Original Article

Bulletin of Environment, Pharmacology and Life Sciences

Online ISSN 2277 – 1808
Bull. Environ. Pharmacol. Life Sci.; Volume 1 [10] September 2012: 50 - 54
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Website: www.bepls.com

Microwave Synthesis of N-Alkyl Aromatic Amines from *p* – Toluene Sulphonamide in Presence of Phase Transfer Catalyst

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ABSTRACT
The substituted p – toluene sulphonamide reacts fast with alkyl halide, base, alcohol and phase transfer catalyst, under microwave irradiation to obtain the corresponding N-alkyl p – toluene sulphonamide, 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.
Keywords: *p–toluene sulphonamide; Alkyl halides; Base; Alcohol; Sulphuric acid; Aromatic amine.*

INTRODUCTION

Microwave synthesis represents a major break-through in synthetic methodology. A dramatic change in the way chemical synthesis is performed and in the way it is perceived in the scientific community. Conventional heating, long known to be inefficient and time-consuming, has been recognized to be creatively limiting as well. Microwave synthesis gives organic chemists more time to expand their scientific creativity, test new theories and develop new processes. Instead of spending hours or even days synthesizing a single compound, chemists can now perform that same reaction in minutes. In concert with rapidly expanding applications, microwave synthesis can be effectively applied to any reaction scheme, creating faster reactions, improving yields, and producing cleaner chemistries [1].

Use of microwave oven as tool for synthetic chemistry is a fast growing area [2,3]. Since the first reports of microwave assisted synthesis in 1986[4,5]. 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 [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 silica 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 (ϵ = 24.3) were used although 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 pollution control etc [9-12].

N-monoalkyl aromatic amines are important intermediates and they find applications in almost every important sector of chemical industry. 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-hypertensive[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 *p*–toluene sulphonamide in presence of solvent under microwave irradiation. The synthesis were carried out by simple mixing of *p*–toluene sulphonamide with 25 % excess of an alkyl halide, base, alcohol and a catalyst amount of tetrabutylammonium hydrogen sulphate ($TBAHSO_4$). These mixtures were irradiated in an open beaker in a microwave oven. The results were summarized in Table-1.

MATERIAL AND METHOD

General procedure for N – alkylation of p – toluene sulphonamides using phase transfer catalyst.

p – toluene sulphonamide (5.0 mmol), sodium hydroxide (20 mmol), 5 ml of alcohol and tetrabutyl ammonium hydrogen sulphate (0.50 mmol) as a catalyst were taken in 50 ml beaker, stirred for few second and placed in microwave oven for irradiation at 300 Watt for 30 seconds to obtain *p* – toluene sulphonamide salt . The mixture was cooled at room temperature. The alkyl halide (7.5 mmol) was mixed with the resulting mixture and was irradiated in microwave oven at 300 Watt for 118 to 140 seconds to obtain *N* – alkyl *p* – toluene sulphonamide. The reaction was monitored by TLC. After completion of the alkylation reaction, the content was cooled at room temperature. The reaction mixture was extracted with benzene (20 ml) and washed with (2 x 25 ml) 2N hydrochloric acid and water to remove unreacted salt. Then it was dried over anhydrous sodium sulphate. On solvent evaporation solid products were obtained. The crude product was purified by crystallization using ethanol as a solvent.

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.

Ie. *N – hexyl p-toluene sulphonamide*

FT-IR (KBr, νcm^{-1}): 3089, 3052, 3007 (C-H aromatic), 2860 (C-H aliphatic), 1593 (C=C aromatic), 1489, 1370, 1348 (-CH2 bending), 1165 (C-N), 1068 (S=O).

^{1}H NMR ($CDCl_3$): δ 7. 476– 7. 028 (m, 10 H, Aromatic), 3.508 (t, 2H), 3.073 (t, 2H), 1.585-1.219 (m, 6H), 0.860 (t, 3H) Mass (ES/MS): m/z 330 (M - H).

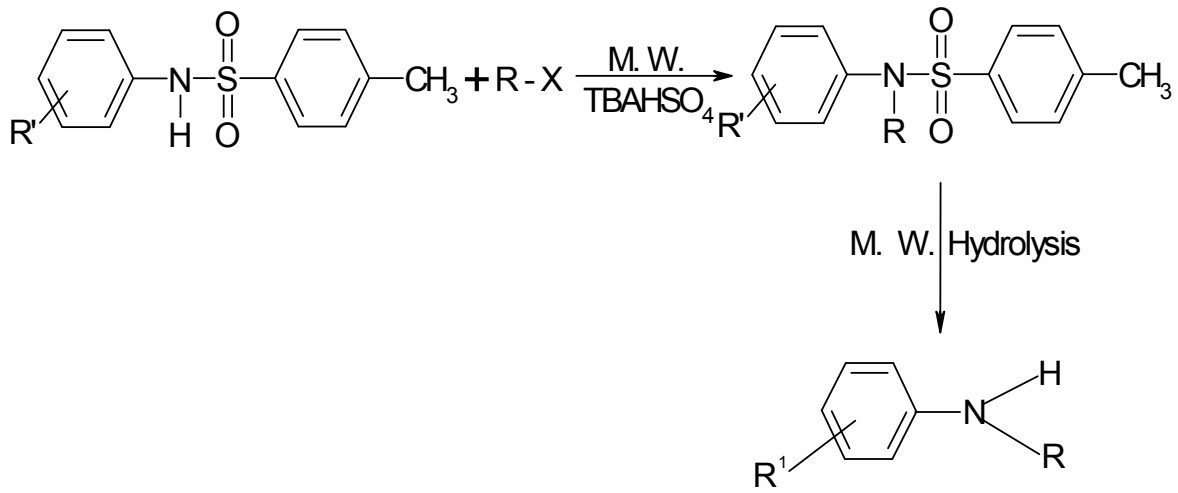
Hd. *N –butyl aniline*

FT-IR (KBr, ν cm^{-1}): 3364 (N-H), 3059, 3037 (C-H aromatic), 2931, 2871 (C-H aliphatic), 1644 (C=C aromatic).

^{1}H NMR ($CDCl_3$): δ 7.256– 6.566 (m, 5H, Aromatic), 3.910 (t, 2H), 3.526 (s, 1H), 3.073 (t, 2H), 1.550 (m, 2H), 1.612(m,2H), 1.398(m,2H), 1.377(q, 2H,), 0.939 (t, 3H,), Mass (ES/MS): m/z 149 (M - H).

RESULT AND DISCUSSION

Under microwave synthesis, number of substituted *p* – toluene sulphonamide reacts fast with alkyl halide, base, alcohol and phase transfer catalyst to give corresponding N-alkyl *p* – toluene sulphonamide, 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 the beaker after 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 *p* – toluene sulphonamide under PTC.

Compd	Substrate	Alkylating Agent	W and T required* For reaction		Product	Yield	M. P./ B. P. (°C)	
			W	Sec.	R	%	Found	Reported
Ia	H	$(CH_3)_2SO_4$	300	118	$-CH_3$	96	96	95
Ib	H	$(C_2H_5)_2SO_4$	300	110	$-C_2H_5$	95	89	88
Ic	H	n-C_3H_7Br	300	130	$-C_3H_7$	94	56	55
Id	H	n-C_4H_9Br	300	125	$-C_4H_9$	94	54	53
Ie	H	n-$C_6H_{13}Br$	300	140	$-C_6H_{13}$	96	66	67
If	H	$C_6H_5CH_2Cl$	300	120	$-CH_2C_6H_5$	95	147	148
Ig	2-Cl	$(CH_3)_2SO_4$	300	130	$-CH_3$	90	98	97
Ih	4-Cl	$(CH_3)_2SO_4$	300	120	$-CH_3$	96	94	93
Ii	2-OCH_3	$(CH_3)_2SO_4$	300	120	$-CH_3$	92	99	100
I	4-OCH_3	$(CH_3)_2SO_4$	300	120	$-CH_3$	95	67	68

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

The hydrolysis of N-alkyl *p* – toluene sulphonamide is carried out under microwave irradiation by simple mixing of N-alkyl *p* – toluene sulphonamide with 20% H_2SO_4 and appropriate time to obtain N-alkyl aniline. The results are sumarised in Table-2

Table 2: Microwave assisted hydrolysis of N-alkyl *p* – toluene sulphonamide 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		93	195	196
Hb	H	$-C_2H_5$	N-Ethyl aniline		92	202	204
Hc	H	n-C_3H_7	N-Propyl aniline		91	220	222
Hd	H	n-C_4H_9	N-Butyl aniline		90	238	240
He	H	n-C_6H_{13}	N-Hexyl aniline	89	157	160	
Hf	H	$-CH_2-C_6H_5$	N-Benzyl aniline		90	37	38
Hg	2-Cl	$-CH_3$	2-Chloro-N-methyl aniline		87	217	218
Hh	4-Cl	$-CH_3$	4-Chloro-N-methyl aniline		90	238	240
Hi	2-OCH_3	$-CH_3$	2-Methoxy-N-methyl aniline	90	33	33	
Hj	4-OCH_3	$-CH_3$	4-Methoxy-N-methyl aniline	91	39	40	

CONCLUSION

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 *p* – toluene sulphonamide 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 thankful to Principal Dr. R. B. Bawdhankar and Dr. P. R. Pawar, Department of Zoology, Veer Wajekar A. S. C. College, Phunde (Uran) for helpful discussions, encouragement and support.

REFERENCES

1. Brittany L Hayes, (2000) *Microwave Synthesis* © CEM Publishing U.S.A. 14.
2. Perreux L., Loupy A., (2001). *Tetrahedron*, 57, 9199.
3. Gabriel S., Grant E. H., Halstead B. S. Mingos D. M., (1998). *P. Chem. Soc. Rev*., 27,213.
4. Gedye R., Simth F., Westaway K., Humera A., Baldisera L., Laberge L. Rousell L.(1996). *Tetrahedron Lett.,* 27, 279.
5. Giguere R., Bray T. L., Duncan S. Majetich G. (1986). *Tetrahedron Lett.,* 27, 4945.
6. Westman J. (2001). *Org Lett.,* 3, 3745.
7. Stadler A., Kappe A. C. (2001). *Eur. J. Org. Chem*., 919.
8. Nicholas E., Leadbeater Torenius M. H. (2002). *J. Org. Chem*., 67, 3145-3148.
9. Starks C. M., Liotta C. L., Halpern M., Chapman Hall. (1994). *Phase Transfer Catalysis*, 23.
10. Dehmlow E. V., Dehmlow S. S. (1993). *Phase Transfer Catalysis*, 65.
11. Sharma M. M., Sasson Y., Neumann R. (1997). Handbook of Phase Transfer Catalysis, 168.
12. Krishna Kumar V. K., Sharma M. M. (1983). *Synthesis*, 558.
13. Koenig K. H., Pommer H. (1962). *Belg Pat*., 606.
14. Baruo Har Toshio N., Koyi F., Kazunobu A. (1972). *Jap. Pat*., 72,26,582.
15. Murai T., Kon Y. (1967). *Jap. Pat*., (67) 3038.
16. Heinz M., Dieter S., Hans S., Hansjoachim T. (1970). *S. Afr. Pat*., 69,04,393.
17. Kutepov D. F., kubinV. K. (1972). (USSR), *Past Massy*,18-20.
18. Cliernik J., (1975). *Czech. Pat.,* 160,528.
19. Iacobescu-ilianu S., Bellu D., Cuiban F. (1965). *Sci. Pharm. Proc*., 25.
20. Julius D., George D. (1976). H U S P., 3,976,643.
21. Julius D., George D. (1980). H U S P., 4,183,956.
22. McMaster P. D., Byrnes E. W., Feldman H. S., Takman B. H., Tenthorey P. A. (1979). *J. Med. Chem*., 22**,** 1177.
23. Straley J. M. (1970). *Chemistry of Synthetic dyes*, Edtd. By Venkataraman K, Vol III ,424.
24. Willoughby O. (1982). *Farm Chemicals Handbook*, Pub By Meister Pub. Co.USA,
25. Kalle A. G. (1964). B P., 977,399.
26. Shinohara J., Aoyagl J. (1973). *Jap. Kokai.,* 73,97,779.
27. Ogawa T., Yatome C., Ishizuka Y., Takase Y. (1973). *Gifu Diagaku Hokuku*, 68-74.
28. Tetsuya I. (1971). Showa Oil Co. Ltd. Tokyo Jap, Sekiyu Gakkai Shi, 14(7), 512-517.

29. Eugeniusz K., Zazislaw B., Witold P. (1980). *Pol. Pat.*, 108,076.

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