : Microwave assisted N-alkylation of benzanilides under PTC

Compd.	Substrate	Alkylating agent	W and T required* for reaction		Product R	Yield %	M. P./ B. P. (°C)	
			W	Sec.			Found	Reported
Ia	H	$(CH_3)_2SO_4$	300	120	$-CH_3$	94	59	60
Ib	H	$(C_2H_5)_2SO_4$	300	110	$-C_2H_5$	93	53	54
Ic	H	$n-C_3H_7Br$	300	110	$-C_3H_7$	92	178	175-80
Id	H	$n-C_4H_9Br$	300	125	$-C_4H_9$	94	52	54
Ie	H	$n-C_6H_{13}Br$	300	150	$-C_6H_{13}$	90	221	220
If	H	CH_2- CH=CH_2-Br	300	130	$-CH_2-CH=CH_2$	92	198	196-98
Ig	H	$C_6H_5CH_2Cl$	300	125	$-CH_2C_6H_5$	95	105	106
Ih	2-Cl	$(CH_3)_2SO_4$	300	120	$-CH_3$	96	65	64
Ii	4-Cl	$(CH_3)_2SO_4$	300	122	$-CH_3$	95	70	69
Ij	2-OCH_3	$(CH_3)_2SO_4$	300	120	$-CH_3$	92	80	80
Ik	3-OCH_3	$(CH_3)_2SO_4$	300	120	$-CH_3$	94	55	56
Il	4-OCH_3	$(CH_3)_2SO_4$	300	125	$-CH_3$	92	74	74-76

***Where W and T indicate watts and time, respectively**

TABLE 2 : Microwave assisted hydrolysis of N-alkyl Benzanilides to N-alkyl anilines

Compd.	Substrate		Product	Yield %	M.P./B.P. (°C)	
	R^1	R			Found	Reported
Ha	H	$-CH_3$	N-Methyl aniline	92	195	196
Hb	H	$-C_2H_5$	N-Ethyl aniline	92	202	204
Hc	H	$n-C_3H_7$	N-Propyl aniline	90	220	222
Hd	H	$n-C_4H_9$	N-Butyl aniline	91	238	240
He	H	$n-C_6H_{13}$	N-Hexyl aniline	87	157	160
Hf	H	$-CH_2-CH=CH_2$	N-Allyl aniline	92	111	112
Hg	H	$-CH_2-C_6H_5$	N-Benzyl aniline	92	37	38
Hh	2-Cl	$-CH_3$	2-Chloro-N-methyl aniline	89	217	218
Hi	4-Cl	$-CH_3$	4-Chloro-N-methyl aniline	92	238	240
Hj	2-OCH_3	$-CH_3$	2-Methoxy-N-methyl aniline	92	33	33
Hk	3-OCH_3	$-CH_3$	3-Methoxy-N-methyl aniline	90	130	131
Hl	4-OCH_3	$-CH_3$	4-Methoxy-N-methyl aniline	89	39	40

The hydrolysis of N-alkyl benzanilides is carried out under microwave irradiation by simple mixing of N-alkyl benzanilide with 20% H_2SO_4 and appropriate time to obtain N-alkyl aniline. The results are sumarised in TABLE 2.

CONCLUSIONS

In conclusion, it is to be stated that the method developed is simple and economical for the synthesis of N-alkyl aniline that occurs under mild conditions using inexpensive reagents and a microwave oven as the irradiation source. Moreover, this synthesis method of N-alkyl aniline is superior and faster as compared to conventional methods because the starting material used here is benzanilide instead of its sodium salt, which makes the synthesis procedure simple, convenient and safe.

AKNOWLEDGEMENTS

The author appreciate financial support provided by University Grants Commission, Western Regional Office Ganeshkhind, Pune for this work [File No: 47-519/08 (WRO) dated 14th Jan. 2009]. The author is greatful to The Principal Dr.R.B.Bawdhankar and Dr.P.R.Pawar, Dept. of Zoology Veer Wajekar A.S.C.College, Phunde (Uran) for helpful discussions, encouragement and support.

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