Termolecular one-pot synthesis of symmetrical azines of 4-acetyl-3-arylsydnone. Hydrazone and azine derivatives of 4-acetyl-3-arylsydnone, their spectral characterization and biological properties

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Hydrazones of 4-acetyl-3-arylsydnone (2a-o) were prepared by heating 4-acetyl-3-arylsydnone (1a-o) with excess of hydrazine hydrate and the corresponding symmetrical azines (3a-o) were obtained by a termolecular reaction of 4-acetyl-3-arylsydnone with hydrazine hydrate (2 : 1 ratio). Hydrazones and azines were screened for their antimicrobial activity and few of these compounds exhibit inhibitory action more than the reference drugs used.

The synthesis, biological and pharmacological studies of a large number of sydnone derivatives have been reported from our laboratory¹⁻³. In continuation of synthetic work on sydnones, we now report the synthesis of some hydrazones of 4-acetyl-3-arylsydnone⁴ and termolecular one-step synthesis of the corresponding symmetrical azines by varying the stoichiometric quantity of 4-acetyl-3-arylsydnone (1a-o) and the reagent hydrazine hydrate.

Results and discussion

The hydrazones (2a-o) were obtained by treating the 4-acetyl-3-arylsydnone (1a-o) with excess of hydrazine hydrate. These hydrazones were resistant to further reaction with aldehyde/ketone and also with another molecule of 4-acetyl-3-arylsydnone, even after prolonged heating and the corresponding azines could not be prepared. The low reactivity of the -NH₂ group of the hydrazones may be attributed to the electron-withdrawing property of the sydnone ring which is a mesoionic dipolar heterocycle (Figs. 1 and 2). Hence, we thought of carrying out a termolecular reaction with two moles of 4-acetyl-3-arylsydnone (1a-o) and one mole of hydrazine hydrate, since hydrazine hydrate is a symmetrical binucleophile it can readily react simultaneously with two carbonyl carbons. The azines (3a-o) were obtained in ~85% yield in about 10 minutes (Scheme 1).

The IR spectra of all the hydrazones (2a-o) showed bands at 3424 cm⁻¹ and 3388 cm⁻¹ for asymmetric and symmetric ν_{NH₂} stretching. The bands at 1727 cm⁻¹ and 1641 cm⁻¹ are due to ν_{C=O} of the sydnone ring and ν_{C=N} respectively. The ¹H NMR (300 MHz) (DMSO-*d*₆) spectra of these

Fig. 1

Fig. 2

1-4 a, R ₁ = H, R ₂ = H	h, R ₁ = H, R ₂ = 4-Br
b, R ₁ = H, R ₂ = 4-CH ₃	i, R ₁ = H, R ₂ = 4-CO ₂ CH ₃
c, R ₁ = H, R ₂ = 2-CH ₃	j, R ₁ = H, R ₂ = 4-CO ₂ C ₂ H ₅
d, R ₁ = H, R ₂ = 4-OCH ₃	k, R ₁ = 3-CH ₃ , R ₂ = 4-CH ₃
e, R ₁ = H, R ₂ = 2-OCH ₃	l, R ₁ = 2-CH ₃ , R ₂ = 5-CH ₃
f, R ₁ = H, R ₂ = 4-Cl	m, R ₁ = 4-CH ₃ , R ₂ = 3-Cl
g, R ₁ = H, R ₂ = 3-Cl	n, R ₁ = 2-OCH ₃ , R ₂ = 4-Cl
	o, R ₁ = 4-Cl, R ₂ = 3-F

Scheme 1

compounds showed a singlet at δ 2.37 (3H) for the methyl protons of the hydrazone group, and another broad peak at δ 10.40 (2H) for amino group (D_2O exchanged). The aromatic protons appeared in the region δ 6.40–7.00. The IR spectra of the azines (**3a-o**) exhibited band at 1741cm^{-1} and 1642cm^{-1} due to $\nu_{C=O}$ of the sydnone ring and $\nu_{C=N}$. The absence of the $-NH_2$ band confirms the formation of azine. The 1H NMR ($DMSO-d_6$) resonance showed magnetic equivalence for the protons of one half of the molecule with the other. All these compounds showed a singlet at δ 3.9 (6H) corresponding to the methyl protons on the azine group and the aromatic protons appeared at δ 7.00–7.30. The formation of the azine was confirmed by the EI-Mass spectrum of a typical compound the *p*-chloro substituted derivative (**3f**). The molecular ion at m/z 472 was not observed but the fragment at m/z 414, accounts for the loss of $-NO$ and $-CO$ from the sydnone ring. This fragmentation is typical of the sydnone ring. The IR spectra of the ar ethyl derivatives of the hydrazones (**4a-o**) showed a broad band at 3300cm^{-1} due to ν_{NH} stretching and 1758cm^{-1} due to $\nu_{C=O}$ of the sydnone ring, while the amide $\nu_{C=O}$ appeared at 1659cm^{-1} . 1HNMR ($DMSO-d_6$) spectra showed a singlet at δ 2.60 (3H) for the methyl protons of $-COCH_3$ and δ 2.20 (3H) of hydrazone group. The $-NH$ proton appeared at δ 10.3 (1H, D_2O exchanged) and the aromatic protons were observed in the region of δ 7.41–7.38.

Antimicrobial activity :

The preliminary antimicrobial testing has been carried out by cup-plate method. The antimicrobial activity was done against two pathogenic bacteria *Escherichia coli* and *Pseudomonas pyocyanous* and *Asperigillus niger* and *Rhizocona bataticola* as the fungal strains. The reference drugs used were Norfloxacin and Griseofulvin respectively. Compounds (**2f**, **g**, **h**, **m**, **n** and **o**) with halogen substitutions on the phenyl ring exhibited antibacterial activity greater than the reference drug against both the bacteria, while only methyl (**2b**, **c**, **k** and **l**) group substitution increased the activity against both the fungi. The halogen substituted azines (**3f**, **g** and **h**) showed enhanced antibacterial activity against both the organisms compared to norfloxacin. Only the *m*-Cl (**3g**) derivative was found to be more active against *R. bataticola* while all the other compounds were moderately active. Amongst the acetyl derivatives (**4a-o**) only one derivative viz. 4-Cl-3-F (**4o**) exhibited activity greater than the reference drug against *E. coli* while all the other compounds were moderately active against both the bacteria. The 4-bromo (**4h**) and 4-carbethoxy (**4j**) substitutions enhanced the antifungal activity against both the fungi, while other derivatives were moderately active (Tables 1–3).

Table 1. Antimicrobial activity of compounds (**2a-o**)

R ₁	R ₂	Antibacterial		Antifungal	
		<i>E. coli</i>	<i>P. pyocyanous</i>	<i>R. bataticola</i>	<i>A. niger</i>
		(mm)	(mm)	(mm)	(mm)
2a	H	14	15	15	16
2b	H	25	17	17	21
2c	H	21	16	19	22
2d	H	26	13	15	16
2e	H	19	19	11	13
2f	H	29	24	13	18
2g	H	28	23	10	17
2h	H	30	22	14	18
2i	H	25	18	14	16
2j	H	18	16	15	14
2k	3-CH ₃	19	18	18	21
2l	2-CH ₃	22	17	19	19
2m	4-CH ₃	29	21	12	13
2n	2-OCH ₃	31	26	11	14
2o	4-Cl	29	23	13	16
		Antibacterial		Antifungal	
		<i>E. coli</i>	<i>P. pyocyanous</i>	<i>R. bataticola</i>	<i>A. niger</i>
		(mm)	(mm)	(mm)	(mm)
Standard					
Norfloxacin		28	20	–	
Griseofulvin		–	–	16	18

Experimental

Melting points were determined in open capillary tube and are uncorrected. The IR spectra were recorded on Nicolet Impact-410 FT-IR spectrophotometer, using KBr pellets. 1H NMR was recorded on Bruker Varian-300 MHz FT-NMR in $DMSO-d_6$ with TMS as an internal standard. Mass spectra were recorded on a MI Ver. 14 on UIC 002002. Elemental analysis was carried out using Heraeus CHN rapid analyzer.

Synthesis of hydrazones of 4-acetyl-3-aryl sydnones (2a-o) : 4-Acetyl-3-aryl sydnones (0.005 mol) were dissolved in ethanol (4 ml) containing 3–4 drops of acetic acid. Hydrazine hydrate (0.025 mol) was added and the reaction mixture warmed on a water-bath for 2 min. The reaction mixture was then diluted with water till turbidity was observed and warmed on water-bath for another 5 min, cooled and filtered. The bright orange crystalline compounds obtained were recrystallised from methanol. **2a** (85%), m.p. 169–170° (Found : C, 55.00; H, 4.60; N, 25.60. $C_{10}H_{10}N_4O_2$ calcd. for : C, 55.03; H, 4.02; N, 25.62%); ν_{max} 3424 and 3388 (NH_2), 1727 (sydnone $C=O$), 1641 ($C=N$); δ_H ($DMSO-d_6$) 10.40 (2H, br, exchanged with

Table 2. Antimicrobial activity of compounds (3a-o)

	R ₁	R ₂	Antibacterial		Antifungal	
			<i>E. coli</i>	<i>P. pyocyanous</i>	<i>R. bataticola</i>	<i>A. niger</i>
			(mm)	(mm)	(mm)	(mm)
3a	H	H	14	15	15	16
3b	H	4-CH ₃	25	17	13	16
3c	H	2-CH ₃	21	16	14	15
3d	H	4-OCH ₃	26	13	15	16
3e	H	2-OCH ₃	19	19	11	13
3f	H	4-Cl	30	23	13	17
3g	H	3-Cl	29	25	19	15
3h	H	4-Br	31	24	14	13
3i	H	4-CO ₂ Me	25	18	14	16
3j	H	4-CO ₂ Et	18	16	15	14
3k	3-CH ₃	4-CH ₃	19	18	15	17
3l	2-CH ₃	5-CH ₃	22	17	13	13
3m	4-CH ₃	3-Cl	25	13	12	13
3n	2-OCH ₃	4-Cl	18	16	11	14
3o	4-Cl	3-F	21	15	13	16
Standard	Antibacterial		Antifungal			
	<i>E. coli</i> (mm)	<i>P. pyocyanous</i> (mm)	<i>R. bataticola</i> (mm)	<i>A. niger</i> (mm)		
Norfloxacin	28	20	—	—		
Griseofulvin	—	—	16	18		

Table 3. Antimicrobial activity of compounds (4a-o)

	R ₁	R ₂	Antibacterial		Antifungal	
			<i>E. coli</i>	<i>P. pyocyanous</i>	<i>R. bataticola</i>	<i>A. niger</i>
			(mm)	(mm)	(mm)	(mm)
4a	H	H	14	15	15	16
4b	H	4-CH ₃	25	17	13	16
4c	H	2-CH ₃	21	16	15	17
4d	H	4-OCH ₃	25	13	15	16
4e	H	2-OCH ₃	19	18	11	13
4f	H	4-Cl	24	17	13	15
4g	H	3-Cl	23	16	10	17
4h	H	4-Br	26	15	19	21
4i	H	4-CO ₂ Me	25	18	14	16
4j	H	4-CO ₂ Et	18	16	21	22
4k	3-CH ₃	4-CH ₃	19	18	16	15
4l	2-CH ₃	5-CH ₃	22	17	15	16
4m	4-CH ₃	3-Cl	24	16	12	13
4n	2-OCH ₃	4-Cl	25	18	11	14
4o	4-Cl	3-F	32	15	13	16
Standard	Antibacterial		Antifungal			
	<i>E. coli</i> (mm)	<i>P. pyocyanous</i> (mm)	<i>R. bataticola</i> (mm)	<i>A. niger</i> (mm)		
Norfloxacin	28	20	—	—		
Griseofulvin	—	—	16	18		

D₂O, NH₂), 6.5–7.41 (5H, m, Ar-H), 2.0 (3H, s, CH₃); *m/z* 218 (M⁺); **2b** (84%), m.p. 171–172° (Found : C, 56.80; H, 5.20; N 24.10. C₁₁H₁₂N₄O₂ calcd. for : C, 56.87; H, 5.21; N, 24.13%); *v*_{max} 3422 and 3380 (NH₂), 1730 (sydnone C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 10.42 (2H, br, exchanged with D₂O, NH₂), 6.40 (2H, d, Ar-H), 7.00 (2H, d, Ar-H), 2.0 (3H, s, CH₃), 2.3 (3H, s, CH₃); δ_{C} (DMSO-*d*₆) 21.8 (q, Ar-CH₃), 28.4 (q, CH₃), 124 (q, Ar-CH₃), 129.2 (q, Ar-sydnone), 130.3 (q, C=N), 143.3 (q, sydnone ring C), 166.6 (q, sydnone C=O), 125.1 and 130.2 (2C each Ar ring); *m/z* 232 (M⁺); **2c** (80%), m.p. 119–120° (Found : C, 56.80; H, 5.20; N, 24.10. C₁₁H₁₂N₄O₂ calcd. for : C, 56.87; H, 5.21; N, 24.13%); *v*_{max} 3421 and 3385 (NH₂), 1732 (sydnone C=O), 1640 (C=N); δ_{H} (DMSO-*d*₆) 10.41 (2H, br, exchanged with D₂O, NH₂), 6.40 (1H, d, Ar-H), 7.20 (1H, d, Ar-H), 7.15 (2H, m, Ar-H), 2.1 (3H, s, CH₃), 2.4 (3H, s, CH₃); *m/z* 232 (M⁺); **2d** (78%), m.p. 174–176° (Found : C, 53.20; H, 4.80; N, 22.60. C₁₁H₁₂N₄O₃ calcd. for : C, 53.21; H, 4.87; N, 22.58%); *v*_{max} 3422 and 3380 (NH₂), 1730 (sydnone C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 10.42 (2H, br, exchanged with D₂O, NH₂), 6.40 (2H, d, Ar-H), 7.00 (2H, d, Ar-H), 2.0 (3H, s, CH₃), 3.8 (3H, s, CH₃); *m/z* 248

(M⁺); **2e** (75%), m.p. 160–161° (Found : C, 53.21; H, 4.79; N, 22.63. C₁₁H₁₂N₄O₃ calcd. for : C, 53.21; H, 4.87; N, 22.58%); *v*_{max} 3420 and 3385 (NH₂), 1735 (sydnone C=O), 1641 (C=N); δ_{H} (DMSO-*d*₆) 10.42 (2H, br, exchanged with D₂O, NH₂), 6.43 (1H, d, Ar-H), 7.35 (1H, d, Ar-H), 7.15 (2H, m, Ar-H), 2.1 (3H, s, CH₃), 3.8 (3H, s, CH₃); *m/z* 248 (M⁺); **2f** (85%), m.p. 192–193° (Found : C, 47.60; H, 3.60; N, 22.18. C₁₀H₉ClN₄O₂ calcd. for : C, 47.61; H, 3.60; N, 22.22%); *v*_{max} 3422 and 3380 (NH₂), 1727 (sydnone C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 10.42 (2H, br, exchanged with D₂O, NH₂), 6.40 (2H, d, Ar-H), 7.00 (2H, d, Ar-H), 2.0 (3H, s, CH₃); *m/z* 252 (M⁺); **2g** (88%), m.p. 145–146° (Found : C, 47.59; H, 3.59; N, 22.23. C₁₀H₉ClN₄O₂ calcd. for : C, 47.61; H, 3.60; N, 22.22%); *v*_{max} 3420 and 3385 (NH₂), 1735 (sydnone C=O), 1641 (C=N); δ_{H} (DMSO-*d*₆) 10.39 (2H, br, exchanged with D₂O, NH₂), 6.41 (1H, d, Ar-H), 7.30 (1H, d, Ar-H), 7.15 (1H, m, Ar-H), 7.8 (1H, s, Ar-H), 2.1 (3H, s, CH₃); *m/z* 252 (M⁺); **2h** (82%), m.p. 146–147° (Found : C, 40.50; H, 3.02; N, 18.90. C₁₀H₉BrN₄O₂ calcd. for : C, 40.54; H, 3.06; N, 18.92%); *v*_{max} 3420 and 3378 (NH₂), 1728 (sydnone C=O), 1642 (C=N); δ_{H} (DMSO-*d*₆) 10.43 (2H, br, exchanged with D₂O, NH₂), 6.43 (2H, d, Ar-H),

7.32 (2H d, Ar-H), 2.2 (3H, s, CH₃); m/z 297 (M⁺); **2i** (70%), m.p. 128–129° (Found : C, 52.10; H, 4.40; N, 20.28). C₁₂H₁₂N₄O₄ calcd. for : C, 52.17; H, 4.38; N, 20.28%; $\nu_{\max}$ 3422 and 3380 (NH₂), 1742 (ester C=O), 1727 (sydnone C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 10.42 (2H, br, exchanged with D₂O, NH₂), 6.87 (2H, d, Ar-H), 7.45 (2H, d, Ar-H), 2.1 (3H, s, CH₃), 3.8 (3H, s, CH₃); m/z 276 (M⁺); **2j** (73%), m.p. 111–112° (Found : C, 53.80; H, 4.80; N, 19.20). C₁₃H₁₄N₄O₄ calcd. for : C, 53.78; H, 4.86; N, 19.30%; $\nu_{\max}$ 3422 and 3380 (NH₂), 1732 (sydnone C=O), 1745 (ester C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 10.42 (2H, br, exchanged with D₂O, NH₂), 6.87 (2H, d, Ar-H), 7.45 (H, d, Ar-H), 2.1 (3H, s, CH₃), 3.8 (2H, q, CH₂), 1.8 (3H, t, CH₃); m/z 290 (M⁺); **2k** (86%), m.p. 159–160° (Found : C, 55.50; H, 5.70; N, 22.70). C₁₂H₁₄N₄O₂ calcd. for : C, 58.51; H, 5.73; N, 22.76%; $\nu_{\max}$ 3422 and 3380 (NH₂), 1732 (C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 10.42 (2H, br, exchanged with D₂O, NH₂), 6.45 (1H, d, Ar-H), 7.21 (1H, d, Ar-H), 7.5 (1H, s, Ar-H), 2.1 (3H, s, CH₃), 2.0 (3H, s, CH₃), 1.9 (3H, s, CH₃); m/z 246 (M⁺); **2l** (68%), m.p. 128–129° (Found : C, 55.50; H, 5.70; N, 22.70). C₁₂H₁₄N₄O₂ calcd. for : C, 58.51; H, 5.73; N, 22.76%; $\nu_{\max}$ 3421 and 3375 (NH₂), 1732 (sydnone C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 10.41 (2H, br, exchanged with D₂O, NH₂), 6.43 (1H, d, Ar-H), 7.18 (1H, d, Ar-H), 7.4 (1H, s, Ar-H), 2.1 (3H, s, CH₃), 2.0 (3H, s, CH₃), 1.9 (3H, s, CH₃); m/z 246 (M⁺); **2m** (80%), m.p. 131–132° (Found : C, 49.60; H, 4.70; N, 21.00). C₁₁H₁₁ClN₄O₂ calcd. for : C, 49.60; H, 4.71; N, 21.05%; $\nu_{\max}$ 3420 and 3375 (NH₂), 1730 (sydnone C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 10.43 (2H, br, exchanged with D₂O, NH₂), 6.41 (1H, d, Ar-H), 7.16 (1H, d, Ar-H), 7.5 (1H, s, Ar-H), 2.1 (3H, s, CH₃), 2.0 (3H, s, CH₃); m/z 266 (M⁺); **2n** (60%), m.p. 147–148° (Found : C, 46.79; H, 3.90; N, 19.80). C₁₁H₁₁ClN₄O₃ calcd. for : C, 46.80; H, 3.93; N, 19.86%; $\nu_{\max}$ 3420 and 3375 (NH₂), 1730 (sydnone C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 10.43 (2H, br, exchanged with D₂O, NH₂), 6.41 (1H, d, Ar-H), 7.16 (1H, d, Ar-H), 7.5 (1H, s, Ar-H), 2.1 (3H, s, CH₃), 3.8 (3H, s, CH₃); m/z 282 (M⁺); **2o** (78%), m.p. 131–133° (Found : C, 44.40; H, 2.90; N, 20.70). C₁₀H₈ClFN₄O₂ calcd. for : C, 44.44; H, 2.99; N, 20.74%; $\nu_{\max}$ 3420 and 3375 (NH₂), 1738 (sydnone C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 10.45 (2H, br, exchanged with D₂O, NH₂), 6.48 (1H, d, Ar-H), 7.24 (1H, d, Ar-H), 7.6 (1H, s, Ar-H), 2.1 (3H, s, CH₃); m/z 270 (M⁺).

Synthesis of azines of 4-acetyl-3-arylsydnone (3a-o) :

4-Acetyl-3-arylsydnone (0.01 mol) were dissolved in ethanol (4 ml) containing 3–4 drops of acetic acid. Hydrazine hydrate (0.005 mol) was then added and the reaction mixture was warmed on a water-bath for 10 min, cooled and the solid separated was filtered. White crystalline com-

pounds were obtained after crystallisation from methanol to give (**3a-o**). **3a** (85%), m.p. 220–221° (Found : C, 59.40; H, 3.90; N, 20.70). C₂₀H₁₆N₆O₄ calcd. for : C, 59.39; H, 3.98; N, 20.78%; $\nu_{\max}$ 1741 (sydnone C=O), 1624 (C=N); δ_{H} (DMSO-*d*₆) 7.0–7.30 (10H, m, Ar-H), 3.9 (6H, s, 2CH₃); m/z 404 (M⁺); **3b** (88%), m.p. 236–237° (Found : C, 61.08; H, 4.60; N, 19.41). C₂₂H₂₀N₆O₄ calcd. for : C, 61.10; H, 4.66; N, 19.43%; $\nu_{\max}$ 1739 (sydnone C=O), 1620 (C=N); δ_{H} (DMSO-*d*₆) 6.80 (4H, d, Ar-H), 7.20 (4H, d, Ar-H), 3.9 (6H, s, 2CH₃), 2.3 (6H, s, 2CH₃); δ_{C} (DMSO-*d*₆) 22.0 (2C, Ar-CH₃), 33.5 (2C, CH₃), 124.5 (q, 2C, Ar-CH₃), 131.2 (q, 2C, Ar-sydnone), 140.1 (q, 2C, C=N), 150.2 (q, 2C, sydnone ring), 168.8 (q, 2C, C=O), 126.0 and 132.3 (4C each, Ar); m/z 432 (M⁺); **3c** (72%) m.p. 210–211° (Found : C, 61.08; H, 4.63; N, 19.40). C₂₂H₂₀N₆O₄ calcd. for : C, 61.10; H, 4.66; N, 19.43%; $\nu_{\max}$ 1740 (sydnone C=O), 1614 (C=N); δ_{H} (DMSO-*d*₆) 6.40 (2H, d, Ar-H), 7.20 (2H, d, Ar-H), 7.15 (4H, m, Ar-H), 3.8 (3H, s, 2CH₃), 2.4 (3H, s, 2CH₃); m/z 432 (M⁺); **3d** (82%), m.p. 229–230° (Found : C, 56.86; H, 4.32; N, 18.08). C₂₂H₂₀N₆O₆ calcd. for : C, 56.89; H, 4.34; N, 18.10%; $\nu_{\max}$ 1740 (sydnone C=O), 1613 (C=N); δ_{H} (DMSO-*d*₆) 6.73 (4H, d, Ar-H), 7.52 (4H, d, Ar-H), 3.9 (6H, s, 2CH₃), 3.8 (6H, s, 2CH₃); m/z 464 (M⁺); **3e** (80%), m.p. 211–212° (Found : C, 56.86; H, 4.32; N, 18.08). C₂₂H₂₀N₆O₆ calcd. for : C, 56.89; H, 4.34; N, 18.10%; $\nu_{\max}$ 1735 (sydnone C=O), 1611 (C=N); δ_{H} (DMSO-*d*₆) 6.43 (2H, d, Ar-H), 7.35 (2H, d, Ar-H), 7.15 (4H, m, Ar-H), 3.9 (6H, s, 2CH₃), 3.8 (6H, s, 2CH₃); m/z 464 (M⁺); **3f** (90%), m.p. 240–241° (Found : C, 50.74; H, 2.95; N, 17.74). C₂₀H₁₄Cl₂N₆O₄ calcd. for : C, 50.76; H, 2.98; N, 17.76%; $\nu_{\max}$ 1745 (sydnone C=O), 1613 (C=N); δ_{H} (DMSO-*d*₆) 6.45 (4H, d, Ar-H), 7.05 (4H, d, Ar-H), 3.7 (6H, s, 2CH₃); m/z 472 (M⁺); **3g** (90%), m.p. 209–210° (Found : C, 50.74; H, 2.95; N, 17.74). C₂₀H₁₄Cl₂N₆O₄ calcd. for : C, 50.76; H, 2.98; N, 17.76%; $\nu_{\max}$ 1745 (sydnone C=O), 1611 (C=N); δ_{H} (DMSO-*d*₆) 6.41 (2H, d, Ar-H), 7.30 (2H, d, Ar-H), 7.15 (2H, m, Ar-H), 7.8 (2H, s, Ar-H), 3.9 (6H, s, 2CH₃); m/z 472 (M⁺); **3h** (85%), m.p. 213–214° (Found : C, 42.70; H, 2.50; N, 14.93). C₂₀H₁₄Br₂N₆O₄ calcd. for : C, 42.73; H, 2.51; N, 14.95%; $\nu_{\max}$ 1748 (sydnone C=O), 1612 (C=N); δ_{H} (DMSO-*d*₆) 6.43 (4H, d, Ar-H), 7.32 (4H, d, Ar-H), 3.9 (6H, s, 2CH₃); m/z 562 (M⁺); **3i** (80%), m.p. 213–214° (Found : C, 55.36; H, 3.84; N, 16.13). C₂₄H₂₀N₆O₈ calcd. for : C, 55.39; H, 3.87; N, 16.15%; $\nu_{\max}$ 1740 (sydnone C=O), 1745 (ester C=O), 1613 (C=N); δ_{H} (DMSO-*d*₆) 6.87 (4H, d, Ar-H), 7.45 (4H, d, Ar-H), 3.88 (6H, s, 2CH₃), 3.8 (6H, s, 2CH₃); m/z 520 (M⁺); **3j** (82%), m.p. 227–228° (Found : C, 56.89; H, 4.40; N, 15.29). C₂₆H₂₄N₆O₈ calcd. for : C, 56.93; H, 4.41; N, 15.32%; $\nu_{\max}$ 1739 (sydnone C=O), 1745 (ester C=O), 1613 (C=N); δ_{H} (DMSO-*d*₆) 6.87

(4H, d, Ar-H), 7.45 (4 H, d, Ar-H), 3.9 (6H, s, 2CH₃), 3.8 (4H, q, 2CH₂), 1.8 (6H, t, 2CH₃); m/z 548 (M⁺); **3k** (70%), m.p. 209–210° (Found : C, 62.56; H, 5.22; N, 18.23. C₂₄H₂₄N₆O₄ calcd. for : C, 62.60; H, 5.25; N, 18.25%); $\nu_{\max}$ 1732 (sydnone C=O), 1643 (C=N); δ_{H} (DMSO-*d*₆) 6.45 (2H, d, Ar-H), 7.21 (2H, d, Ar-H), 7.5 (2H, s, Ar-H), 3.74 (6H, s, 2CH₃), 2.0 (6H, s, 2CH₃), 1.9 (6H, s, 2CH₃); m/z 460 (M⁺); **3l** (68%), m.p. 214–215° (Found : C, 62.56; H, 5.22; N, 18.23. C₂₄H₂₄N₆O₄ calcd. for : C, 62.60; H, 5.25; N, 18.25%); $\nu_{\max}$ 1742 (sydnone C=O), 1613 (C=N); δ_{H} (DMSO-*d*₆) 6.43 (2H, d, Ar-H), 7.18 (2H, d, Ar-H), 7.4 (2H, s, Ar-H), 3.9 (6H, s, 2CH₃), 2.0 (6H, s, 2CH₃), 1.9 (6H, s, 2CH₃); m/z 460 (M⁺); **3m** (80%), m.p. 219–220° (Found : C, 52.70; H, 3.60; N, 16.74. C₂₂H₁₈Cl₂N₆O₄ calcd. for : C, 52.71; H, 3.62; N, 16.76%); $\nu_{\max}$ 1739 (sydnone C=O), 1613 (C=N); δ_{H} (DMSO-*d*₆) 6.41 (2H, d, Ar-H), 7.16 (2H, d, Ar-H), 7.5 (2H, s, Ar-H), 3.87 (6H, s, 2CH₃), 2.0 (6H, s, 2CH₃); m/z 501 (M⁺); **3n** (70%), m.p. 213–214° (Found : C, 49.53; H, 3.38; N, 15.75. C₂₂H₁₈Cl₂N₆O₆ calcd. for : C, 49.55; H, 3.40; N, 15.76%); $\nu_{\max}$ 1745 (sydnone C=O), 1610 (C=N); δ_{H} (DMSO-*d*₆) 6.41 (2H, d, Ar-H), 7.16 (2H, d, Ar-H), 7.5 (2H, s, Ar-H), 3.89 (6H, s, 2CH₃), 3.8 (6H, s, 2CH₃); m/z 533 (M⁺); **3o** (75%), m.p. 208–209° (Found : C, 47.13; H, 2.32; N, 16.47. C₂₀H₁₂Cl₂F₂N₆O₄ calcd. for : C, 47.17; H, 2.37; N, 16.50%); $\nu_{\max}$ 1738 (sydnone C=O), 1613 (C=N); δ_{H} (DMSO-*d*₆) 6.48 (2H, d, Ar-H), 7.24 (2H, d, Ar-H), 7.6 (2H, s, Ar-H), 3.8 (3H, s, CH₃); m/z 509 (M⁺).

Synthesis of N-acetyl hydrazones of 4-acetyl-3-aryl sydnone (4a-o) : Hydrazones of 4-acetyl-3-arylsydnes (0.002 mol) were heated with acetic anhydride (3 ml) on water-bath for 15 min. The reaction mixture was cooled, poured into ice-water and the resultant solid separated was filtered. Bright yellow crystalline compounds were obtained after crystallisation from ethanol. **4a** (76%), m.p. 189–190° (Found : C, 55.35; H, 4.60; N, 21.50. C₁₂H₁₂N₄O₃ calcd. for : C, 55.38; H, 4.65; N, 21.53%); $\nu_{\max}$ 3300 (NH), 1755 (sydnone C=O), 1656 (amide C=O); δ_{H} (DMSO-*d*₆) 10.20 (1H, br, exchanged with D₂O, NH), 6.5–7.41 (5H, m, Ar-H), 2.50 (3H, s, CH₃), 2.0 (3H, s, CH₃); m/z 260 (M⁺); **4b** (80%), m.p. 171–172° (Found : C, 56.90; H, 5.12; N, 20.40. C₁₃H₁₄N₄O₃ calcd. for : C, 56.93; H, 5.14; N, 20.43%); $\nu_{\max}$ 3310 (NH), 1750 (sydnone C=O), 1658 (amide C=O); δ_{H} (DMSO-*d*₆) 10.25 (1H, br, exchanged with D₂O, NH), 6.35 (2H, d, Ar-H), 6.95 (2H, d, Ar-H), 2.50 (3H, s, CH₃), 2.0 (3H, s, CH₃), 2.3 (3H, s, CH₃); m/z 274 (M⁺); **4c** (60%), m.p. 121–122° (Found : C, 56.90; H, 5.11; N, 20.40. C₁₃H₁₄N₄O₃ calcd. for : C, 56.93; H, 5.14; N, 20.43%); $\nu_{\max}$ 3305 (NH), 1752 (sydnone C=O), 1650 (amide C=O); δ_{H} (DMSO-*d*₆) 10.25 (1H, br, exchanged with D₂O, NH),

6.40 (1H, d, Ar-H), 7.20 (1H, d, Ar-H), 7.25 (2H, m, Ar-H), 2.50 (3H, s, CH₃), 2.1 (3H, s, CH₃), 2.4 (3H, s, CH₃); m/z 274 (M⁺); **4d** (68%), m.p. 174–175° (Found : C, 53.75; H, 4.85; N, 19.28. C₁₃H₁₄N₄O₄ calcd. for : C, 53.79; H, 4.86; N, 19.30%); $\nu_{\max}$ 3300 (NH), 1755 (sydnone C=O), 1653 (amide C=O); δ_{H} (DMSO-*d*₆) 10.21 (1H, br, exchanged with D₂O, NH), 6.40 (2H, d, Ar-H), 7.00 (2H, d, Ar-H), 2.50 (3H, s, CH₃), 2.0 (3H, s, CH₃), 3.8 (3H, s, CH₃); m/z 290 (M⁺); **4e** (70%), m.p. 160–161° (Found : C, 53.75; H, 4.85; N, 19.28. C₁₃H₁₄N₄O₄ calcd. for : C, 53.79; H, 4.86; N, 19.30%); $\nu_{\max}$ 3305 (NH), 1755 (sydnone C=O), 1651 (amide C=O); δ_{H} (DMSO-*d*₆) 10.21 (1H, br, exchanged with D₂O, NH), 6.45 (2H, d, Ar-H), 7.37 (1H, d, Ar-H), 7.85 (2H, m, Ar-H), 2.50 (3H, s, CH₃), 2.1 (3H, s, CH₃), 3.8 (3H, s, CH₃); m/z 290 (M⁺); **4f** (82%), m.p. 142–143° (Found : C, 48.90; H, 3.74; N, 19.00. C₁₂H₁₁ClN₄O₃ calcd. for : C, 48.91; H, 3.76; N, 19.01%); $\nu_{\max}$ 3300 (NH), 1757 (C=O), 1653 (C=O); δ_{H} (DMSO-*d*₆) 10.20 (1H, br, exchanged with D₂O, NH), 6.40 (2H, d, Ar-H), 7.00 (2H, d, Ar-H), 2.50 (3H, s, CH₃), 2.0 (3H, s, CH₃); m/z 294 (M⁺); **4g** (86%), m.p. 157–158° (Found : C, 48.90; H, 3.74; N, 19.00. C₁₂H₁₁ClN₄O₃ calcd. for : C, 48.91; H, 3.76; N, 19.01%); $\nu_{\max}$ 3305 (NH), 1755 (sydnone C=O), 1651 (amide C=O); δ_{H} (DMSO-*d*₆) 10.25 (1H, br, NH), 6.41 (1H, d, Ar-H), 7.30 (1H, d, Ar-H), 7.25 (1H, m, Ar-H), 7.8 (1H, s, Ar-H), 2.50 (3H, s, CH₃), 2.1 (3H, s, CH₃); m/z 294 (M⁺); **4h** (85%), m.p. 106–107° (Found : C, 42.47; H, 3.22; N, 16.50. C₁₂H₁₁BrN₄O₃ calcd. for : C, 42.50; H, 3.27; N, 16.52%); $\nu_{\max}$ 3308 (NH), 1758 (sydnone C=O), 1652 (amide C=O); δ_{H} (DMSO-*d*₆) 10.43 (1H, br, exchanged with D₂O, NH), 6.43 (2H, d, Ar-H), 7.32 (2H, d, Ar-H), 2.50 (3H, s, CH₃), 2.2 (3H, s, CH₃); m/z 239 (M⁺); **4i** (70%), m.p. 113–114° (Found : C, 52.80; H, 4.40; N, 17.58. C₁₄H₁₄N₄O₅ calcd. for : C, 52.83; H, 4.43; N, 17.60%); $\nu_{\max}$ (NH), 1757 (sydnone C=O), 1740 (ester C=O), 1653 (amide C=O); δ_{H} (DMSO-*d*₆) 10.42 (1H, br, exchanged with D₂O, NH), 6.75 (2H, d, Ar-H), 7.37 (2H, d, Ar-H), 2.49 (3H, s, CH₃), 2.1 (3H, s, CH₃), 3.8 (3H, s, CH₃); m/z 318 (M⁺); **4j** (74%), m.p. 117–118° (Found : C, 54.20; H, 4.81; N, 16.84. C₁₅H₁₆N₄O₅ calcd. for : C, 54.21; H, 4.85; N, 16.86%); $\nu_{\max}$ 3300 (NH), 1752 (sydnone C=O), 1745 (ester C=O), 1653 (amide C=O); δ_{H} (DMSO-*d*₆) 10.45 (1H, br, exchanged with D₂O, NH), 6.87 (2H, d, Ar-H), 7.45 (2H, d, Ar-H), 2.50 (3H, s, CH₃), 2.1 (3H, s, CH₃), 3.8 (2H, q, CH₂), 1.8 (3H, t, CH₃); m/z 332 (M⁺); **4k** (80%), m.p. 179–180° (Found : C, 58.30; H, 5.57; N, 19.40. C₁₄H₁₆N₄O₃ calcd. for : C, 58.32; H, 5.59; N, 19.43%); $\nu_{\max}$ 3300 (NH), 1752 (sydnone C=O), 1653 (amide C=O); δ_{H} (DMSO-*d*₆) 10.35 (1H, br, exchanged with D₂O, NH), 6.45 (1H, d, Ar-H), 7.21 (1H, d, Ar-H), 7.5 (1 H, s, Ar-H), 2.4 (3H, s, CH₃), 2.1 (3H,

s, CH₃), 2.0 (3H, s, CH₃), 1.9 (3H, s, CH₃); m/z 288 (M⁺); **4l** (70%), m.p. 153–154° (Found : C, 58.30; H, 5.57; N, 19.40. C₁₄H₁₆N₄O₃ calcd. for : C, 58.32; H, 5.59; N, 19.43%); $\nu_{\max}$ 3315 (NH), 1750 (sydnone C=O), 1656 (amide C=O); δ_{H} (DMSO-*d*₆) 10.41 (1H, br, exchanged with D₂O, NH), 6.43 (1H, d, Ar-H), 7.18 (1H, d, Ar-H), 7.4 (1H, s, Ar-H), 2.50 (3H, s, CH₃), 2.1 (3H, s, CH₃), 2.0 (3H, s, CH₃), 1.9 (3H, s, CH₃); m/z 288 (M⁺); **4m** (72%), m.p. 151–152° (Found : C, 50.55; H, 4.20; N, 18.10. C₁₃H₁₃ClN₄O₃ calcd. for : C, 50.58; H, 4.24; N, 18.15%); $\nu_{\max}$ 3302 (NH), 1755 (sydnone C=O), 1660 (amide C=O); δ_{H} (DMSO-*d*₆) 10.43 (1H, br, exchanged with D₂O, NH), 6.41 (1H, d, Ar-H), 7.16 (1H, d, Ar-H), 7.5 (1H, s, Ar-H), 2.50 (3H, s, CH₃), 2.1 (3H, s, CH₃), 2.0 (3H, s, CH₃); m/z 308 (M⁺); **4n** (60%), m.p. 147–148° (Found : C, 48.05; H, 4.01; N, 17.22. C₁₃H₁₃ClN₄O₄ calcd. for : C, 48.08; H, 4.04; N, 17.25%); $\nu_{\max}$ 3312 (NH), 1754 (sydnone C=O), 1655 (amide C=O); δ_{H} (DMSO-*d*₆) 10.43 (1H, br, exchanged with D₂O, NH), 6.41 (1H, d, Ar-H), 7.16 (1H, d, Ar-H), 7.5 (1H, s, Ar-H), 2.50 (3H, s, CH₃), 2.1 (3H, s, CH₃), 3.8 (3H, s, CH₃); m/z 324 (M⁺); **4o** (70%), m.p. 181–183° (Found : C, 46.06; H, 3.20; N, 17.90. C₁₂H₁₀ClFN₄O₃ calcd. for : C, 46.09; H, 3.22; N, 17.92%); $\nu_{\max}$ 3375 (NH), 1758 (sydnone C=O),

1652 (amide C=O); δ_{H} (DMSO-*d*₆) 10.45 (1H, br, exchanged with D₂O, NH), 6.48 (1H, d, Ar-H), 7.24 (1H, d, Ar-H), 7.6 (1H, s, Ar-H), 2.50 (3H, s, CH₃), 2.1 (3H, s, CH₃), m/z 312 (M⁺).

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References

1. B. G. Ugarkar, B. V. Badami and G. S. Puranik, *Arch. Pharm. (Weinheim)*, 1978, **311**, 109.
2. S. V. Badachihar and G. S. Puranik, *Indian. J. Chem., Sect. B*, 1985, **24**, 228.
3. (a) Shanta G. Mullur and Bharati V. Badami, *Indian J. Heterocyclic Chem.*, 1999, **8**, 343; (b) J. R. Kavali and B. V. Badami, *Il Farmaco.*, 2000, **55**, 406.
4. C. V. Greco, J. Tobias and L. B. Kier, *J. Het. Chem.*, 1967, **4**, 160.