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Efficient classical synthesis of aminoazines under microwave irradiation

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Abstract

In the present study, Aminoazines were prepared from the reaction of amidrazone hydroiodide with various aromatic aldehydes in the presence of a solid base under microwave irradiation with power level of 850 W for 2-7 min in high yields. The amidrazone hydroiodide can also be prepared by the reaction of *S*-methyl isothiobenzamide hydroiodide and hydrazine in methanol under nitrogen gas. All synthesized compounds were characterized on the basis of IR and ^{1}H NMR spectral data. The significant features of this method are short reaction times, high yields of the products, solvent free reaction, easy work-up procedure, direct production of aminoazines.

Key words: Aminoazine, aldehyde, microwave irradiation.

Introduction

In the last few years, there has been a growing interest in the use of microwave irradiation in organic synthesis [1-4]. Reaction under dry condition, i.e. in the absence of solvent, on solid support with or without catalyst, is of great interest and increasingly widespread due to the improved efficiency of many surface bound reagents [5,6]. Further, with the advent of the microwave dielectric heating technique, the synthesis of organic compounds under microwave irradiation has been developed [7-9]. In this exploration, the use of inorganic solid supports such as SiO_2 has become a landmark as the reactions can be performed in "dry media" or solvent-free conditions [10,11]. The

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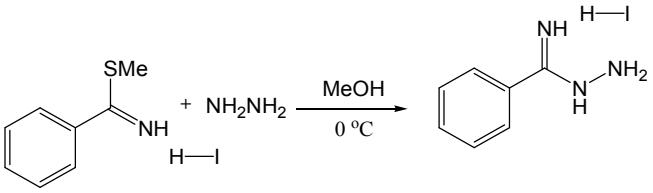
coupling of microwave irradiation (MWI) with the use of inorganic solid support offers benefits of shorter reaction time, milder reaction conditions, yield enhancement, and high catalytic activity with optimum utilization of energy [12,13]. In view of the eco-friendly role of dry condition using microwave irradiation and our ongoing exploration towards green synthesis, the reaction of amidrazone hydroiodide with benzaldehydes was carried out under microwave irradiation using solid support (SiO_2).

Aminoazines are important intermediates in the preparation of heterocyclic compounds such as 1,2,4-triazoles[14,15]and triazines [14]. Triazoles derived from azines have been used to produce the compounds with herbicidal, fungicidal, bactericidal, germicidal, antitoxin, anti-inflammatory and analgesic properties [16]. In general, amidrazones are monoacid bases, which produce salt by mineral acids [17]. Amidrazones are unstable and hydrolyzed in alkaline solution, so they are named according to the acid that is obtained from hydrolysis [18,19]. Aminoazines can be considered as amidrazone derivatives. In another attempt to synthesize the amidrazones, these compounds were also obtained by reaction of benzaldehydehydrazone with *S*-methyl isothiobenzamide hydroiodide [20]. Amidrazone salt can be prepared by the reaction of *S*-methyl isothiobenzamide hydroiodide with hydrazine in methanol at 0 ºC (Scheme 1). For example, benzamidrazone hydroiodide is obtained by reaction of *S*-methyl isothiobenzamide hydroiodide with hydrazine in 90% yields [21].



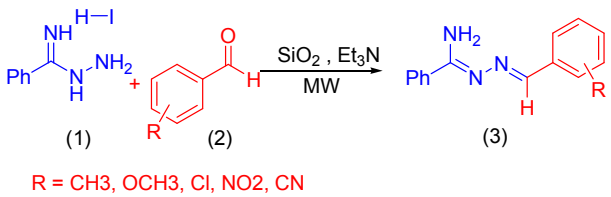
Scheme 1. Synthesis of benzamidrazone hydroiodide

Aminoazines are also obtained by reaction of amidrazones with aldehydes and ketones in the weak acidic solution. In regarding to the contradictions in literatures, in most methods, aminoazine synthesis in high purity is difficult and the final yield is low. As a part of our continuous efforts in laboratory relating the synthesis of aminoazine derivatives, we report here in the synthesis aminoazines under microwave irradiation in high yields. Synthesis without solvents under microwave irradiation offers several advantages. The absence of solvent reduces the risk of explosions when the reaction takes place in a closed vessel in an oven. During microwave induction of reactions under dry conditions, the reactants are adsorbed on the surface of silica gel whereas the support does not, nor does it restrict the transmission of microwaves. Consequently,

such supported reagents efficiently induce reactions under safe and simple conditions with domestic microwave ovens instead of specialised expensive commercial microwave systems.

Results and discussion

Aminoazine (3) is synthesized in the reaction of amidrazone hydroiodide(1) with aromatic aldehydes (2) on a basic solid under microwave irradiation in high yields (Scheme 2).



Scheme 2. Microwave-assisted synthesis of aminoazines

The significant features of this method are direct production of aminoazines, high yields of the products, solvent free reaction, short reaction times and easy extraction of products. This is confirmed by the appearance of the proton peak (-N ⇧CH-) at δ= 8-9 in ^{1}H NMR; carbonyl group's peak in the FT-IR spectra is removed. Reactions with electron-deficient aldehydes with substitution at the para-position resulted in the formation of products, whereas unsubstituted, electron rich, and heterocyclic aldehydes as well as electron-deficient aldehydes with substitution at ortho- and meta-positions gave corresponding aminoazines (Table 1).

Experimental

General

Melting points were taken on an electrothermal 9100 melting point apparatus without further correction. The IR spectra were recorded on a Rayleigh WQF-510 spectrometer using KBr discs. The ^{1}H NMR spectra were recorded in DMSO on a FT-NMR Bruker DRX (^{1}H NMR, 400 MHz). Microwave irradiation was carried out using the commercial microwave oven (Moulinex 2735A) at 2450 MHz (100% power corresponding to 850 W). TLC was carried out on pre-coated plates (Merck silica gel 60, GF254).The physical data (mp, NMR, IR) of these known compounds were found to be identical with those reported in the literature.

Synthesis of benzamidrazone hydroiodide

S-Methyl isothiobenzamide hydroiodide (6 mmol) in methanol (7 mL) was added to hydrazine (6 mmol) in methanol (5 mL) at 0-5 ^{o}C under nitrogen gas. After 2 hours, TLC monitoring with dichloromethane eluent indicated that product is formed. Then, diethylether (8 mL) was added to the reaction flask and the resulting mixture was kept at 0 ^{o}C for 3 h. The mixture was diluted with ether (100 mL) and filtered. The residue was purified by recrystallization in ethanol. Benzamidrazone hydroi-

odide was obtained in 80% yield; mp 178-180 ^{o}C [20,22].

General procedure for the Synthesis of aminoazines

A mixture of amidrazone hydroiodide**(1)** (2 mmol), aldehydes (**2a-g**) (2 mmol), triethylamine (2 mL) and silica gel (2 g)was well-grounded with a pestle and introduced to the microwave irradiation at full power (850 W) in an open Pyrex beaker for the appropriate time (Table 1). After complete conversion, as indicated by TLC, the mixture was extracted with dichloromethane. The solvent was evaporated in vacuo and the product was purified by chromatography on silica gel column eluting with a mixture of n-hexane and ethyl acetate (70/30), or recrystallised directly from an ethanol-water mixture. The results are summarized in Table 1.

Table 1. Synthesis of aminoazine derivatives using different aldehydes using microwave irradiated[a]

Product	R	Time (min)	Yields (%)	Mp (°C)
3b	C_6H_5	2	89	133-135
3c	*p*-$NO_2C_6H_4$	4	94	187
3d	*p*-ClC_6H_4	4	92	148-151
3e	*p*-MeC_6H_4	6	86	142-145
3f	*p*-$OMeC_6H_4$	7	88	147.5-150
3g	*p*-CNC_6H_4	4	91	194-197
	o-CNC_6H_4	4	92	218-220

[a] Reaction conditions: 2.0 mmol of amidrazonehydroiodide, 2.0 mmol of compounds (2), triethylamine(2mL); [b] Isolated yield.

In order to optimize the reaction conditions, the effect of microwave irradiation was examined with amidrazone hydroiodide and benzaldehyde as the substrate and the reaction mixtures were irradiated for variable powers (Table 2). It was observed that the formation of aminoazine is favored as the microwave power increases.

Table 2. Effect of irradiation power and time on the synthesis of aminoazine in the microwave-assisted reaction

Entry	Power (W)	Time (min)	Yields (%)
1	450	2	72
2	450	4	77
3	650	2	80
4	650	4	82
5	850	2	89
6	850	4	89

Spectroscopic data of products

1-Amino-1-phenyl-4-phenyl-2,3diazo buta-1,3-diene (3a): Pale yellow solid,Yield: 89%, mp 133-135 °C. IR (KBr):3504 (NH_2), 3300, 1642 (C=N), 1580 cm^{-1}; ^{1}HNMR (400 MHz DMSO) δ 5.71 (2H, s, NH_2), 6.91-7.60 (m, 10H, Ar), 8.53 (1H, s).

1-Amino-1-phenyl-4-p-nitrophenyl-2,3diazo buta-1,3-diene (3b): Yellow solid,Yield: 94%,mp 187 °C. IR (KBr): 3500 (NH_2), 3250, 1620(C=N), 1515, 1340 cm^{-1};

^{1}HNMR (400 MHz DMSO) δ 5.80 (2H, s, NH_2), 7.10-8.05 (9H, m, Ar), 8.66 (1H, s).

1-Amino-1-phenyl-4-p-chlorophenyl-2,3diazo buta-1,3-diene (3c): Pale yellow solid,Yield: 92%, mp 148-151 °C. IR (KBr): 3506 (NH_2), 3314, 1621 (C=N), 1510, 757 (C-Cl)cm^{-1}; ^{1}HNMR (400 MHz DMSO) δ 5.73 (2H, s, NH_2), 6.81-8.04 (9H, m, Ar), 8.53 (1H, s).

1-Amino-1-phenyl-4-p-methylphenyl-2,3diazo buta-1,3-diene (3d): Pale yellow solid, Yield: 86%, mp 142-145 °C. IR(KBr):3491 (NH_2),3274, 1650(C=N), 1511, 1310 cm^{-1}; ^{1}H NMR (400 MHz DMSO) δ 2.38 (3H,s), 5.75 (2H, s, NH_2), 7.11-7.94 (9H, m,Ar), 8.59 (1H, s).

1-Amino-1-phenyl-4-p-methoxyphenyl-2,3diazo buta-1,3-diene (3e): Pale yellow solid, Yield: 88%, mp 147.5-150 °C. IR(KBr): 3490 (NH_2), 1625 (C=N), 1484, 1249 cm^{-1}; ^{1}H NMR (400 MHz DMSO) δ 4.04 (3H,s,-OCH_3), 5.80 (2H, s, NH_2), 7.26-7.87 (9H, m, Ar), 8.62 (1H, s).

1-Amino-1-phenyl-4-p-cyanophenyl-2,3diazo buta-1,3-diene (3f): Pale yellow solid,Yield: 91%, mp 194-197 °C. IR(KBr): 3374 (NH_2), 2254 (C⇩N), 1685 (C=N), 1284 cm^{-1}; ^{1}H NMR (400 MHz DMSO) δ 5.92 (2H,s,NH_2), 7.31-8.09 (9H, m, ArH), 8.57 (1H, s).

1-Amino-1-phenyl-4-o-cyanophenyl-2,3diazo buta-1,3-diene (3g): Pale yellow solid,Yield: 92%, mp 218-220 °C. IR(KBr): 3442 (NH_2), 2239 (C⇩N), 1637 (C=N), 1527 cm^{-1}; ^{1}H NMR (400 MHz DMSO) δ 7.46-8.41 (2H, s, NH_2), 7.80-8.46 (9H, m, ArH), 8.93 (1H, s).

Conclusion

In conclusion, we have developed a simple, inexpensive and effective method for the synthesis of aminoazine by using amidrazone hydroiodide and various aldehydes as the substrates on a basic solid under microwave irradiation. The reactions were performed smoothly to generate the corresponding products in high yields under safe experimental conditions. This method offers several advantages including mild reaction conditions, high yields of products, short reaction times, solvent free conditions and easy extraction of products.

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