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Ultrasound mediated Green Synthesis of Hexa-hydro Triazines

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Abstract

Sym-triazines have been documented for their antitumor, antimicrobial and anti-cancer actions. The present work aims to derive a variety of 1,3,5-triaryl-1,3,5-hexahydrotriazine using ultrasound assisted reactions from the reactions of aryl amines with aqueous formaldehyde. Furthermore, a special study on the different solvents and revealed that mixture of water and ethanol was found to be the best solvent.

*Key words***:** Green synthesis; Non-hazardous; Solvent; Triazines; Ultrasound mediated synthesis

Introduction

In early 1990's, Green chemistry is defined as the utilisation of a set of principles that reduces or eliminates the use of hazardous substances in the design, manufacture and application of chemical products [1]. Among the methods in chemical synthesis that have been recognized to have a green value, are the ones that make use of (a) ultrasound and (b) the non-hazardous microwave irradiation [1-2].

Ultrasonic irradiation has been found useful as support for quite a few organic reactions [3]. In recent decades, ultrasound has been used more and more frequently in organic synthesis [4-6]. Ultrasound irradiation enables many chemical reactions to proceed, even with some reactions which could not be carried out under conventional condition. The use of ultrasound in organic transformations is well known because it can enhance the reaction rate and can alter selectivity performance of the reaction [7-9]. Ultrasonic irradiation has been increasingly used in organic synthesis in last three decades. Comparing with traditional methods, this method is more convenient and easily controlled. A large no. of organic reactions has been carried out in higher yield, shorter reaction time and milder condition under ultrasound irradiation [10-12]. In all reactions, organic solvents are always being used. Recently organic reactions in water without use of harmful organic solvents have drawn much more attention, because water is cheap, safe and environmentally benign solvent [13-14]. sym-triazine derivatives are reported to show a broad spectrum of biological activity in particular, antitumor, antimicrobial, and anticancer activities [15]. It is also used as herbicides, carcenolytics, growth stimulating and antidote activity [16]. In the course of our investigation to develop new

green synthetic method, we would like to report ultrasound assisted synthesis of 1,3,5-triaryl hexa hydro triazines in different solvents (Scheme 1). It can also felicitates reactions at ambient conditions that otherwise require higher temperature, pressure or concentrations. To the best of our knowledge, the use of ultrasound has not been extended to the synthesis of triazines.

Experimental

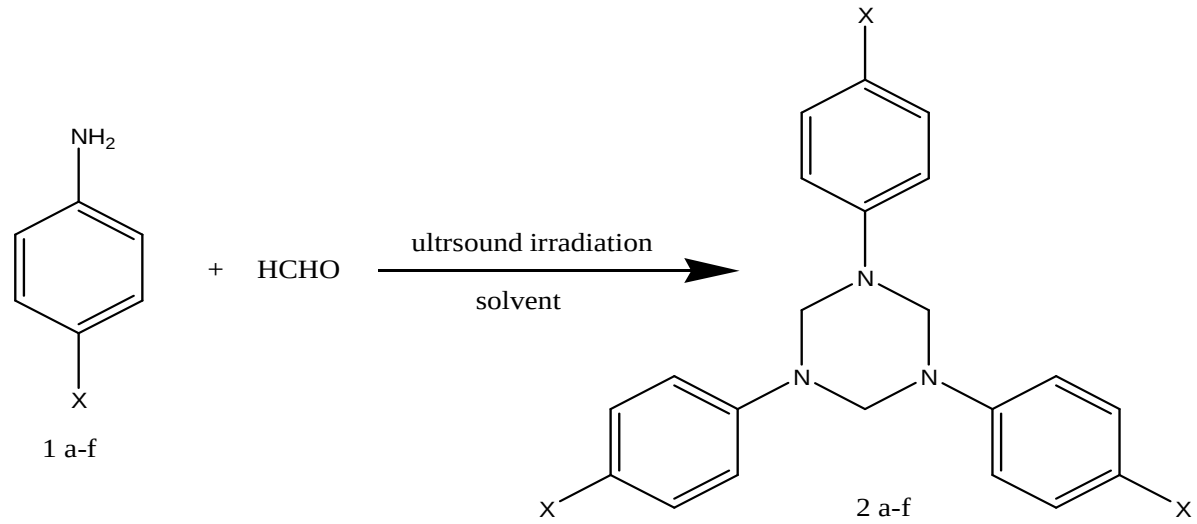
Melting points were measured in open capillaries and are uncorrected. IR spectra were recorded on Jasco FT/IR-5300 spectrophotometer. ^{1}H-NMR spectra were run on a Jeol AL 300 FT NMR and the chemical shifts are expressed as δ ppm using TMS as internal reference. Elemental analyses were performed on Exter Analytical Inc "Model CE-440 CHN analyzer. All commercially available chemicals were purchased from E. Merck and Aldrich.

General Procedure for the Preparation of 1,3,5-triaryl-1,3,5-hexahydrotriazines:
Ultrasound assisted Method:

A mixture of aryl amines (0.01mol) and formaldehyde (0.011mol) contained in Erlenmayer flask was introduced in to Sonicator. Reactions were done in different solvent medium reported in Table1. After completion of reaction (as monitored by TLC), filtered the product and washed with ethanol to afford the product 2a-f.

Conventional Method:

To a mixture of aryl amines (0.01mol) in ethanol, 37% HCHO solution (0.011mol), the reaction mixture was stirred with gentle refluxing for 2 hrs. The precipitated product was filtered off the next day. The products were extracted rapidly with 5 parts of ethanol to give the pure products 2a-f.



X = H ; a
X = CH3 ; b
X = OCH3 ; c
X = NH2 ; d
X = Cl ; e
X = NO2 ; f

Scheme: 1

Results and Discussion

Aryl amines underwent smooth reactions with aqueous formaldehyde in different solvents to produce 1,3,5-triaryl-1,3,5-hexahydrotriazines in reasonably good yields (Scheme 1). All the products displayed the IR and ^{1}H-NMR spectra consistent with their assigned structures. The physical data and yield of the products are given in Table1. It is evident from the Table 1 that mixture of ethyl alcohol and water (60:40) produce

maximum yield in comparison to the other solvents used in study in reasonably less time.

Spectral and elemental data:

Hexahydro-1,3,5-triphenyl-s-triazine (2a):
M.P. 141-142^{o}C;
IR (KBr)- 3032, 2937, 2844, 2574, 1596, 1498, 1227, 1163;
^{1}H-NMR (DMSO-d_6): δ: 5.32 (s,6H,CH_2), 6.8, 7.2, and 6.9 (15H, Ar-H)
Anal.calc. for- $C_{21}H_{21}N_3$ (315.33) C,79.93; H,7.19; N,12.88. Found: C,79.68; H,7.13; N,13.186

Hexahydro-1,3,5-tolyl-s-triazine (2b):
M.P. 127-128^{o}C;
IR (KBr)- 3069, 3024, 2860, 2735, 1618, 1473, 1239, 1008
^{1}H-NMR (DMSO-d_6): δ:5.32 (s, 6H,CH_2), 6.75 and 6.9 (AA'BB', 12H,Ar-H) and 2.5(CH_3):
Anal. calc. For $C_{24}H_{27}N_3$ (357.32) C,81.13; H7.61; N, 11.26 Found: C,80.98; H,7.63; N,11.39

Hexahydro-1,3,5-p-methoxyphenyl-s-triazine (2c):
M.P. 132-134^{o}C;
IR (KBr)- 3037, 2997, 2826, 1612, 1443, 1293, 1150
^{1}H-NMR (DMSO-d_6): δ:5.31(s, 6H, CH_2),6.7 and 6.8 (AA'BB', 12H,Ar-H) and 3.45(OCH_3)
Anal. Calc. For $C_{24}H_{27}N_3O_3$ (404.97) C,71.11; H,6.72; N, 10.37; O,11.8 Found: C,71.03; H,6.68; N,10.38, O,11.91.

Hexahydro-1,3,5-p-aminophenyl-s-triazine (2d):
M.P. 240-242^{o}C;
IR (KBr)- 3384, 3032, 2863, 1616, 1513, 1226, 1069
^{1}H-NMR (DMSO-d_6): δ:5.27 (s, 6H, CH_2), 6.5 and 6.45 (AA'BB', 12H, Ar-H) and 3.8 (-NH_2)
Anal. Calc. For $C_{21}H_{24}N_6$ (360.43) C,69.86; H,6.67; N,23.4; Found: C,69.92; H,6.74; N,23.34

Hexahydro-1,3,5-p-chlorophenyl-s-triazine (2e):
M.P. 130-132^{o}C;
IR (KBr)- 3038, 2932, 1592, 1494, 1227, 1164
^{1}H-NMR (DMSO-d_6): δ: 5.35 (s, 6H, CH_2), 7.10 and 7.85 (AA'BB', 12H, Ar-H)
Anal. Calc. For $C_{21}H_{18}Cl_3N_3$ C,60.19; H,4.38; N,10.07; Found: C,60.21; H,4.45; N,10.14.

Hexahydro-1,3,5-p-nitrophenyl-s-triazine (2f):
M.P.285-286^{o}C;
IR (KBr)- 3060, 2922, 1531, 1470, 1297, 1267, 1187
^{1}H-NMR(DMSO-d_6): δ: 5.35 (s, 6H, CH_2), 7.23 and 8.10 (AA'BB', 12H, Ar-H); Anal.Calcd. for $C_{21}H_{18}N_6O_6$ (450.18) C,56.87; H,4.46; N, 18.69; Found: C,56.84; H,4.51; N,18.71.

Table 1: Yield and physical data of the product in different solvent

Name of compound	Name of Solvent								M.P. (°C)
	EtOH (Rectified)		60% EtOH + 40% Water		Water		Acetonitrile		
	Time (sec.)	Yield (%)	Time (sec.)	Yield (%)	Time (sec.)	Yield (%)	Time (sec.)	Yield (%)	
2a	220	75	180	84	250	68	230	70	141-142
2b	200	80	180	86	240	70	220	74	127-128
2c	180	82	160	90	220	80	200	78	132-134
2d	150	84	140	92	180	82	170	82	240-242
2e	250	72	220	78	280	68	270	70	130-132
2f	300	74	280	78	320	68	310	72	285-286

Conclusion

The use of ultrasound provides an efficient, clean and quick methodology for the synthesis of various 1,3,5-hexahydrotriazine derivatives with greater yields than the previously reported conventional methods.

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