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# Environmentally benign synthesis of sydnone containing 1,3,4-thiadiazines under microwave and solvent-free conditions

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**Abstract.** Novel, convenient and benign synthesis of 2-arylamino-5-(3′-arylsydnone-4-yl)-1,3,4-thiadiazines **3a–l** by the interaction of 3-substituted-4-bromoacetyl sydnones **1** with substituted thiosemicarbazides **2** under MW irradiation and solvent-free condition is described.

**Keywords.** Sydnones; microwave synthesis; thiosemicarbazides; thiadiazines.

## 1. Introduction

The application of microwave as an energy source for chemical reactions and processes has been extensively studied during recent years.[1] The combination of solvent-free conditions and microwave irradiation leads to large reduction in reaction time, enhancement in conversion, easier work up and sometimes in selectivity with several advantages of an eco-friendly approach.[2] Further, its unique capabilities allow its applications in transformations which are difficult or impossible to carry out by means of conventional methods.

Sydnones are a novel class of meso-ionic compounds with unique chemical and physical properties. A vast array of sydnone derivatives have been found to show varied biological properties,[3] antioxidant activity[4] and liquid crystalline properties.[5] Furthermore, sydnones have been used as precursors in 1,3-dipolar additions,[6] material chemistry[7] and in battery applications.[8] However, the use of microwave technique in sydnone chemistry has not been explored to date. In continuation of our effort to develop benign synthetic methods for sydnone derivatives,[9] we report here a new series of sydnone containing 1,3,4-thiadiazines by microwave irradiation under solvent-free conditions.

## 2. Experimental

### 2.1 *General remarks*

Melting points were determined by open capillary method and are uncorrected. All compounds were analysed satisfactorily for C, H, and N. IR spectra (KBr disc) were recorded on a JASCO FT IR 430 spectrophotometer. $^1$H NMR spectra were recorded on Bruker AC 300 F (300 MHz) NMR spectrometer using DMSO-$d_6$ as a solvent and TMS as an internal standard. The chemical shifts are expressed in $\delta$ scale downfield from TMS and proton signals are indicated as *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *m* = multiplet. Mass spectra were recorded either on a Jeol JMS-D 300 Mass spectrometer or API 3000 LCMS instrument operating at 70 eV.

### 2.2 *Typical procedure for the synthesis 2-arylamino-5-(3′-arylsydnone-4-yl)-1,3,4-thiadiazines (***3a–l***)*

3-Aryl-4-bromoacetylsydnone **1** (0·005 mol) and aryl thiosemicrabazide **2** (0·005 mol) were ground in a mortar using a pestle for uniform mixing. The powdered mixture was transferred to a 50 mL beaker and made a slurry using 4–5 drops of water. The slurry was kept inside a microwave oven (LG make – Little Chef) operating at 160 W for about one minute. After completion of the reaction, the product was poured into cold water and allowed to stand for 15 min. The products were collected by filtration, washed with water and re-crystallized from ethanol-DMF mixture. The characterization data is given in table 1.

### 2.3 *Spectral data for compounds* **3a–l**

2.3a *2-Phenylamino-5-(3′-phenylsydnone-4-yl)-1,3,4-thiadiazines (***3a***)*: IR (KBr, $\nu$ cm$^{-1}$) 3000–3200

*For correspondence

(NH), 1739 (sydnone C=O), 1616 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 3·88 (*s*, 2H, S-$CH_2$), 6·88–7·63 (*m*, 11H, Ar-H&NH). MS *m/z*: 351 ($M^+$), 321 ($M^+$–NO), 293 ($M^+$–NO–CO). Anal. calcd. for $C_{17}H_{13}N_5O_2S$: C, 58·12; H, 3·70; N, 19·94. Found C, 58·05; H, 3·72; N, 19·91.

2.3b *2-p-tolylamino-5-(3'-phenylsydnone-4-yl)-1,3,4-thiadiazines (**3b**)*: IR (KBr, $\nu$ cm$^{-1}$) 3212 (NH), 1744 (sydnone C=O), 1627 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 2·33 (*s*, 3H, $CH_3$), 3·87 (*s*, 2H, S-$CH_2$), 6·80 (*d*, 2H, *o*-protons of *p*-tolyl group), 7·10 (*d*, 2H, *m*-protons of *p*-tolyl group) 7·52–7·60 (*m*, 6H, Ar-H & NH). LCMS *m/z*: 366 ($M^+$ + 1), 336 ($M^+$–NO + 1), 308 ($M^+$–NO–CO + 1). Anal. calcd. for $C_{18}H_{15}N_5O_2S$: C, 59·18; H, 4·11; N, 19·17. Found C, 59·11; H, 4·09; N, 19·14.

2.3c *2-p-anisylamino-5-(3'-phenylsydnone-4-yl)-1, 3,4-thiadiazines (**3c**)*: IR (KBr, $\nu$ cm$^{-1}$) 3130 (NH), 1741 (sydnone C=O), 1622 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 3·79 (*s*, 3H, $OCH_3$), 3.87 (*s*, 2H, S–$CH_2$), 6·84–7·63 (*m*, 10H, Ar-H&NH). LCMS *m/z*: 382 ($M^+$ + 1), 352 ($M^+$–NO + 1), 323 ($M^+$–NO–CO + 1). Anal. calcd. for $C_{18}H_{15}N_5O_3S$: C, 56·69; H, 3·94; N, 18·37. Found C, 56·60; H, 3·97; N, 18·34.

2.3d *2-p-chlorophenylamino-5-(3'-phenylsydnone-4-yl)-1,3,4-thiadiazines (**3d**)*: IR (KBr, $\nu$ cm$^{-1}$) 3236 (NH), 1739 (sydnone C=O), 1620 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 3·91 (*s*, 2H, S–$CH_2$), 6·82 (*d*, 2H, *o*-protons of *p*-chlorophenyl group), 7·57 (*d*, 2H, *m*-protons of *p*-chlorophenyl group), 7·24–7·65 (*m*, 6H, Ar-H & NH). LCMS *m/z*: 386 & 388 ($M^+$ + 1 & $M^+$ + 3), 329 ($M^+$–NO–CO). Anal. calcd. for $C_{17}H_{12}ClN_5O_2S$: C, 52·93; H, 3·11; N, 18·16. Found C, 52·82; H, 3·13; N, 18·12.

2.3e *2-Phenylamino-5-(3$^1$-tolylsydnone-4-yl)-1,3,4-thiadiazines (**3e**)*: IR (KBr, $\nu$ cm$^{-1}$) 3180 (NH), 1743 (sydnone C=O), 1623 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 2·51 (*s*, 3H, $CH_3$), 3·89 (*s*, 2H, S-$CH_2$), 6·78–7·60 (*m*, 10H, Ar-H & NH). LCMS *m/z*: 366 ($M^+$ + 1), 307 ($M^+$–NO–CO + 1). Anal. calcd. for $C_{18}H_{15}N_5O_2S$: C, 59·18; H, 4·11; N, 19·18. Found C, 59.10; H, 4·09; N, 19·14.

2.3f *2-p-tolylamino-5-(3'-tolylsydnone-4-yl)-1,3,4-thiadiazines (**3f**)*: IR (KBr, $\nu$ cm$^{-1}$) 3252 (NH), 1737 (sydnone C=O), 1617 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 2·51 (*s*, 3H, $CH_3$), 2·81 (*s*, 3H, $CH_3$), 3·78 (*s*, 2H, S–$CH_2$), 6·78–7·60 (*m*, 9H, Ar-H&NH). Anal. calcd. for $C_{19}H_{17}N_5O_2S$: C, 60·16; H, 4·49; N, 18·47. Found C, 60·23; H, 4·47; N, 18·42.

2.3g *2-p-anisylamino-5-(3'-tolylsydnone-4-yl)-1,3,4-thiadiazines (**3g**)*: IR (KBr, $\nu$ cm$^{-1}$) 3139 (NH), 1749 (sydnone C=O), 1613 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 2·46 (*s*, 3H, $CH_3$), 3·80 (*s*, 3H, $OCH_3$), 3·87 (*s*, 2H, S–$CH_2$), 6·67–7·89 (*m*, 9H, Ar–H & NH). LCMS *m/z*: 396 ($M^+$ + 1), 337 ($M^+$-NO-CO). Anal. calcd. For $C_{19}H_{17}N_5O_3S$: C, 57·72; H, 4·30; N, 17·72. Found C, 57·62; H, 4·33; N, 17·70.

2.3h *2-p-chlorophenylamino-5-(3'-tolylsydnone-4-yl)-1,3,4-thiadiazines (**3h**)*: IR (KBr, $\nu$ cm$^{-1}$) 3139 (NH), 1741 (sydnone C=O), 1627 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 2·52 (*s*, 3H, $CH_3$), 3·82 (*s*, 2H, S-$CH_2$), 6·78–7·60 (*m*, 9H, Ar-H & NH). Anal. calcd. for $C_{18}H_{14}ClN_5O_2S$: C, 54·07; H, 3·50; N, 17·52. Found C, 54·00; H, 3·53; N, 17·47.

2.3i *2-phenylamino-5-(3'-anisylsydnone-4-yl)-1,3,4-thiadiazines (**3i**)*: IR (KBr, $\nu$ cm$^{-1}$) 3185 (NH), 1737 (sydnone C=O), 1628 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 3·27 (*s*, 3H, $OCH_3$), 3·91 (*s*, 2H, S-$CH_2$), 6·73–7·82 (*m*, 10H, Ar-H&NH). LCMS *m/z*: 382 ($M^+$ + 1), 323 ($M^+$–NO–CO). Anal. calcd. for $C_{18}H_{15}N_5O_3S$: C, 56·69; H, 3·94; N, 18·37. Found C, 56·60; H, 3·91; N, 18·33.

2.3j *2-p-tolylamino-5-(3'-anisylsydnone-4-yl)-1,3,4-thiadiazines (**3j**)*: IR (KBr, $\nu$ cm$^{-1}$) 3204 (NH), 1743 (sydnone C=O), 1627 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 2·72 (*s*, 3H, $CH_3$), 3·58 (*s*, 3H, $OCH_3$), 3·74 (*s*, 2H, S-$CH_2$), 6·74–7·96 (*m*, 9H, Ar-H & NH); Anal. calcd. For $C_{19}H_{17}N_5O_3S$: C, 57·72; H, 4·30; N, 17·72. Found C, 57·82; H, 4·32; N, 17·78.

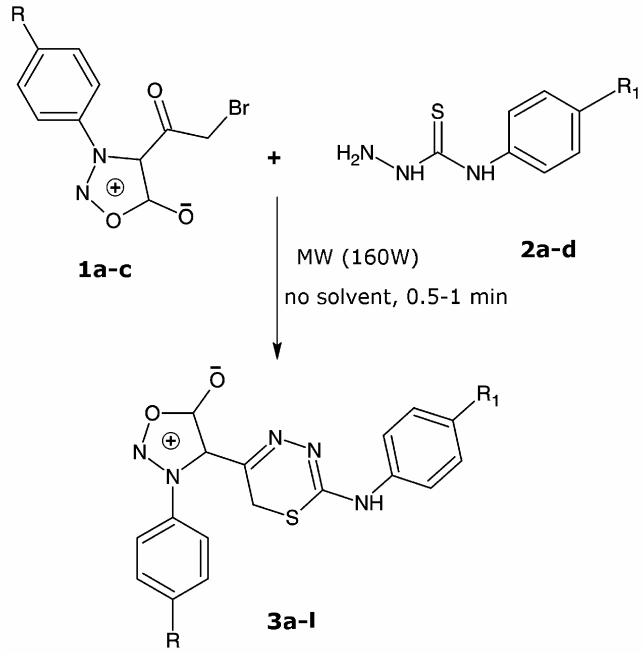
2.3k *2-p-anisylamino-5-(3'-anisylsydnone-4-yl)-1,3,4-thiadiazines (**3k**)*: IR (KBr, $\nu$ cm$^{-1}$) 3125 (NH), 1729 (sydnone C=O), 1616 (C=N); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 3·41 (*s*, 3H, $OCH_3$), 3·62 (*s*, 3H, $OCH_3$), 3·83 (*s*, 2H, S-$CH_2$), 6·36–8·12 (*m*, 9H, Ar-H & NH); LCMS *m/z*: 413 ($M^+$ + 1), 354 ($M^+$–NO–CO); Anal. calcd. For $C_{19}H_{17}N_5O_4S$: C, 55·47; H, 4·14; N, 17·03. Found C, 55·40; H, 4·11; N, 17·09.

2.3l *2-p-chorophenylamino-5-(3'-anisylsydnone-4-yl)-1,3,4-thiadiazines (**3l**)*: IR (KBr, $\nu$ cm$^{-1}$) 3142 (NH), 1743 (sydnone C=O), 1617 (C=N); $^1$H NMR

**Table 1.** Characterization data of 2-arylamino-5-(3′-arylsydnone-4-yl)-1,3,4-thiadiazines **3a–l**.

| Compound[a] | R | $R_1$ | Nature | % Yield[b] | mp (°C) |
|---|---|---|---|---|---|
| **3a** | H | H | Yellow crystals | 80 (64) | 190–92 |
| **3b** | H | $CH_3$ | Yellow crystals | 82 (58) | 164–65 |
| **3c** | H | $OCH_3$ | Pale-yellow crystals | 82 (69) | 179–80 |
| **3d** | H | Cl | Yellow shining crystals | 90 (54) | 182–84 |
| **3e** | $CH_3$ | H | Light-brown crystals | 87 (70) | 189–90 |
| **3f** | $CH_3$ | $CH_3$ | Yellow crystals | 84 (64) | 175–76 |
| **3g** | $CH_3$ | $OCH_3$ | Brown crystals | 84 (67) | 185 |
| **3h** | $CH_3$ | Cl | Brownish-yellow crystals | 88 (58) | 165–67 |
| **3i** | $OCH_3$ | H | Dark-yellow crystals | 80 (70) | 160–62 |
| **3j** | $OCH_3$ | $CH_3$ | Yellow crystals | 86 (62) | 167–68 |
| **3k** | $OCH_3$ | $OCH_3$ | Brown crystals | 87 (67) | 172–74 |
| **3l** | $OCH_3$ | Cl | Brown crystals | 85 (56) | 180–82 |

[a]All compounds were satisfactorily analysed for C, H and N and well-characterized by IR, $^1$H NMR & MS. [b]Yields inside the bracket indicate the yields in solvent phase




**Scheme 1.**

(300 MHz, DMSO-$d_6$): $\delta$ 3·52 (*s*, 3H, $OCH_3$), 3·94 (*s*, 2H, S–$CH_2$), 6·89–7·52 (*m*, 9H, Ar–H & NH). Anal. calcd. for $C_{18}H_{14}ClN_5O_3S$: C, 52·05; H, 3·37; N, 16·85. Found C, 52·13; H, 3·32; N, 16·80.

## 3. Results and discussion

The reaction of 3-aryl-4-bromoacetyl sydnones **1a–c** with arylthiosemicarbazides **2a–d** afforded 2-arylamino-5-(3′-arylsydnone-4-yl)-1,3,4-thiadiazines **3a–l** under MW irradiation at 160 W without using any catalyst and solvent (scheme 1). Progress of the reaction was monitored by TLC. The scope and generality of this method with respect to various precursors are summarized in table 1. 3-aryl-4-bromoacetylsydnones were prepared by photochemical bromination of 3-aryl-4-acetylsydnone.[3e] arylthiosemicarbazides **2a–d** were synthesized following the reported method.[10]

In the present protocol, we observed better yields in a shorter period compared to the reactions carried out in ethanol medium. Interestingly, the decomposition of sydnone ring was much slower under solvent-free conditions. However, prolonged MW irradiation caused decomposition of the products. The compounds have been characterized by comparing their melting points and mixed melting points with the products obtained in ethanol medium, and by spectral and analytical data (provided in experimental part).

In conclusion, we have described efficient and benign synthesis of 1,3,4-thiadiazines containing sydnone moiety under MW irradiation and solvent-free condition without using any catalyst. Further, this method is simple and safe from green chemistry point of view.

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