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Studies on the syntheses of heterocycles from 3-arylsydnone-4-carbohydroximic acid chlorides with *N*-arylmaleimides, [1,4]naphthoquinone and aromatic amines

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Abstract—3-Arylsydnone-4-carbohydroximic acid chlorides (**1**) could react with *N*-arylmaleimides (**3a**–**b**) or 2-methyl-*N*-phenylmaleimide (**3c**) to give 3-(3-arylsydnon-4-yl)-5-aryl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-diones (**4a**–**h**) or 6a-methyl-3-(3-arylsydnon-4-yl)-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-diones (**4i**–**l**), respectively. However, 3-(arylsydnon-4-yl)-naphtho[2,3-*d*]isoxazole-4,9-diones (**6a**–**d**) were obtained in good yield by the reaction of carbohydroximic acid chlorides **1** with [1,4]naphthoquinone. Furthermore, 2-(3-arylsydnon-4-yl)benzoxazoles (**9a**–**d**) and 2-(3-arylsydnon-4-yl)benzothiazoles (**9e**–**h**) were obtained via the reaction of carbohydroximic acid chlorides **1** with *ortho*-substituted aromatic amines **7a** and **b**.

1. Introduction

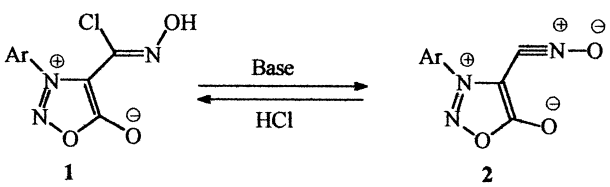
3-Arylsydnone-4-carbohydroximic acid chlorides (**1**) have been extensively studied since they were discovered in 1988.[1] They are versatile precusors for the syntheses of corresponding nitrile oxides **2** which can undergo various dipolar 1,3-cycloaddition and 1,3-addition reactions, leading to cyclic and open chain products, respectively.[2–8] Recently, we have reported the 1,3-dipolar cycloaddition of nitrile oxides **2** with electron-withdrawing or electron-donating substituted cycloalkenes[9] and explained the concerted mechanism based on the frontier molecular orbitals.[10,11] In this paper, the syntheses of 3-(3-arylsydnon-4-yl)-5-aryl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-diones (**4a**–**h**) and 6a-methyl-3-(3-arylsydnon-4-yl)-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-diones (**4i**–**l**) via the reaction of carbohydroximic acid chlorides **1** with various *N*-arylmaleimides (**3a**–**c**) in the presence of triethylamine are reported. The reaction is also a typical 1,3-dipolar cycloaddition of nitrile oxides **2**.

Many sydnone compounds have been found to exhibit pharmacological and biological activities.[12–17] Quinones have been used as plant growth regulators and parthenocarpy stimulants for tomatoes.[18] Treating compounds **1** with [1,4]naphthoquinone (**3d**) in the presence of triethylamine to obtain the desired fused ring heterocycles, should have significant results. Fortunately, the products 3-(3-arylsydnon-4-yl)-naphtho[2,3-*d*]isoxazole-4,9-diones (**6a**–**d**) were directly obtained. However, benzoxazoles, benzothiazoles and their derivatives are manufactured worldwide for several range of applications. They are used, among other things, as fungicides, herbicides or antialgal agents.[19] Benzothiazole is also found to be flavoring compound produced by the fungus, *Aspergillus claratus*.[20] Due to so many biological and pharmacological activities of benzoxazoles and benzothiazoles, focusing on the syntheses of sydnones by directly substituted with 4-benzothiazolyl or 4-benzoxazolyl group, is interesting.

2. Results and discussion

The compounds **1** are stable at room temperature and are easily converted into the corresponding carbonitrile oxides **2** in a polar solvent or basic aqueous solution (Scheme 1).[1]

In our previous work, the active nitrile oxides **2** generated in this way could undergo 1,3-dipolar cycloaddition with electron-withdrawing or electron-donating substituted cycloalkenes to give 4-isoxazolinyl sydnones.[9] In this paper, the reaction of carbohydroximic acid chlorides **1**



1 **2**

Scheme 1.

Keywords: nitrile oxides; benzoxazoles; benzothiazoles; 3-arylsydnone-4-carbohydroximic acid chlorides; 5-aryl-3-(3-arylsydnone-4-yl)-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-diones; 3-(arylsydnon-4-yl)naphtho-[2,3-*d*]isoxazole-4,9-diones.

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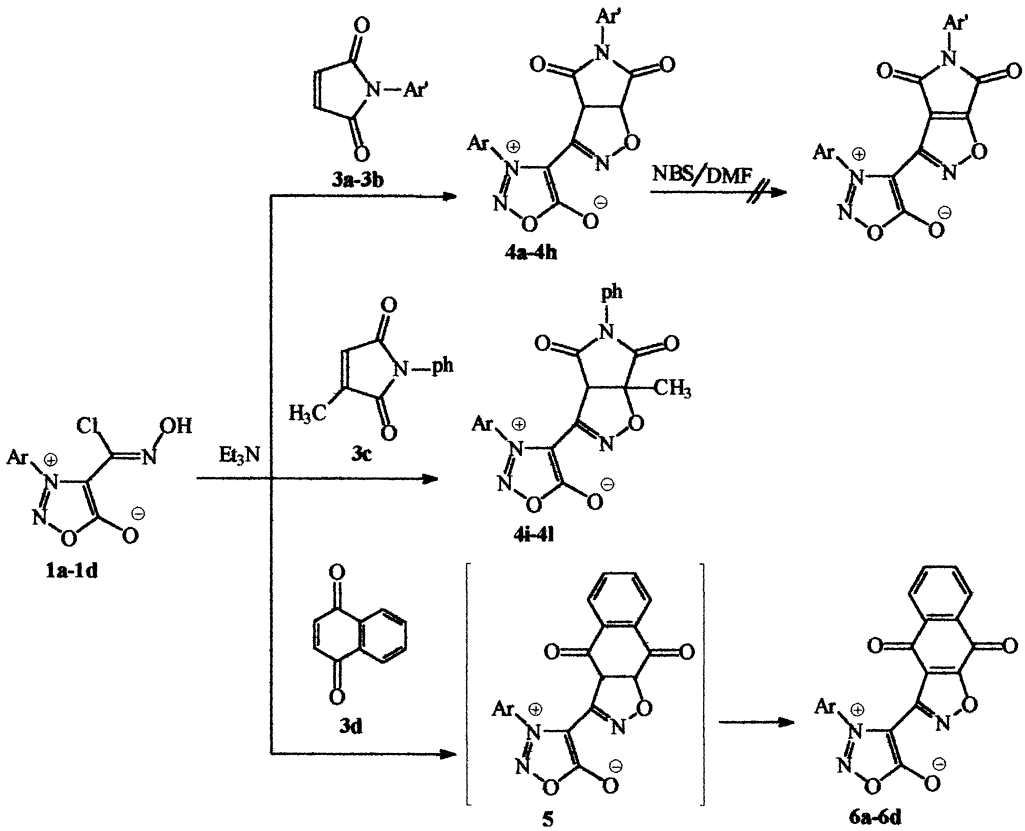


Scheme 2. **1a**: Ar=C_6H_5; **1b**: Ar=*p*-$CH_3C_6H_4$; **1c**: Ar=*p*-$CH_3OC_6H_4$; **1d**: Ar=*p*-$C_2H_5OC_6H_4$; **3a**: Ar′=C_6H_5; **3b**: Ar′=*p*-BrC_6H_4.

with some dipolarophiles such as *N*-arylmaleimides and [1,4]naphthoquinone was studied. Thus, treatment of **1** with *N*-arylmaleimides (**3a** and **b**) or 2-methyl-*N*-phenylmaleimide (**3c**) in the presence of triethylamine produced 3-(3-aryl-sydnon-4-yl)-5-aryl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-diones (**4a**–**h**) or 6a-methyl-3-(3-arylsydnon-4-yl)-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-diones (**4i**–**l**) in high yields (Scheme 2). Among these new products, the yellow crystal **4l** obtained was analytically pure and suitable for X-ray structure determination. Fig. 1 shows the ORTEP drawing of 6a-methyl-3-[3-(4′-ethoxyphenyl)sydnon-4-yl]-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]-isoxazole-4,6-dione (**4l**).

The experimental results indicated that the reaction of nitrile oxides **2** with various *N*-arylmaleimides (**3a**–**c**) is a typical 1,3-dipolar cycloaddition. Furthermore, the X-ray structure of **4l** has a *cis*-isoxazolinyl group, implying the concerted mechanism of 1,3-dipolar cycloaddition.[9–11] However, acid chlorides **1** reacted with [1,4]naphthoquinone (**3d**) to give 3-(3-arylsydnon-4-yl)-naphtho[2,3-*d*]isoxazole-4,9-diones (**6a**–**d**) directly, but not 1,3-dipolar cycloaddition adducts 3-(3-arylsydnon-4-yl)-naphtho[2,3-*d*]isoxazole-4,9-diols (**5**), as shown in Scheme 2. Although the compounds **5** were not found and isolated in the reaction, one might speculate that compounds **5** contain hydroquinone moiety, which is readily undergoing air oxidation to form the more stable

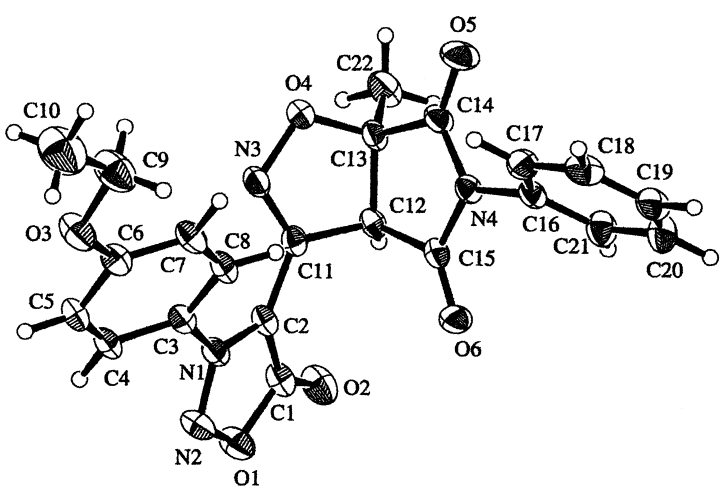


Figure 1. Crystal structure of compound **4l**.

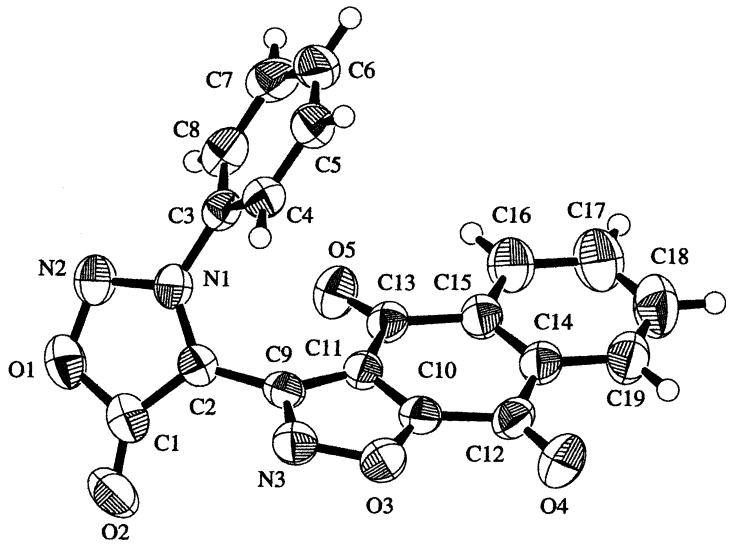
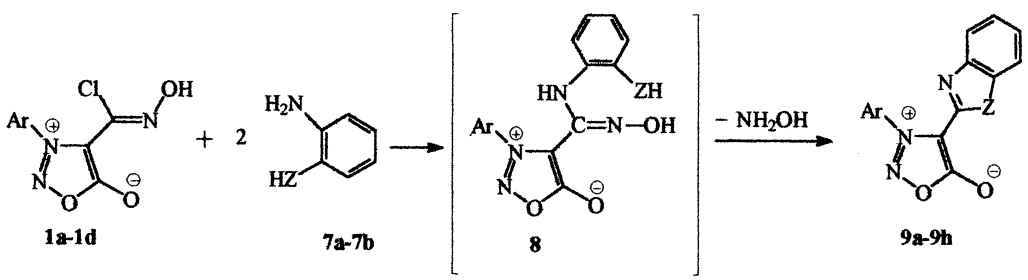


Figure 2. Crystal structure of compound **6a**.

compounds **6**. However, the isoxazolinyl compounds **4a–h** are relatively stable and could not converted into the corresponding isoxazoles by oxidation with *N*-bromosuccinimide (NBS).[21] The structure of compound **6a** was also verified by X-ray diffraction and is displayed in Fig. 2.

C-2-substituted benzoxazole and benzothiazole derivatives exhibit interesting antiviral, antibacterial and herbicidal activities[19,22] and can be widely applied in medicine.[23] Several synthetic methods are known for the syntheses of such derivatives. Benzoxazole and benzothiazole derivatives are generally prepared by the action of acid chlorides, aldehydes, nitriles and other compounds, with *o*-aminophenol and *o*-aminothiophenol, respectively, either by heating in a solvent or by thermal fusion in the presence or absence of an auxiliary base.[24–31] However, the various synthetic methods show varying degrees of success and different limitations, due to both the side reaction and difficulties with purification.

In this study, a useful and general methodology for new and efficient reactions of hydroxamoyl chlorides with aromatic amines had been established. First, 3-arylsydnone-4-carbohydroximic acid chlorides (**1**) were treated with the stoichiometric amount of *o*-aminophenol in ethanol, in the presence of triethylamine, to give the desired products. Triethylamine was used to scavenge the released hydrochloric acid which might protonate the amino group of the *o*-aminophenol and the reactivity of *o*-aminophenol was thus inhibited. However, the cyclization was unsuccessful in such condition. The polar and weakly basic solvent, *N*-methyl-2-pyrrolidinone (NMP) is well known for its good acceptance of strong protonic acid, such as HCl. Furthermore, the polarity of such solvent (ϵ=32 at 25°C) should facilitate the cyclization reaction.[27] However, treatment of carbohydroximic acid chlorides **1** with the stoichiometric amount of *o*-aminophenol using NMP as a reaction solvent, caused the reaction solution to darken and increased difficulty of purifying the recovered colored material. Treatment of 3-arylsydnone-4-carbohydroximic acid chlorides (**1a–d**) with 2 equiv. of *o*-aminophenol (**7a**) in dichloromethane–ethanol gave 2-(3-arylsydnon-4-yl)benzoxazoles (**9a–d**) in good yields (Scheme 3). An excess of *o*-aminophenol was used to trap the hydrogen chloride released during the reaction. 3-Arylsydnone-4-carbohydroximic acid chlorides (**1**) was added slowly to the solution of *o*-aminophenol at 0°C to minimize the dimerization of nitrile oxides **2**. The nucleophilic substitution of *o*-aminophenol with **1** was very rapid. The starting materials **1a–d** reacted completely to give intermediates **8** within 1 h by TLC survey. Then the reaction mixture was stirred or left standing at room temperature over 3–4 days for further cyclization. Experimental tests showed that adding 2–3 drops of sulfuric acid to the reaction solution at this stage would accelerate the cyclization to give the desired products. The crystals of benzoxazoles **9a–d** would automatically precipitate out in the solution and the isolation and purification of **9a–d** then become very easy. The benzoxazoles **9a–d** could be proved to be produced by the corresponding intermediates **8** after elimination of



Scheme 3. 1a: Ar=C_6H_5; **1b**: Ar=*p*-$CH_3C_6H_4$; **1c**: Ar=*p*-$CH_3OC_6H_4$; **1d**: Ar=*p*-$C_2H_5OC_6H_4$; **7a**: ZH=OH; **7b**: ZH=SH.

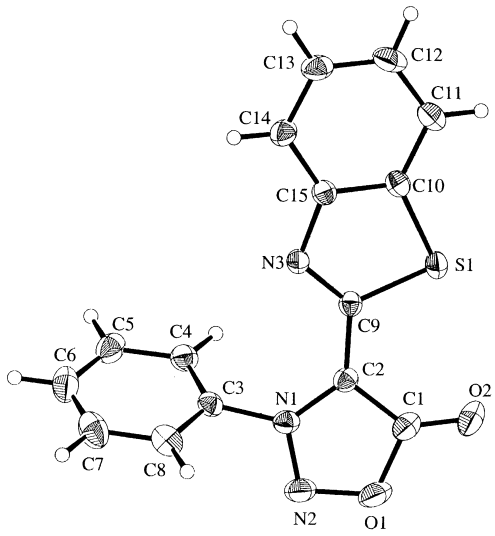


Figure 3. Crystal structure of compound **9e**.

hydroxylamine moiety (Scheme 3). The intermediates **8** would be precipitated out in situ and could be isolated due to using the less amount of solvent or changing the polarity of the reaction solvent. Therefore, the reaction of **1** with *o*-aminophenol should be conducted in much more solvent to prevent the intermediate **8** from precipitating out and to ensure a cyclization reaction step proceed successfully. The ^{1}H NMR spectra of isolated intermediates **8** taken at room temperature in the DMSO-d_6 solution revealed two singlet signals of OH protons, each of about δ=7.50 and 10.83 ppm, in addition to a singlet signal of NH proton at δ=9.60 ppm. Dissolved in CH_2Cl_2/EtOH and kept standing for several days, the isolated compounds **8** would cyclize automatically to the desired products **9**. Similar treatment of 3-arylsydnone-4-carbohydroximic acid chlorides (**1**) with 2 equiv. of *o*-aminothiophenol (**7b**) produced the corresponding benzothiazoles **9e–h** as described in Scheme 3. The structure of compound **9e** was also verified by X-ray diffraction and is displayed in Fig. 3. Details of complete lists of crystal data of compounds **4l**, **6a** and **9e** are given in Table 1.

3. Conclusions

In summary, the compounds **1** reacted with [1,4]naphthoquinone in the presence of triethylamine to give fused ring heterocycles **6a–d** directly, but not 1,3-dipolar cycloaddition adducts **5** which were not found and isolated in the reaction. One might speculate that compounds **5** contain hydroquinone moiety and are readily undergoing air oxidation to form the more stable compounds **6**. However, the acid chlorides **1** reacted with *N*-arylmaleimides (**3a** and **b**) or 2-methyl-*N*-phenylmaleimide (**3c**) to give the 1,3-dipolar cycloaddition products **4a–h** or **4i–l**, respectively. Based on the frontier molecular orbitals concept and X-ray structure of **4l** with a *cis*-isoxazolinyl group, the reaction mechanism of the 1,3-dipolar cycloaddition should be proved to be concerted again. Furthermore, the isoxazolinyl compounds **4a–h** are very stable and could not converted into the corresponding isoxazoles by oxidation with NBS. Besides that, C-2-substituted benzoxazole **9a–d** and benzothiazole derivatives **9e–h** were obtained in good yields via the reaction of carbohydroximic acid chlorides **1** with *ortho*-substituted aromatic amines **7a** and **b**. The fused ring heterocycles **9** were produced by the corresponding intermediates **8** after elimination of hydroxylamine moiety.

Table 1. Crystal data of compounds **4l**, **6a** and **9e**

Compound	**4l**	**6a**	**9e**
Diffractometer	Rigaku AFC7S	Rigaku AFC7S	Rigaku AFC7S
Formula	$C_{22}H_{18}N_4O_6$	$C_{19}H_9N_3O_5$	$C_{15}H_9N_3O_2S$
Formula weight	434.41	359.30	295.32
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	$P\bar{1}$ (#2)	$P2_1/n$ (#14)	$P2_1/n$ (#14)
a (Å)	8.312 (2)	14.417 (2)	11.130 (2)
b (Å)	12.110 (5)	6.991 (2)	5.997 (2)
c (Å)	12.566 (5)	17.152 (2)	19.756 (2)
α (°)	61.14 (3)		
β (°)	74.25 (3)	114.436 (9)	101.53 (1)
γ (°)	74.33 (3)		
V (Å^3)	1028.7 (8)	1574.0 (5)	1291.9 (5)
Z	2	4	4
D_{calc} (g cm^{-3})	1.402	1.516	1.518
F_{000}	452.00	736.00	608.00
μ (Mo K$_\alpha$) (cm^{-1})	0.98	1.06	2.46
Crystal size (mm^3)	0.38×0.40×0.82	0.58×0.76×0.80	0.38×0.62×0.80
Temperature (K)	298	298	298
Scan type	ω–2θ	ω–2θ	ω–2θ
2θ_{max} (°)	52.1	50.0	52.0
Reflections measured	4241	3147	2953
Unique reflections	4039	3020	2808
No. observations (I>3.00σ(I))	2003	2256	2097
No. variables	289	244	190
Residuals: R; Rw	0.048; 0.049	0.048; 0.061	0.037; 0.053
GoF	1.64	4.35	1.94

4. Experimental

4.1. General

All melting points were determined on a Yanaco MP-J3 micromelting point apparatus and are uncorrected. IR spectra were recorded on a MATTSON/SATELLITE 5000 FT-IR Spectrophotometer. Mass spectra were measured on a VG 70-250S GC/MS/MS spectrometer. ^{1}H NMR spectra were run on a Bruker AMX-200 NMR spectrometer, using TMS as internal standard. ^{13}C NMR spectra were carried out with complete ^{1}H decoupling and the assignments were made by additional DEPT experiments. Elemental analyses were taken with a Heraeus CHN–O-Rapid Analyzer. X-Ray spectra were performed on a Rigaku AFC7S diffractometer.

4.2. Starting materials

3-Phenylsydnone-4-carbohydroximic acid chloride (**1a**), 3-(4′-methylphenyl)sydnone-4-carbohydroximic acid chloride (**1b**), 3-(4′-methoxyphenyl)sydnone-4-cabohydroximic acid chloride (**1c**) and 3-(4′-ethoxyphenyl)sydnone-4-carbohydroximic acid chloride (**1d**) were prepared according to the literature.[1]

4.3. Syntheses of 3-(3-arylsydnon-4-yl)-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-diones (4a–d)

To an ice cooled solution of *N*-phenylmaleimide (86.6 mg, 0.50 mmol) in absolute ethanol (1.5 mL) and dichloromethane (0.5 mL), triethylamine (81.0 mg, 0.80 mmol) was added. The mixed basic solution was stirred at 0°C. Then 3-phenylsydnone-4-carbohydroximic acid chloride (120 mg, 0.50 mmol) was slowly added to the above basic solution over 0.5 h. After the addition was completed, stirring was continued at 0°C for additional 3–4 h. The precipitating solid was collected by filtration and then recrystallized from dichloromethane–ethanol to afford 133 mg (70%) of 3-(3-phenylsydnon-4-yl)-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (**4a**) as white crystalline. The chemical and physical spectral characteristics of these products are given below.

4.3.1. 3-(3-Phenylsydnon-4-yl)-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4a). White crystals from CH_2Cl_2/EtOH; yield 70%; mp 180–181°C; IR (KBr) 3070, 2980, 1758, 1728, 1596, 1497, 1380, 1194 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 5.03 (d, J=9.7 Hz, 1H), 5.59 (d, J=9.7 Hz, 1H), 7.23–7.28 (m, 2H), 7.43–7.51 (m, 3H), 7.67–7.83 (m, 5H); ^{13}C NMR (DMSO-d_6) δ 54.82, 80.79, 98.74, 125.76, 127.02, 129.08, 129.23, 129.98, 131.58, 132.84, 134.32, 142.00, 164.95, 169.96, 171.36; FABMS$^+$ m/z (%): 377 (M^++H, 100), 318 (M^+−NO−CO, 88). Anal. calcd for $C_{19}H_{12}N_4O_5$: C, 60.64; H, 3.21; N, 14.89. Found: C, 60.35; H, 3.27; N, 14.67.

4.3.2. 3-[3-(4′-Methylphenyl)sydnon-4-yl]-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4b). White crystals from CH_2Cl_2/EtOH; yield 73%; mp 227–228°C; IR (KBr) 3064, 2981, 2940, 2923, 1744, 1728, 1492, 1379, 1198 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.42 (s, 3H), 5.00 (d, J=9.7 Hz, 1H), 5.59 (d, J=9.7 Hz, 1H), 7.22–7.27 (m, 2H), 7.30–7.51 (m, 5H), 7.67 (d, J=8.4 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 21.08, 54.85, 80.77, 98.62, 125.48, 127.01, 129.08, 129.24, 130.37, 131.56, 131.84, 142.03, 143.16, 164.93, 169.97, 171.38; FABMS$^+$ m/z (%): 391 (M^++H, 100), 332 (M^+−NO−CO, 30). Anal. calcd for $C_{20}H_{14}N_4O_5$: C, 61.54; H, 3.62; N, 14.35. Found: C, 61.37; H, 3.67; N, 14.26.

4.3.3. 3-[3-(4′-Methoxyphenyl)sydnon-4-yl]-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4c). White powder from CH_2Cl_2/EtOH; yield 60%; mp 201–203°C; IR (KBr) 3079, 2987, 2938, 2844, 1757, 1729, 1603, 1512, 1493, 1381, 1263, 1200 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.85 (s, 3H), 5.00 (d, J=9.7 Hz, 1H), 5.59 (d, J=9.7 Hz, 1H), 7.19 (d, J=9.0 Hz, 2H), 7.23–7.27 (m, 2H), 7.43–7.54 (m, 3H), 7.73 (d, J=9.0 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 54.84, 56.00, 80.70, 98.72, 114.98, 126.84, 127.02, 127.35, 129.08, 129.23, 131.57, 142.09, 162.24, 164.96, 169.97, 171.39; FABMS$^+$ m/z (%): 407 (M^++H, 100), 348 (M^+−NO−CO, 51). Anal. calcd for $C_{20}H_{14}N_4O_6$: C, 59.12; H, 3.47; N, 13.79. Found: C, 58.85; H, 3.49; N, 13.67.

4.3.4. 3-[3-(4′-Ethoxyphenyl)sydnon-4-yl]-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4d). White powder from CH_2Cl_2/EtOH; yield 60%; mp 234–235°C; IR (KBr) 3076, 2986, 2932, 1767, 1728, 1602, 1512, 1497, 1392, 1260, 1227, 1212 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.36 (t, J=7.0 Hz, 3H), 4.13 (q, J=7.0 Hz, 2H), 4.99 (d, J=9.8 Hz, 1H), 5.59 (d, J=9.8 Hz, 1H), 7.17 (d, J=9.0 Hz, 2H), 7.21–7.28 (m, 2H), 7.44–7.54 (m, 3H), 7.72 (d, J=9.0 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 14.61, 54.82, 64.09, 80.69, 98.69, 115.30, 126.64, 126.99, 127.32, 129.05, 129.21, 131.55, 142.08, 161.55, 164.93, 169.95, 171.37; FABMS$^+$ m/z (%): 421 (M^++H, 100), 362 (M^+−NO−CO, 49). Anal. calcd for $C_{21}H_{16}N_4O_6$: C, 60.00; H, 3.84; N, 13.33. Found: C, 59.78; H, 3.84; N, 13.22.

4.4. Syntheses of 5-(4-bromophenyl)-3-(3-arylsydnon-4-yl)-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-diones (4e–h)

5-(4-Bromophenyl)-3-(3-phenylsydnon-4-yl)-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (**4e**) were synthesized in 70% yield (160 mg, 0.35 mmol) by the reaction of 3-phenylsydnone-4-carbohydroximic acid chlorides (**1a**, 120 mg, 0.50 mmol) with *N*-(4-bromophenyl)maleimide (**3b**, 126 mg, 0.50 mmol) in a manner similar to that for compound **4a** as mentioned above. Properties and analytical data of these compounds **4e–h** are given below.

4.4.1. 5-(4-Bromophenyl)-3-(3-phenylsydnon-4-yl)-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4e). Pale yellow needles from CH_2Cl_2/EtOH; yield 70%; mp 239–240°C; IR (KBr) 3098, 3073, 2964, 1758, 1716, 1586, 1490, 1385, 1226, 1185 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 5.04 (d, J=9.6 Hz, 1H), 5.59 (d, J=9.6 Hz, 1H), 7.25 (d, J=8.7 Hz, 2H), 7.64–7.83 (m, 7H); ^{13}C NMR (DMSO-d_6) δ 54.82, 80.71, 98.72, 122.11, 125.79, 129.14, 129.95, 130.86, 132.25, 132.83, 134.33, 141.83, 164.92, 169.60, 171.11; FABMS$^+$ m/z (%): 457 (M^++2+H, 100), 455 (M^++H, 96). Anal. calcd for $C_{19}H_{11}N_4O_5Br$: C, 50.13; H, 2.44; N, 12.31. Found: C, 49.87; H, 2.53; N, 12.13.

4.4.2. 5-(4-Bromophenyl)-3-[3-(4′-methylyphenyl)sydnon-4-yl]-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4f). White needles from CH_2Cl_2/EtOH; yield 72%;

mp 219–220°C; IR (KBr) 3093, 3074, 2961, 2913, 1767, 1726, 1509, 1488, 1392, 1212 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.44 (s, 3H), 5.01 (d, J=9.7 Hz, 1H), 5.59 (d, J=9.7 Hz, 1H), 7.24 (d, J=8.7 Hz, 2H), 7.47 (d, J=8.2 Hz, 2H), 7.67 (d, J=8.2 Hz, 2H), 7.71 (d, J=8.7 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 21.06, 54.83, 80.68, 98.59, 122.08, 125.49, 129.11, 130.31, 130.83, 131.83, 132.24, 141.86, 143.12, 164.89, 169.62, 171.11; FABMS$^+$ m/z (%): 471 (M^++2+H, 99), 469 (M^++H, 100), 412 (M^++2−NO−CO, 31), 410 (M^+−NO−CO, 31). Anal. calcd for $C_{20}H_{13}N_4O_5Br$: C, 51.19; H, 2.79; N, 11.94. Found: C, 50.94; H, 2.86; N, 11.79.

4.4.3. 5-(4-Bromophenyl)-3-[3-(4′-methoxyphenyl)sydnon-4-yl]-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4g). White needles from CH_2Cl_2/EtOH; yield 72%; mp 225–227°C; IR (KBr) 3116, 2976, 2848, 1750, 1727, 1513, 1490, 1365, 1262, 1180 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.85 (s, 3H), 5.00 (d, J=9.7 Hz, 1H), 5.59 (d, J=9.7 Hz, 1H), 7.18 (d, J=9.1 Hz, 2H), 7.25 (d, J=8.7 Hz, 2H), 7.71 (d, J=8.7 Hz, 2H) 7.74 (d, J=9.1 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 54.83, 55.98, 80.62, 98.68, 114.93, 122.08, 126.83, 127.35, 129.11, 130.85, 132.23, 141.92, 162.21, 164.92, 169.62, 171.12; FABMS$^+$ m/z (%): 487 (M^++2+H, 97), 485 (M^++H, 100). Anal. calcd for $C_{20}H_{13}N_4O_6Br$: C, 49.50; H, 2.70; N, 11.55. Found: C, 49.28; H, 2.74; N, 11.45.

4.4.4. 5-(4-Bromophenyl)-3-[3-(4′-ethoxyphenyl)sydnon-4-yl]-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4h). Yellow crystals from CH_2Cl_2/EtOH; yield 56%; mp 235–237°C; IR (KBr) 3094, 2980, 2926, 1767, 1726, 1605, 1511, 1489, 1380, 1258, 1217 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.34 (t, J=7.0 Hz, 3H), 4.11 (q, J=7.0 Hz, 2H), 4.99 (d, J=9.7 Hz, 1H), 5.58 (d, J=9.7 Hz, 1H), 7.15 (d, J=8.8 Hz, 2H), 7.24 (d, J=8.8 Hz, 2H), 7.71 (d, J=8.8 Hz, 4H); ^{13}C NMR (DMSO-d_6) δ 14.62, 54.83, 64.09, 80.62, 98.68, 115.27, 122.08, 126.65, 127.34, 129.11, 130.85, 132.24, 141.92, 161.53, 164.92, 169.62, 171.12; FABMS$^+$ m/z (%): 501 (M^++2+H, 100), 499 (M^++H, 100), 442 (M^++2−NO−CO, 39), 440 (M^+−NO−CO, 39). Anal. calcd for $C_{21}H_{15}N_4O_6Br$: C, 50.52; H, 3.03; N, 11.22. Found: C, 50.22; H, 3.14; N, 10.98.

4.5. Syntheses of 6a-methyl-3-(3-arylsydnon-4-yl)-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-diones (4i–l)

6a-Methyl-3-(3-phenylsydnon-4-yl)-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (**4i**) were synthesized in 58% yield (113 mg, 0.29 mmol) by the reaction of 3-phenylsydnone-4-carbohydroximic acid chlorides (**1a**, 120 mg, 0.50 mmol) with 2-methyl-*N*-phenylmaleimide (**3c**, 93.6 mg, 0.50 mmol) in a procedure similar to that for compound **4a** as mentioned above. Properties and analytical data of these compounds **4i–l** are given below.

4.5.1. 6a-Methyl-3-(3-phenylsydnon-4-yl)-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4i). Yellow needles from CH_2Cl_2/EtOH; yield 58%; mp 202–203°C; IR (KBr) 3070, 2986, 2932, 1767, 1725, 1494, 1479, 1389, 1245, 1218 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.64 (s, 3H), 4.90 (s, 1H), 7.26–7.82 (m, 10H); ^{13}C NMR (DMSO-d_6) δ 17.62, 58.23, 87.79, 99.14, 125.76, 127.04, 129.14, 129.26, 130.00, 131.63, 132.87, 134.44, 142.00, 165.12, 169.24, 172.46; FABMS$^+$ m/z (%): 391 (M^++H, 100), 332 (M^+−NO−CO, 40). Anal. calcd for $C_{20}H_{14}N_4O_5$: C, 61.54; H, 3.62; N, 14.35. Found: C, 61.28; H, 3.62; N, 14.30.

4.5.2. 6a-Methyl-3-[3-(4′-methylphenyl)sydnon-4-yl]-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4j). White plates from CH_2Cl_2/EtOH; yield 67%; mp 215–216°C; IR (KBr) 3064, 2974, 2926, 1758, 1722, 1503, 1491, 1386, 1239, 1209 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.64 (s, 3H), 2.42 (s, 3H), 4.88 (s, 1H), 7.23–7.51 (m, 7H), 7.67 (d, J=8.4 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 17.63, 21.12, 58.26, 87.78, 99.02, 125.47, 127.03, 129.15, 129.28, 130.37, 131.62, 131.97, 142.04, 143.17, 165.13, 169.28, 172.49; FABMS$^+$ m/z (%): 405 (M^++H, 100), 346 (M^+−NO−CO, 26). Anal. calcd for $C_{21}H_{16}N_4O_5$: C, 62.37; H, 3.99; N, 13.85. Found: C, 62.11; H, 3.99; N, 13.77.

4.5.3. 6a-Methyl-3-[3-(4′-methoxyphenyl)sydnon-4-yl]-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4k). White crystals from CH_2Cl_2/EtOH; yield 62%; mp 208–209°C; IR (KBr) 3052, 2952, 1757, 1723, 1509, 1492, 1387, 1253, 1226 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.64 (s, 3H), 3.85 (s, 2H), 4.87 (s, 1H), 7.18 (d, J=9.1 Hz, 2H), 7.25–7.51 (m, 5H), 7.73 (d, J=9.1 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 17.62, 56.02, 58.26, 87.69, 99.11, 114.97, 126.91, 127.01, 127.32, 129.12, 129.24, 131.62, 142.09, 162.25, 165.12, 169.24, 172.47; FABMS$^+$ m/z (%): 421 (M^++H, 100), 362 (M^+−NO−CO, 37). Anal. calcd for $C_{21}H_{16}N_4O_6$: C, 60.00; H, 3.84; N, 13.33. Found: C, 59.94; H, 3.90; N, 13.23.

4.5.4. 6a-Methyl-3-[3-(4′-ethoxyphenyl)sydnon-4-yl]-5-phenyl-3a,6a-dihydro-pyrrolo[3,4-*d*]isoxazole-4,6-dione (4l). Yellow crystals from CH_2Cl_2/EtOH; yield 60%; mp 204–205°C; IR (KBr) 3074, 2977, 2940, 1753, 1726, 1511, 1475, 1381, 1258, 1244 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.35 (t, J=6.9 Hz, 3H), 1.64 (s, 3H), 4.12 (q, J=6.9 Hz, 2H), 4.86 (s, 1H), 7.16 (d, J=9.1 Hz, 2H), 7.25–7.54 (m, 5H), 7.71 (d, J=9.1 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 14.86, 17.84, 58.49, 64.33, 87.90, 99.31, 115.51, 126.97, 127.22, 127.52, 129.33, 129.45, 131.82, 142.30, 161.76, 165.33, 169.45, 172.68; FABMS$^+$ m/z (%): 435 (M^++H, 100), 376 (M^+−NO−CO, 37). Anal. calcd for $C_{22}H_{18}N_4O_6$: C, 60.83; H, 4.17; N, 12.90. Found: C, 60.64; H, 4.12; N, 12.82. X-Ray analytical data are listed in Table 1. Further details have been deposited at the Cambridge Crystallographic Data Center and allocated the deposition number CCDC 191966.

4.6. Syntheses of 3-(3-arylsydnon-4-yl)-naphtho[2,3-*d*]-isoxazole-4,9-diones (6a–d)

To an ice cooled solution of 1,4-naphthoquinone (87.0 mg, 0.55 mmol) in 2 mL of absolute ethanol/dichloromethane (1:1), triethylamine (81.0 mg, 0.80 mmol) was added. The mixed basic solution was stirred at 0°C. Then an ice-cooled solution of 3-phenylsydnone-4-carbohydroximic acid chloride (120 mg, 0.50 mmol) in absolute ethanol (2 mL) was slowly added to the above basic solution over 0.5 h. After the addition was completed, stirring was continued at 0°C for additional 3–4 h. The reaction mixture was

concentrated, the precipitating solid was collected by filtration, washed with 95% ethanol and a practically pure solid (131 mg) was obtained. The solid could be recrystallized from dichloromethane/ethanol to afford 3-(3-penylsydnon-4-yl)-naphtho[2,3-*d*]isoxazole-4,9-dione (**6a**) as yellow crystals (119 mg, 66%). The chemical and physical spectral characteristics of these products are given below.

4.6.1. 3-(3-Phenylsydnon-4-yl)-naphtho[2,3-*d*]isoxazole-4,9-dione (6a). Yellow crystals from CH_2Cl_2/EtOH; yield 66%; mp 203–204°C; IR (KBr) 3082, 1767, 1749, 1692, 1596, 1332, 1203, 921 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.57–7.75 (m, 5H), 7.89–7.97 (m, 3H), 8.12–8.15 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 95.49, 119.75, 124.64, 126.65, 127.01, 130.15, 132.39, 132.79, 132.97, 133.93, 134.82, 135.31, 147.29, 164.75, 166.86, 172.72, 177.20; FABMS$^+$ *m/z* (%): 360 (M^++H, 100), 301 (M^+−NO−CO, 23). Anal. calcd for $C_{19}H_9N_3O_5$: C, 63.52; H, 2.52; N, 11.69. Found: C, 63.22; H, 2.60; N, 11.54. X-Ray analytical data are listed in Table 1. Further details have been deposited at the Cambridge Crystallographic Data Center and allocated the deposition number CCDC 191967.

4.6.2. 3-[3-(4′-Methylphenyl)sydnon-4-yl]-naphtho[2,3-*d*]-isoxazole-4,9-dione (6b). Pale yellow needles from CH_2Cl_2/EtOH; yield 68%; mp 193–194°C; IR (KBr) 3076, 2920, 1755, 1692, 1599, 1326, 1206, 921 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.34 (s, 3H), 7.38 (d, J=8.4 Hz, 2H), 7.60 (d, J=8.4 Hz, 2H), 7.90–7.99 (m, 3H), 8.13–8.18 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 20.98, 95.33, 119.89, 124.40, 126.71, 127.04, 130.54, 131.57, 132.42, 133.03, 134.83, 135.33, 143.15, 147.39, 164.80, 166.85, 172.74, 177.25; FABMS$^+$ *m/z* (%): 374 (M^++H, 100), 315 (M^+−NO−CO, 21). Anal. calcd for $C_{20}H_{11}N_3O_5$: C, 64.35; H, 2.97; N, 11.26. Found: C, 64.30; H, 3.04; N, 11.28.

4.6.3. 3-[3-(4′-Methoxyphenyl)sydnon-4-yl]-naphtho-[2,3-*d*]isoxazole-4,9-dione (6c). Yellow crystals from CH_2Cl_2/EtOH; yield 70%; mp 194–196°C; IR (KBr) 3016, 2986, 2938, 1752, 1692, 1602, 1323, 1260, 1206, 918 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.79 (s, 3H), 7.09 (d, J=9.1 Hz, 2H), 7.66 (d, J=9.1 Hz, 2H), 7.90–8.03 (m, 3H), 8.13–8.18 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 55.95, 95.32, 115.15, 119.88, 126.25, 126.60, 126.70, 127.02, 132.39, 133.01, 134.81, 135.32, 147.45, 162.14, 164.80, 166.82, 172.74, 177.24; FABMS$^+$ *m/z* (%): 390 (M^++H, 100), 331 (M^+−NO−CO, 23). Anal. calcd for $C_{20}H_{11}N_3O_6$: C, 61.70; H, 2.85; N, 10.79. Found: C, 61.66; H, 2.92; N, 10.63.

4.6.4. 3-[3-(4′-Ethoxyphenyl)sydnon-4-yl]-naphtho[2,3-*d*]-isoxazole-4,9-dione (6d). Yellow crystals from CH_2Cl_2/EtOH; yield 72%; mp 218–220°C; IR (KBr) 3076, 2986, 2926, 1755, 1683, 1602, 1329, 1263, 1203, 921 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.28 (t, J=7.0 Hz, 3H), 4.04 (q, J=7.0 Hz, 2H), 7.05 (d, J=9.0 Hz, 2H), 7.63 (d, J=9.0 Hz, 2H), 7.89–7.99 (m, 3H), 8.12–8.16 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 14.52, 64.07, 95.32, 115.52, 119.87, 126.26, 126.45, 126.70, 127.05, 132.44, 133.04, 134.84, 135.33, 147.46, 161.45, 164.81, 166.86, 172.76, 177.26; FABMS$^+$ *m/z* (%): 404 (M^++H, 100), 345 (M^+−NO−CO, 33). Anal. calcd for $C_{21}H_{13}N_3O_6$: C, 62.53; H, 3.25; N, 10.42. Found: C, 62.59; H, 3.24; N, 10.36.

4.7. Syntheses of 2-(3-arylsydnon-4-yl)benzoxazoles (9a–d)

To an ice cooled solution of *o*-aminophenol (109 mg, 1.00 mmol) in 6 mL of absolute ethanol/dichloromethane (2:1), 3-phenylsydnone-4-carbohydroximic acid chloride (**1a**, 120 mg, 0.50 mmol) was gradually added. The reaction solution was kept stirring at 0°C for additional 1 h, and then two drops of sulfuric acid (98%) was added. The resulting mixture was further stirred for another 2 h and then allowed to stand at room temperature for 3–4 days. The resulting solid was collected, washed with ethanol, and recrystallized from dichloromethane/ethanol to afford 2-(3-phenylsydnon-4-yl)benzoxazole (**9a**, 91.0 mg, 65%). The chemical and physical spectral characteristics of these products are given below.

4.7.1. 2-(3-Phenylsydnon-4-yl)benzoxazole (9a). Yellow crystals from CH_2Cl_2/EtOH; yield 65%; mp 234–236°C; IR (KBr) 3064, 1773, 1625, 1581, 1452, 1239, 1044 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.33–7.38 (m, 2H), 7.59–7.66 (m, 2H), 7.71–7.78 (m, 3H), 7.87–7.92 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 99.83, 111.08, 120.09, 125.59, 125.90, 126.21, 129.99, 133.01, 134.96, 140.85, 149.37, 151.92, 164.64; EIMS (30 eV) *m/z* (%): 279 (M^+, 24), 221 (M^+−NO−CO, 100), 77 ($C_6H_5^+$, 90). Anal. calcd for $C_{15}H_9N_3O_3$: C, 64.52; H, 3.25; N, 15.05. Found: C, 64.40; H, 3.16; N, 15.02.

4.7.2. 2-[3-(4′-Methylphenyl)sydnon-4-yl]benzoxazole (9b). Yellow needles from CH_2Cl_2/EtOH; yield 64%; mp 217–218°C; IR (KBr) 3070, 2920, 1776, 1620, 1575, 1455, 1278, 1020 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.47 (s, 3H), 7.30–7.41 (m, 2H), 7.50 (d, J=8.4 Hz, 2H), 7.61–7.68 (m, 2H), 7.76 (d, J=8.4 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 21.15, 99.36, 110.84, 119.83, 125.30, 125.64, 125.95, 130.07, 132.26, 140.61, 142.88, 149.11, 151.69, 164.42; EIMS (30 eV) *m/z* (%): 293 (M^+, 13), 235 (M^+−NO−CO, 100). Anal. calcd for $C_{16}H_{11}N_3O_3$: C, 65.53; H, 3.78; N, 14.33. Found: C, 65.42; H, 3.82; N, 14.26.

4.7.3. 2-[3-(4′-Methoxyphenyl)sydnon-4-yl]benzoxazole (9c). Yellow needles from CH_2Cl_2/EtOH; yield 80%; mp 229–230°C; IR (KBr) 3070, 2980, 2938, 1791, 1605, 1575, 1455, 1263, 1038 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.89 (s, 3H), 7.22 (d, J=8.9 Hz, 2H), 7.33–7.39 (m, 2H), 7.62–7.69 (m, 2H), 7.82 (d, J=8.9 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 56.00, 99.46, 110.87, 114.75, 119.85, 125.32, 125.94, 127.32, 127.48, 140.66, 149.13, 151.81, 162.18, 164.47; EIMS (30 eV) *m/z* (%): 309 (M^+, 7), 251 (M^+−NO−CO, 100). Anal. calcd for $C_{16}H_{11}N_3O_4$: C, 62.14; H, 3.58; N, 13.59. Found: C, 62.11; H, 3.55; N, 13.48.

4.7.4. 2-[3-(4′-Ethoxyphenyl)sydnon-4-yl]benzoxazole (9d). Yellow needles from CH_2Cl_2/EtOH; yield 76%; mp 187–188°C; IR (KBr) 3076, 2980, 2926, 1800, 1620, 1575, 1455, 1248, 1044 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.38 (t, J=7.0 Hz, 3H), 4.16 (q, J=7.0 Hz, 2H), 7.19 (d, J=9.0 Hz, 2H), 7.33–7.39 (m, 2H), 7.62–7.68 (m, 2H), 7.81 (d, J=9.0 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 14.67, 64.09, 99.75, 110.87, 115.11, 119.87, 125.34, 125.97, 127.17, 127.48, 140.67, 149.15, 151.83, 161.50, 164.49; EIMS (30 eV) *m/z* (%): 323 (M^+, 20), 265 (M^+−NO−CO, 100). Anal. calcd for $C_{17}H_{13}N_3O_4$: C, 63.16; H, 4.05; N, 13.00. Found: C, 63.11; H, 4.12; N, 12.89.

4.8. Syntheses of 2-(3-arylsydnon-4-yl)benzothiazoles (9e–h)

Typical procedures for the syntheses of sydnone derivatives **9e–h** were as follows: 2-(3-phenylsydnon-4-yl)benzothiazole (**9e**) was synthesized in 86% yield (128 mg, 0.43 mmol) from 3-phenylsydnone-4-carbohydroximic acid chloride (**1a**, 120 mg, 0.50 mmol) and *o*-aminothiophenol (125 mg, 1.00 mmol) in the presence of sulfuric acid catalyst by a procedure similar to that for compound **9a**. The chemical and physical spectral characteristics of these products are given below.

4.8.1. 2-(3-Phenylsydnon-4-yl)benzothiazole (9e). Yellow plates from CH_2Cl_2/EtOH; yield 86%; mp 180–181°C; IR (KBr) 3058, 1749, 1598, 1534, 1443, 1272, 978 cm^{-1};^{1}H NMR (DMSO-d_6) δ 7.36–7.45 (m, 2H), 7.59–7.92 (m, 6H), 8.10–8.14 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 105.08, 122.33, 122.56, 125.68, 126.33, 126.89, 129.58, 132.59, 133.28, 134.77, 151.66, 152.28, 165.88; EIMS (30 eV) *m/z* (%): 295 (M^+, 15), 237 (M^+-58, 100), 77 ($C_6H_5^+$, 40). Anal. calcd for $C_{15}H_9N_3O_2S$: C, 61.01; H, 3.07; N, 14.23; S, 10.86. Found: C, 61.00; H, 3.16; N, 14.18; S, 10.78. X-Ray analytical data are listed in Table 1. Further details have been deposited at the Cambridge Crystallographic Data Center and allocated the deposition number CCDC 191970.

4.8.2. 2-[3-(4′-Methylphenyl)sydnon-4-yl]benzothiazole (9f). Yellow needles from CH_2Cl_2/EtOH; yield 52%; mp 190–191°C; IR (KBr) 3064, 2920, 1758, 1533, 1446, 1257, 978 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.49 (s, 3H), 7.39–7.46 (m, 2H), 7.51 (d, J=8.4 Hz, 2H), 7.65–7.69 (m, 1H), 7.77 (d, J=8.4 Hz, 2H), 8.10–8.14 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 21.22, 104.90, 122.28, 122.60, 125.64, 126.05, 126.84, 129.93, 132.26, 133.28, 142.75, 151.71, 152.29, 165.86; EIMS (30 eV) *m/z* (%): 309 (M^+, 36), 251 ($M^+-NO-CO$, 100), 91 ($CH_3C_6H_4^+$, 66). Anal. calcd for $C_{16}H_{11}N_3O_2S$: C, 62.12; H, 3.58; N, 13.58; S, 10.36. Found: C, 62.03; H, 3.61; N, 13.52; S, 10.42.

4.8.3. 2-[3-(4′-Methoxyphenyl)sydnon-4yl]benzothiazole (9g). Light green rod from CH_2Cl_2/EtOH; yield 82%; mp 175–176°C; IR (KBr) 3076, 2926, 1773, 1611, 1533, 1515, 1452, 1251, 972 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.88 (s, 3H), 7.21 (d, J=9.0 Hz, 2H), 7.25–7.44 (m, 2H), 7.66–7.71 (m, 1H), 7.81 (d, J=9.0 Hz, 2H), 8.07–8.12 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 55.98, 104.95, 114.58, 122.22, 122.61, 125.59, 126.80, 127.21, 127.86, 133.25, 151.80, 152.29, 162.14, 165.81; EIMS (30 eV) *m/z* (%): 325 (M^+, 12), 267 ($M^+-NO-CO$, 100). Anal. calcd for $C_{16}H_{11}N_3O_3S$: C, 59.07; H, 3.41; N, 12.92; S, 9.85. Found: C, 58.91; H, 3.45; N, 12.87; S, 9.88.

4.8.4. 2-[3-(4′-Ethoxyphenyl)sydnon-4-yl]benzothiazole (9h). Yellow needles from CH_2Cl_2/EtOH; yield 65%; mp 187–188°C; IR (KBr) 3062, 2988, 1774, 1606, 1536, 1510, 1448, 1256, 976 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.39 (t, J=7.0 Hz, 3H), 4.17 (q, J=7.0 Hz, 2H), 7.20 (d, J=8.9 Hz, 2H), 7.36–7.49 (m, 2H), 7.68–7.72 (m, 1H), 7.81 (d, J=8.9 Hz, 2H), 8.09–8.13 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 14.67, 64.07, 104.99, 114.98, 122.27, 122.63, 125.63, 126.84, 127.07, 127.89, 133.28, 151.83, 152.32, 161.47, 165.84; EIMS (30 eV) *m/z* (%): 339 (M^+, 20), 281 ($M^+-NO-CO$, 100). Anal. calcd for $C_{17}H_{13}N_3O_3S$: C, 60.17; H, 3.86; N, 12.38; S, 9.45. Found: C, 60.24; H, 3.87; N, 12.34; S, 9.50.

4.9. Isolation of intermediates (2-hydroxyphenylamino)-(3-arylsydnon-4-yl)methanone oximes (8b–d)

Typical procedures for the isolation of intermediates **8b–d** were as follows. To an ice cooled solution of *o*-aminophenol (109 mg, 1.00 mmol) in 3 mL absolute ethanol, 3-(4′-methylphenyl)sydnone-4-carbohydroximic acid chloride (127 mg, 0.50 mmol) was slowly added over 0.5 h. After the addition was completed, stirring was continued at 0°C for additional 1 h. The resulting solid was collected by filtration and washed with ice water, ethanol to afford 115 mg (70%) of (2-hydroxyphenylamino)-[3-(4′-methylphenyl)sydnon-4-yl]methanone oxime (**8b**). The chemical and physical spectral characteristics of these products are given below.

4.9.1. (2-Hydroxyphenylamino)-[3-(4′-methylphenyl)-sydnon-4-yl]methanone oxime (8b). Pale yellow powder; yield 70%; mp 172–173°C; IR (KBr) 3401, 3335, 1735, 1639, 1600, 1515, 1454, 1330, 952 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.37 (s, 3H), 6.49–6.84 (m, 4H), 7.29–7.44 (m, 4H), 7.52 (s, 1H), 9.61 (s, 1H), 10.83 (s, 1H); FABMS$^+$ *m/z* (%): 327 (M^++H, 100); HRMS (FAB) calcd for $C_{16}H_{14}N_4O_4$: 327.1093. Found: 327.1095.

4.9.2. (2-Hydroxyphenylamino)-[3-(4′-methoxyphenyl)-sydnon-4-yl]methanone oxime (8c). Pale yellow powder; yield 75%; mp 170–171°C; IR (KBr) 3324, 3286, 1736, 1639, 1624, 1599, 1255 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.81 (s, 3H), 6.49–6.83 (m, 4H), 7.06 (d, J=9.1 Hz, 2H), 7.35 (d, J=9.1 Hz, 2H), 7.49 (s, 1H), 9.59 (s, 1H), 10.83 (s, 1H); FABMS$^+$ *m/z* (%): 343 (M^++H, 100); HRMS (FAB) calcd for $C_{16}H_{14}N_4O_5$: 343.1042. Found: 343.1047.

4.9.3. (2-Hydroxyphenylamino)-[3-(4′-ethoxyphenyl)-sydnon-4-yl]methanone oxime (8d). Yellow powder; yield 78%; mp 172–173°C; IR (KBr) 3397, 3299, 1737, 1725, 1639, 1604, 1511, 1257, 952 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.33 (t, J=7.0 Hz, 3H), 4.08 (q, J=7.0 Hz, 2H), 6.42–6.84 (m, 4H), 7.03 (d, J=9.0 Hz, 2H), 7.33 (d, J=9.0 Hz, 2H), 7.50 (s, 1H), 9.59 (s, 1H), 10.83 (s, 1H); FABMS$^+$ *m/z* (%): 357 (M^++H, 100); HRMS (FAB) calcd for $C_{17}H_{16}N_4O_5$: 357.1199. Found: 357.1197.

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