Mild Oxidative Cyclization of Sydnone-Benzoylhydrazone with Lead Oxide to 2,5-Disubstituted-1,3,4-Oxadiazole–Sydnone Hybrid Derivatives

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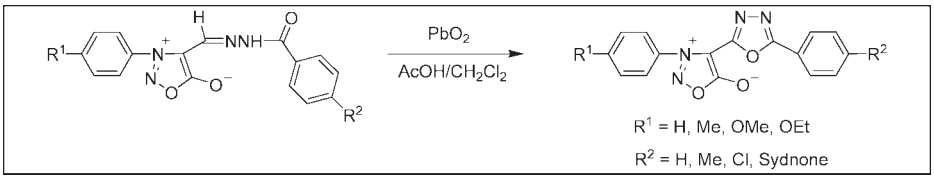

The mild oxidation of sydnone-benzoylhydrazone hybrids with lead oxide in acetic acid/dichloromethane solution inducted their intramolecular cyclization to provide the corresponding 2,5-disubstituted-1,3,4-oxidiazole derivatives. The sydnone moiety has been efficient preserved for the future work in the mild oxidation.

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INTRODUCTION

Sydnones attract attention due to their wildly useful properties, including biological and pharmaceutical usage [1], synthetic application [2], photochromic properties [3], and preparation of electroluminescent materials [4]. Sydones, also considered as the masked hydrazines, can react with HCl for de-masking for the further formation of heterocycles [5].

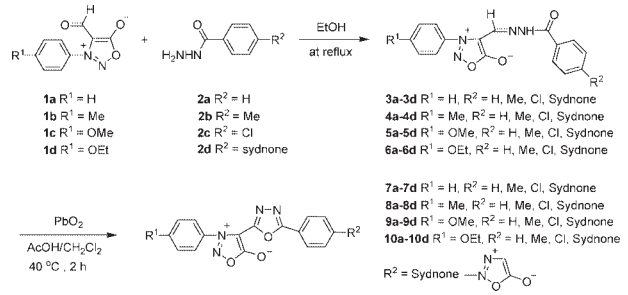
1,3,4-Oxadiazoles have been reported to be biologically versatile compounds displaying a variety of biological effects, which include anti-inflammatory [6], antifungal [7], antiparasitic [8], and antimicrobial activities [9]. In addition, they have been used as bioisosteres on the carboxamide moiety [10]. The most common synthetic approach to 1,3,4-oxidiazoles involves cyclodehydration of 1,2-diacylhydrazines. Typically, the reaction is carried out by using thionyl chloride [11], phosphorous oxychloride [12], phosphorous pentoxide [13], triphenylphosphine [14], or trifluoromethane–sulfonic anhydride as the dehydrating agent [15].

Another alternative route to 1,3,4-oxadiazoles by oxidative cyclization from the corresponding aldehyde *N*-acylhydrazones proceeds with lead tetraacetate [16], lead oxide [17], potassium permanganate [18], electrochemical methods [19], iodobenzene diacetate [20], or chloramine T [21]. The azines were used as oxidative cyclization precursors. Herein, we report the aldehyde *N*-acylhydrazone containing sydnone moiety with lead oxide reagent, at 40°C for 2 h to afford 2,5-disubstituted-1,3,4-oxadiazole–sydnone hybrids in 51–63%. In this mild oxidative cyclization, the sydnone moiety is able to be successful preserved without decomposition.

RESULTS AND DISCUSSION

The synthetic pathway of the 2,5-disubstituted-1,3,4-oxadiazole–sydnone hybrid derivatives (**7–10**) was depicted in Scheme 1. Following by the published procedure [2,22], the sydnone compounds were easily converted to the 3-aryl-4-formyl-sydnone derivatives **1a–1d** in a solution of $POCl_3$ and DMF by the Schmidt reaction. And benzoyl chloride reacted with hydrazine monohydrate to generate benzoylhydrazones **2a–2d**. Then various 3-aryl-4-formyl-sydnone derivatives **1a–1d** (p-R^1 = H, Me, OMe, and OEt) were mixed with benzoylhydrazones **2a–2d** (p-R^2 = H, Me, Cl, and sydnone) and stirred for 2.0–6.0 h in an EtOH solution to achieve the elimination and give the corresponding products **3–6** in good yields (74–86%, see Table 1) [23].

Scheme 1. The synthetical route of 2,5-disubstituted-1,3,4-oxadiazole–sydnone hybrid derivatives.



Aldehyde *N*-acylhydrazones **3–6** were performed the oxidative–cyclization by using fresh $KMnO_4$ in acetic acid/dichloromethane solution. The low isolable oxidative–cyclization products were provided because of the further oxidation formation and the damage of sydnone ring by $KMnO_4$. In the controllable and improvable experiment, the commercially available reagent lead oxide (PbO_2) was selected for the mild oxidative–cyclization agent [17,24]. When the aldehyde *N*-acylhydrazones **3–6** were oxidized with 2.5 equiv of lead oxide (PbO_2), the 2,5-disubstituted-1,3,4-oxadiazole–sydnone hybrid derivatives **7–10** were formed in 50–63% yields. The long range of the substitution effects on R^1 (H, Me, OMe, and OEt) and R^2 (H, Me, Cl, and sydnone) positions are not clearly a function of the isolated yield and the results are shown in Table 1.

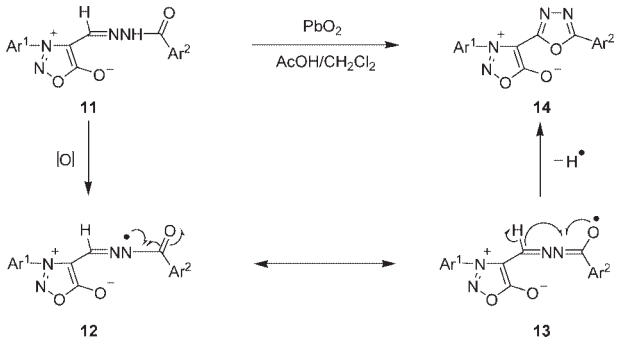
The proposed oxidative–cyclization mechanism is shown in the Scheme 2. The aldehyde *N*-acylhydrazone **11** can be oxidized by lead oxide (PbO_2) to trap the hydrogen and afford the hydrazonyl radical **12** [17].

Table 1

The yields of aldehyde *N*-acylhydrazones **3–6** and 2,5-disubstituted-1,3,4-oxadiazole–sydnone hybrid derivatives **7–10**.

Entry		Compounds	Yield	Compounds	Yield
R^1	R^2	**3–6**	(%)	**7–10**	(%)
H	H	**3a**	80	**7a**	57
	Me	**3b**	86	**7b**	57
	Cl	**3c**	77	**7c**	50
	Sydnone	**3d**	84	**7d**	51
Me	H	**4a**	83	**8a**	59
	Me	**4b**	83	**8b**	58
	Cl	**4c**	75	**8c**	51
	Sydnone	**4d**	87	**8d**	53
OMe	H	**5a**	82	**9a**	61
	Me	**5b**	85	**9b**	60
	Cl	**5c**	75	**9c**	53
	Sydnone	**5d**	89	**9d**	58
OEt	H	**6a**	82	**10a**	63
	Me	**6b**	84	**10b**	62
	Cl	**6c**	74	**10c**	53
	Sydnone	**6d**	89	**10d**	57

Scheme 2. The proposed mechanism of the oxidative cyclization.



Because of the electron radical can be stabilized by the strong electronegativity of oxygen atom, the electron radical migrates from nitrogen to oxygen atom to form the radical intermediate **13**. The intermediate **13** undergoes the further oxidative cyclization to yield 2,5-disubstituted-1,3,4-oxadiazole–sydnone hybrid **14** [23].

In conclusion, we have developed a mild and efficient oxidative–cyclization method for the synthesis of 2,5-disubstituted-1,3,4-oxadiazole–sydnone hybrid derivatives. Using this mild radical cyclization, the sydnone ring was successfully preserved to provide 1,3,4-oxadiazole–sydnone hybrids in the core molecular.

EXPERIMENTAL

General procedure. Analytical thin-layer chromatography was performed on precoated plates (silica gel 60 F-254), purchased from Merck Inc. Purification by gravity column chromatography was carried out by use of Merck Reagents Silica Gel 60 (particle size 0.063–0.200 mm, 70–230 mesh ASTM). Infrared (IR) spectra were measured on a Bomem Michelson Series FT-IR spectrometer. The wave numbers reported are referenced to the polystyrene 1601 cm^{-1} absorption. Absorption intensities are recorded by the following abbreviations: s, strong; m, medium; w, weak. Proton NMR spectra were obtained on a Bruker-300 (400 MHz) spectrometer by use of $CDCl_3$ and d_6-DMSO as solvent. Carbon-13 NMR spectra were obtained on a Varian a Bruker-300 (100 MHz) spectrometer by used of $CDCl_3$ as solvent. Carbon-13 chemical shifts are referenced to the center of the $CDCl_3$ triplet (δ 77.0 ppm). Multiplicities are recorded by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; *J*, coupling constant (hertz). Elemental analyses were carried out on a Heraeus CHN–O RAPID element analyzer. Mass spectra were measured on a VG Platform II GC-MS Instruments. FAB mass and High-resolution mass spectra were obtained by means of a Finnigan/Thermo Quest MAT 95XL mass spectrometer.

Standard procedure for the substitution reaction. To a solution of 3-aryl-4-formyl-sydnone derivatives (**1a–1d**, 0.38 g, 2.00 mmol, 1.0 equiv) and benzoylhydrazones (**2a–2d**, 0.27 g, 2.00 mmol, 1.6 equiv) in EtOH (10 mL) was stirred and added one drop of aqueous H_2SO_4 solution.

The reaction mixture was stirred at room temperature for 2.0 h. After the reaction was completed, the resultant precipitate was filtrated, washed with cold EtOH (20 mL × 2), and dried in vacuum oven. The residue was purified by recrystallization from EtOAc to give pure aldehyde *N*-acylhydrazones **3–6** as white powder in 74–86% yields.

3-Phenyl-4-formylsydnone benzoylhydrazone (3a). Mp (recrystallized from EtOAc) 196–198°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.40–7.82 (m, 10 H), 8.11 (s, 1 H), 11.69 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 106.1, 125.9, 127.7, 128.7, 130.3, 132.1, 133.2, 133.4, 134.5, 142.1, 162.9, 164.3; IR (KBr) 3370 (s, NH), 1755 (m, C=O), 1695 m cm^{-1}; FABMS *m*/*z* (relative intensity) 309 (M + 1, 59), 308 (M$^+$, 15).

3-Phenyl-4-formylsydnone p-methylbenzoylhydrazone (3b). Mp (recrystallized from EtOAc) 197–199°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.21 (s, 3H, CH_3), 7.12–7.72 (m, 9 H), 8.03 (s, 1 H), 11.56 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.2, 106.2, 125.9, 127.5, 127.7, 129.2, 130.3, 132.8, 133.4, 134.3, 142.2, 162.8, 164.1; IR (KBr) 3338 (s, NH), 1754 (m, C=O), 1692 m cm^{-1}; FABMS *m*/*z* (relative intensity) 323 (M + 1, 74), 322 (M$^+$, 35).

3-Phenyl-4-formylsydnone p-chlorolbenzoylhydrazone (3c). Mp (recrystallized from EtOAc) 200–202°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.10–7.80 (m, 9 H), 7.86 (s, 1 H), 11.68 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 106.0, 125.3, 125.8, 127.1, 128.5, 130.2, 132.1, 133.2, 133.5, 142.3, 161.8, 163.9; IR (KBr) 3364 (s, NH), 1755 (m, C=O), 1689 m cm^{-1}.

3-Phenyl-4-formylsydnone 4-(sydnon-3-yl)benzoylhydrazone (3d). Mp (recrystallized from MeOH) 183–185°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.05–8.68 (m, 11 H, ArH + sydnone), 12.35 (s, 1 H, NH); IR (KBr) 3091 (s, NH), 1745 (m, C=O), 1681 m cm^{-1}; FABMS *m*/*z* (relative intensity) 393 (M + 1, 3), 392 (M$^+$, 24).

3-(p-Methylphenyl)-4-formylsydnone benzoylhydrazone (4a). Mp (recrystallized from EtOAc) 191–193°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.46 (s, 3H, CH_3), 7.25–7.75 (m, 9 H), 8.11 (s, 1 H), 11.66 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.1, 106.1, 125.7, 127.3, 127.7, 129.0, 129.3, 130.3, 131.1, 134.5, 143.2, 162.8, 164.7; IR (KBr) 3352 (s, NH), 1758 (m, C=O), 1692 m cm^{-1}.

3-(p-Methylphenyl)-4-formylsydnone p-methylbenzoylhydrazone (4b). Mp (recrystallized from EtOAc) 197–199°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.20 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 7.25–7.75 (m, 8 H), 8.16 (s, 1 H), 11.67 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.0, 21.2, 106.3, 126.2, 127.3, 127.9, 129.8, 130.4, 132.6,134.5, 142.6, 162.5, 164.0; IR (KBr) 3345 (s, NH), 1752 (m, C=O), 1695 m cm^{-1}.

3-(p-Methylphenyl)-4-formylsydnone p-chlorolbenzoylhydrazone (4c). Mp (recrystallized from EtOAc) 201–203°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.43 (s, 3H, CH_3), 7.28–7.90 (m, 8 H), 7.98 (s, 1 H), 11.63 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.0, 106.0, 125.1, 127.0, 127.4, 128.8, 129.1, 130.2, 130.9, 134.2, 143.1, 162.4, 164.1; IR (KBr) 3359 (s, NH), 1752 (m, C=O), 1695 m cm^{-1}.

3-(p-Methylphenyl)-4-formylsydnone 4-(sydnon-3-yl)benzoylhydrazone (4d). Mp (recrystallized from MeOH) 210–212°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.43 (s, 3H, CH_3), 7.39–8.15 (m, 10 H, ArH + sydnone), 11.93 (s, 1 H, NH); IR (KBr) 3095 (s, NH), 1751 (m, C=O), 1679 m cm^{-1}.

3-(p-Methoxyphenyl)-4-formylsydnone benzoyl-hydrazone (5a). Mp (recrystallized from EtOAc) 183–185°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.88 (s, 3H, OCH_3), 7.12–7.72 (m, 9 H), 8.03 (s, 1 H), 11.56 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 56.8, 106.2, 121.2, 121.7, 127.7, 129.3, 130.5, 130.6, 133.7, 134.8, 142.3, 162.8, 164.0; IR (KBr) 3334 (s, NH), 1755 (m, C=O), 1704 m cm^{-1}; FABMS *m*/*z* (relative intensity) 339 (M + 1, 68), 338 (M$^+$, 6).

3-(p-Methoxyphenyl)-4-formylsydnone p-methylbenzoylhydrazone (5b). Mp (recrystallized from EtOAc) 178–180°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.34 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 7.25–7.79 (m, 8 H), 8.02 (s, 1 H), 11.66 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.1, 56.7, 106.4, 121.3, 121.8, 127.7, 129.1, 130.3, 131.8, 133.8, 134.5, 142.1, 162.7, 164.0; IR (KBr) 3332 (s, NH), 1748 (m, C=O), 1701 m cm^{-1}; FABMS *m*/*z* (relative intensity) 353 (M + 1, 21), 352 (M$^+$, 2).

3-(p-Methoxyphenyl)-4-formylsydnone p-chlorolbenzoylhydrazone (5c). Mp (recrystallized from EtOAc) 191–193°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.87 (s, 3H, OCH_3), 7.03–7.70 (m, 8 H), 7.90 (s, 1 H), 11.52 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 56.6, 106.1, 121.1, 121.2, 127.4, 129.2, 130.1, 130.5, 132.9, 134.5, 142.0, 161.7, 163.8; IR (KBr) 3361 (s, NH), 1755 (m, C=O), 1699 m cm^{-1}; FABMS *m*/*z* (relative intensity) 373 (M + 1, 62), 372 (M$^+$, 13).

3-(p-Methoxyphenyl)-4-formylsydnone 4-(sydnon-3-yl)benzoylhydrazone (5d). Mp (recrystallized from MeOH) 204–206°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.87 (s, 3H, OCH_3), 7.24–8.15 (m, 10 H, ArH + sydnone), 11.92 (s, 1 H, NH); IR (KBr) 3092 (s, NH), 1746 (m, C=O), 1683 m cm^{-1}; FABMS *m*/*z* (relative intensity) 423 (M + 1, 6), 422 (M$^+$, 1).

3-(p-Ethoxyphenyl)-4-formylsydnone benzoyl-hydrazone (6a). Mp (recrystallized from EtOAc) 192–194°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.37 (t, 3 H, J = 7.0 Hz, CH_3), 4.15 (q, 2 H, J = 7.0 Hz, CH_2), 7.20–7.83 (m, 9 H), 8.15 (s, 1 H), 11.70 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 14.7, 64.2, 106.2, 125.8, 127.5, 127.7, 128.7, 129.1, 132.2, 133.2, 134.9, 142.3, 161.5, 163.0; IR (KBr) 3352 (s, NH), 1749 (m, C=O), 1698 m cm^{-1}; FABMS *m*/*z* (relative intensity) 353 (M + 1, 21), 352 (M$^+$, 3).

3-(p-Ethoxyphenyl)-4-formylsydnone p-methylbenzoylhydrazone (6b). Mp (recrystallized from EtOAc) 189–191°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.33 (t, 3 H, J = 7.0 Hz, CH_3), 2.44 (s, 3H, CH_3), 4.13 (q, 2 H, J = 7.0 Hz, CH_2), 7.20–7.78 (m, 9 H), 8.15 (s, 1 H), 11.65 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 14.7, 21.2, 64.2, 106.1, 125.8, 127.4, 127.7, 128.7, 129.2, 130.2, 133.2, 134.6, 142.3, 164.0; IR (KBr) 3358 (s, NH), 1740 (m, C=O), 1695 m cm^{-1}; FABMS *m*/*z* (relative intensity) 367 (M + 1, 19), 366 (M$^+$, 4).

3-(p-Ethoxyphenyl)-4-formylsydnone p-chlorolbenzoylhydrazone (6c). Mp (recrystallized from EtOAc) 195–197°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.36 (t, 3 H, J = 7.0 Hz, CH_3), 4.13 (q, 2 H, J = 7.0 Hz, CH_2), 7.13–7.80 (m, 8 H), 7.91 (s, 1 H), 11.66 (s, 1 H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 14.6, 64.1, 105.8, 125.5, 127.2, 127.7, 128.8, 129.4, 132.2, 133.0, 134.6, 142.1, 160.8, 162.9; IR (KBr) 3350 (s, NH), 1745 (m, C=O), 1699 m cm^{-1}; FABMS *m*/*z* (relative intensity) 387 (M + 1, 51), 386 (M$^+$, 3).

3-(p-Ethoxyphenyl)-4-formylsydnone 4-(sydnon-3-yl)benzoylhydrazone (6d). Mp (recrystallized from MeOH) 178–180°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.37 (t, 3 H, J = 6.9 Hz, CH_3), 4.14 (q, 2 H, J = 6.9 Hz, CH_2), 7.21–8.16 (m, 10 H, ArH + sydnone), 11.93 (s, 1 H, NH); IR (KBr) 3094 (s, NH), 1749 (m, C=O), 1677 m cm^{-1}; FABMS *m*/*z* (relative intensity) 437 (M + 1, 6), 436 (M$^+$, 4).

Standard procedure for the oxidative–cyclization. Aldehyde *N*-acylhydrazones **3–6** (0.31 g, 1.00 mmol, 1.0 equiv) was dissolved in glacial acetic acid/dichloromethane (1/1, 15 mL). Lead oxide (PbO_2, 0.60 g, 2.50 mmol, 2.5 equiv) was added to the reaction mixture and stirred at 35–40°C for 1.5–6 h. After the reaction was completed, the reaction mixture was filtrated to remove the lead oxide residue and washed with cold dichloromethane (10 mL × 3). The filtrate was washed and extracted with saturated $NaHCO_3$ aqueous solution (20 mL × 2) to remove the residue glacial acetic acid. The combined organic layer was dried with $MgSO_{4\ (s)}$ and concentrated under reduced pressure. The residue was purified by recrystallization from dichloromethane to give pure 2,5-disubstituted-1,3,4-oxidiazole–sydnone hybrid derivatives **7–10** as a white powder in 50–63% yields.

3-Phenyl-4-(5-phenyl-1,3,4-oxadiazol-2-yl)sydnone (7a). Mp (recrystallized from CH_2Cl_2) 177–179°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.51–7.96 (m, 10 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 97.6, 120.6, 126.0, 126.5, 129.7, 129.9, 132.5, 133.0, 134.5, 154.1, 163.1, 163.9; IR (KBr) 1749 m cm^{-1}; FABMS *m*/*z* (relative intensity) 307 (M + 1, 77), 306 (M^+, 9); *Anal*. Calcd for $C_{16}H_{10}N_4O_3$: C, 62.74; H, 3.72; N, 18.30. Found: C, 62.51; H, 3.35; N, 18.04.

3-Phenyl-4-[5-(p-methylphenyl)-1,3,4-oxadiazol-2-yl]-sydnone (7b). Mp (recrystallized from CH_2Cl_2) 205–207°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.42 (s, 3H, CH_3), 7.34–7.94 (m, 9 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.2, 106.2, 125.9, 127.5, 127.7, 129.2, 130.3, 132.8, 133.4, 134.3, 142.2, 162.8, 164.1; IR (KBr) 1743 m cm^{-1}; FABMS *m*/*z* (relative intensity) 321 (M + 1, 48), 320 (M^+, 14); *Anal*. Calcd for $C_{17}H_{12}N_4O_3$: C, 63.75; H, 3.75; N, 17.50. Found: C, 63.91; H, 3.87; N, 17.81.

3-Phenyl-4-[5-(p-chlorophenyl)-1,3,4-oxadiazol-2-yl]sydnone (7c). Mp (recrystallized from CH_2Cl_2) 187–189°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.43–7.99 (m, 9 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 97.4, 121.3, 126.2,128.4, 129.5, 132.0, 133.1, 136.5, 154.5, 162.9, 164.0; IR (KBr) 1755 m cm^{-1}; *Anal*. Calcd for $C_{16}H_9N_4O_3Cl$: C, 56.38; H, 2.64; N, 16.45. Found: C, 56.63; H, 2.41; N, 16.64.

3-Phenyl-4-[5-(p-chlorophenyl)-1,3,4-oxadiazol-2-yl]-sydnone (7c). Mp (recrystallized from CH_2Cl_2) 187–189°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 7.43–7.99 (m, 9 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 97.4, 121.3, 126.2,128.4, 129.5, 132.0, 133.1, 136.5, 154.5, 162.9, 164.0; IR (KBr) 1755 m cm^{-1}; *Anal*. Calcd for $C_{16}H_9N_4O_3Cl$: C, 56.38; H, 2.64; N, 16.45. Found: C, 56.62; H, 2.41; N, 16.64.

3-p-Methylphenyl-4-(5-phenyl-1,3,4-oxadiazol-2-yl)sydnone (8a). Mp (recrystallized from CH_2Cl_2) 204–206°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.43 (s, 3H, CH_3), 7.41–7.78 (m, 9 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.2, 97.5, 122.6, 125.8, 126.7, 129.3, 129.9, 132.1, 133.5, 134.6, 154.5, 162.8, 163.6; IR (KBr) 1752 m cm^{-1}; FABMS *m*/*z* (relative intensity) 321 (M + 1, 45), 320 (M^+, 13); *Anal*. Calcd for $C_{17}H_{12}N_4O_3$: C, 63.75; H, 3.75; N, 17.50. Found: C, 63.68; H, 3.42; N, 17.86.

3-p-Methylphenyl-4-(5-phenyl-1,3,4-oxadiazol-2-yl)sydnone (8a). Mp (recrystallized from CH_2Cl_2) 204–206°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.43 (s, 3H, CH_3), 7.41–7.78 (m, 9 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.2, 97.5, 122.6, 125.8, 126.7, 129.3, 129.9, 132.1, 133.5, 134.6, 154.5, 162.8, 163.6; IR (KBr) 1752 m cm^{-1}; FABMS *m*/*z* (relative intensity) 321 (M + 1, 45), 320 (M^+, 13); *Anal*. Calcd for $C_{17}H_{12}N_4O_3$: C, 63.75; H, 3.75; N, 17.50. Found: C, 63.68; H, 3.42; N, 17.86.

3-(p-Methylphenyl)-4-[5-(p-chlorophenyl)-1,3,4-oxadiazol-2-yl]sydnone (8c). Mp (recrystallized from CH_2Cl_2) 202–205°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.42 (s, 3H, CH_3), 7.43–7.99 (m, 9 H); IR (KBr) 1749 m cm^{-1}; FABMS *m*/*z* (relative intensity) 357 (M + 1, 51), 356 (M^+, 16); *Anal*. Calcd for $C_{17}H_{11}N_4O_3Cl$: C, 57.55; H, 3.10; N, 15.80. Found: C, 57.33; H, 3.07; N, 15.72.

4-[5-(4-Sydnon-3-yl-phenyl)-1,3,4-oxadiazol-2-yl]-3-(4-methylphenyl)sydnone (8d). Mp (recrystallized from CH_2Cl_2) 215–217°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.45 (s, 3H, CH_3), 7.52 (d, 2 H, *J* = 8.2 Hz), 7.79 (d, 2 H, *J* = 8.2 Hz), 7.88 (s, 1 H), 8.01 (d, 2 H, *J* = 8.6 Hz), 8.14 (d, 2 H, *J* = 8.6 Hz); IR (KBr) 1753 m cm^{-1}; FABMS *m*/*z* (relative intensity) 397 (M + 1, 64), 396 (M^+, 11); *Anal*. Calcd for $C_{18}H_{10}N_6O_5$: C, 56.43; H, 2.97; N, 20.79. Found: C, 56.18; H, 3.24; N, 20.96.

3-p-Methoxyphenyl-4-(5-phenyl-1,3,4-oxadiazol-2-yl)-sydnone (9a). Mp (recrystallized from CH_2Cl_2) 224–226°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.89 (s, 3H, OCH_3), 7.25–7.78 (m, 9 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 56.6, 97.4, 122.3, 125.9, 126.3, 129.1, 130.2, 132.1, 133.6, 134.7, 154.8, 162.2, 164.0; IR (KBr) 1748 m cm^{-1}; FABMS *m*/*z* (relative intensity) 337 (M + 1, 37), 336 (M^+, 4); *Anal*. Calcd for $C_{17}H_{12}N_4O_4$: C, 60.71; H, 3.57; N, 16.67. Found: C, 60.87; H, 3.67; N, 16.54.

3-(p-Methoxyphenyl)-4-[5-(p-methylphenyl)-1,3,4-oxadiazol-2-yl]sydnone (9b). Mp (recrystallized from CH_2Cl_2) 188–190°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.38 (s, 3H, CH_3), 3.87 (s, 3H, OCH_3), 7.19–7.88 (m, 8 H); IR (KBr) 1755 m cm^{-1}; FABMS *m*/*z* (relative intensity) 350 (M + 1, 28), 349 (M^+, 8); *Anal*. Calcd for $C_{18}H_{13}N_4O_4$: C, 61.71; H, 3.71; N, 16.00. Found: C, 61.52; H, 3.54; N, 15.86.

3-(p-Methoxyphenyl)-4-[5-(p-chlorophenyl)-1,3,4-oxadiazol-2-yl]sydnone (9c). Mp (recrystallized from CH_2Cl_2) 203–205°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.88 (s, 3H, OCH_3), 7.25–7.75 (m, 8 H); IR (KBr) 1744 m cm^{-1}; FABMS *m*/*z* (relative intensity) 372 (M + 1, 31), 371 (M^+, 9); *Anal*. Calcd for $C_{17}H_{11}N_4O_4Cl$: C, 55.06; H, 2.97; N, 15.11. Found: C, 54.94; H, 2.81; N, 14.89.

4-[5-(4-Sydnon-3-yl-phenyl)-1,3,4-oxadiazol-2-yl]-3-(4-methoxyphenyl)sydnone (9d). Mp (recrystallized from CH_2Cl_2) 225–227°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.86 (s, 3H, OCH_3), 7.35 (d, 2 H, *J* = 8.2 Hz), 7.82 (d, 2 H, *J* = 8.2 Hz), 7.88 (s, 1 H), 8.03 (d, 2 H, *J* = 8.5 Hz), 8.13 (d, 2 H, *J* = 8.5 Hz); IR (KBr) 1749 m cm^{-1}; FABMS *m*/*z* (relative intensity) 421 (M + 1, 3), 420 (M^+, 1); *Anal*. Calcd for $C_{19}H_{12}N_6O_6$: C, 53.77; H, 2.83; N, 22.64. Found: C, 53.97; H, 2.96; N, 22.81.

3-p-Ethoxyphenyl-4-(5-phenyl-1,3,4-oxadiazol-2-yl)sydnone (9a). Mp (recrystallized from CH_2Cl_2) 187–189°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.38 (t, 3 H, *J* = 6.9 Hz, CH_3), 4.16 (q, 2 H, *J* = 6.9 Hz, CH_2), 7.18–7.84 (m, 9 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 14.6, 64.2, 97.5, 115.3, 122.7, 126.5, 126.8, 127.5, 129.7, 132.5, 154.2, 161.7, 163.1, 164.0; IR (KBr) 1751 m cm^{-1}; FABMS *m*/*z* (relative intensity) 351 (M + 1, 49), 350 (M^+, 4); *Anal*. Calcd for $C_{18}H_{14}N_4O_4$: C, 61.71; H, 4.00; N, 16.00. Found: C, 61.58; H, 4.10; N, 15.89.

3-(p-Ethoxyphenyl)-4-[5-(p-methylphenyl)-1,3,4-oxadiazol-2-yl]sydnone (10b). Mp (recrystallized from CH_2Cl_2) 204–206°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.38 (t, 3 H, *J* = 6.9 Hz, CH_3), 2.43 (s, 3H, CH_3), 4.19 (q, 2 H, *J* = 6.9 Hz, CH_2), 7.22 (d, 2 H, *J* = 9.0 Hz), 7.36 (d, 2 H, *J* = 8.1 Hz), 7.64 (d, 2 H, *J* = 8.1 Hz), 7.82 (d, 2 H, *J* = 9.0 Hz); ^{13}C

NMR (DMSO-d_6, 75 MHz) δ 14.6, 21.3, 64.2, 97.5, 115.2, 120.0, 126.5, 126.8, 127.5, 130.2, 142.8, 153.9, 161.7, 163.2, 164.0; IR (KBr) 1751 m cm^{-1}; FABMS *m*/*z* (relative intensity) 365 (M + 1, 91), 364 (M^+, 7); *Anal*. Calcd for $C_{19}H_{16}N_4O_4$: C, 62.64; H, 4.40; N, 15.37. Found: C, 62.19; H, 4.08; N, 15.01.

3-(p-Ethoxyphenyl)-4-[5-(p-chlorophenyl)-1,3,4-oxadiazol-2-yl]sydnone (10c). Mp (recrystallized from CH_2Cl_2) 190–192°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.39 (t, 3 H, J = 7.0 Hz, CH_3), 4.17 (q, 2 H, J = 7.0 Hz, CH_2), 7.21–7.89 (m, 8 H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 14.7, 64.3, 97.6, 114.8, 122.9, 125.9, 127.0, 127.8, 130.0, 132.1, 154.4, 161.5, 163.2, 164.1; IR (KBr) 1749 m cm^{-1}; FABMS *m*/*z* (relative intensity) 385 (M + 1, 11), 384 (M^+, 3); *Anal*. Calcd for $C_{18}H_{13}N_4O_4Cl$: C, 56.17; H, 3.38; N, 15.43. Found: C, 56.54; H, 3.68; N, 15.94.

4-[5-(4-Sydnon-3-yl-phenyl)-1,3,4-oxadiazol-2-yl]-3-(4-ethoxyphenyl)sydnone (10d). Mp (recrystallized from CH_2Cl_2) 178–181°C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.38 (t, 3 H, J = 7.0 Hz, CH_3), 4.16 (q, 2 H, J = 7.0 Hz, CH_2), 7.25 (d, 2 H, J = 8.2 Hz), 7.85 (d, 2 H, J = 8.2 Hz), 7.88 (s, 1 H), 8.03 (d, 2 H, J = 8.5 Hz), 8.16 (d, 2 H, J = 8.5 Hz); IR (KBr) 1746 m cm^{-1}; FABMS *m*/*z* (relative intensity) 437 (M + 1, 28), 436 (M^+, 13); *Anal*. Calcd for $C_{20}H_{16}N_6O_6$: C, 55.05; H, 3.67; N, 19.27. Found: C, 55.37; H, 3.84; N, 19.47.

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