Synthesis of Sydnone Compounds Having Alternating Carbon-Nitrogen Chain and Heterocyclic Groups at the 4-Position[1)]

Toshio FUCHIGAMI,* Mou-Yung YEH,† Takushi GOTO,
Tsutomu NONAKA,* and Hsien-Ju TIEN†
Department of Electronic Chemistry, Graduate School at Nagatsuta, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227
†*Department of Chemistry, National Cheng Kung University, Tainan, Taiwan, Republic of China*
(Received July 11, 1983)

Entirely new type sydnones having alternating carbon-nitrogen chain groups such as 3-aryl-4-(arylcarbonimidoylcarbamoyl)sydnones, 3-aryl-4-(dimethylaminomethylenecarbamoyl)sydnones, and 4-(dimethylaminomethylenethiocarbamoyl)-3-phenylsydnone were prepared in high yields from 3-aryl-4-chloroformylsydnone, 3-aryl-4-carbamoylsydnone, and 3-phenyl-4-thiocarbamoylsydnone, respectively. The cyclization of the alternating carbon-nitrogen chain groups provided new sydnone derivatives having heterocyclic substituents such as 1,2,4-oxadiazol-5-yl, 1,2,4-triazol-3-yl, and 1,2,4-thiadiazol-5-yl groups in good yields.

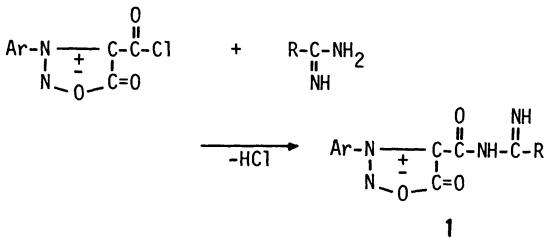
Sydnone is a typical mesoionic compound and its chemical and physical properties are very unique.[2,3)] Recently, many sydnone derivatives have been found to have biological and pharmacological activities.[2,4)] In addition, alternating carbon-nitrogen chain and nitrogen-containing heterocyclic compounds are also well known to show similar activities.

It therefore should be significant to establish some methods for synthesizing sydnone compounds having alternating carbon-nitrogen chain and heterocyclic groups as their substituents. However, a sydnone ring is so sensitive to acids, alkalies, and heat that reaction conditions for the preparation of sydnone compounds seem to be limited in cases. One of excellent methods for preparing alternating carbon-nitrogen chain compounds is to start from amino compounds but 4-aminosydnone compounds have been unknown, though some attempts had been done.[5)] Both amidines and imidates are also useful as precusors for the alternating carbon-nitrogen chain compounds, but their preparations have been unsuccesfully tried in the case of sydnone compounds.[6)]

In this work, the synthesis of sydnones attached to a carbon atom of the alternating carbon-nitrogen groups was aimed.

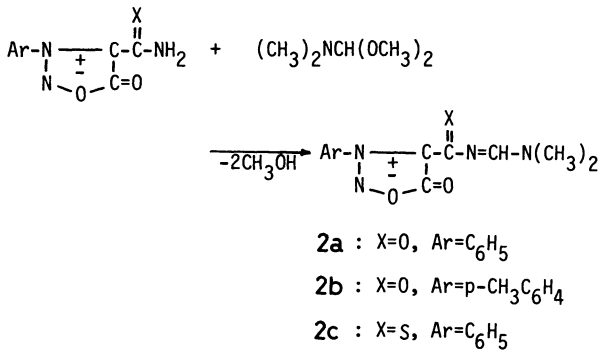
Results and Discussion

Synthesis of Sydnone Compounds Having Alternating Carbon-Nitrogen Chain Groups. 3-Aryl-4-(arylcarbonimidoylcarbamoyl)sydnones (1): Using a method similar to the preparation of *N*-acylamidines,[7,8)] the reaction of amidine hydrochloride with 3-aryl-4-chloroformylsydnone was carried out in aqueous solution in the presence of sodium hydroxide at room temperature. However, the yield was very low because of low solubility of the chloride and its instability in an alkaline solution. It was found that **1** could be prepared in good yields by changing the solvent and base into DMF and two equiv of triethylamine, respectively. Table 1 summarizes synthetic results of **1**.



Scheme 1.

*3-Aryl-4-(dimethylaminomethylenecarbamoyl)sydnones (**2a**, **2b**) and 3-Aryl-4-(dimethylaminomethylenethiocarbamoyl)sydnone (**2c**)*: Recently Lin *et al.*[8)] found that amides reacted readily with *N*,*N*-dimethylalkanamide dimethyl acetal to give N^2-acyl-N^1,N^1-dimethylamidines in good yields. Using this new amination method, **2a** and **2b** were prepared quantitatively by heating 3-aryl-4-carbamoylsydnone in large excess amount of *N*,*N*-dimethylformamide dimethyl acetal. In a similar manner, **2c** was also obtained quantitatively from 3-phenyl-4-thiocarbamolsydnone at room temperature. Physical properties and spectral data of **2** are summarized in Table 2.



Scheme 2.

Cyclization of Sydnone Compounds Having Alternating Carbon-Nitrogen Chain Groups. The alternating carbon-nitrogen chains of the sydnone compounds synthesized above could be converted into the corresponding heterocyclic groups without any decomposition of their sydnone rings.

*Synthesis of Sydnone Derivatives Having 1,2,4-Oxadiazol-5-yl Groups (**3**) from **1***: We previously developed a novel synthesis of 1,2,4-oxadiazoles from *N*-haloamidino compounds.[7,8)] In this work, this synthetic reaction could be successfully extended to the

TABLE 1. SYNTHESIS OF 3-ARYL-4-(ARYLCARBONIMIDOYLCARBAMOYL) SYDNONES (1)

	Compd 1		Yield	Mp	MS	IR (KBr)		
	Ar	R	%	θ_m/°C	(*m/e*)	ν_{NH}/cm^{-1}	$\nu_{C=O}$/cm^{-1}	$\nu_{C=N}$/cm^{-1}
1a	C_6H_5	C_6H_5	74	198—199	—[a]	3380 3280	1780, 1765 1630	1600
1b	C_6H_5	*p*-$NO_2C_6H_4$	60	193—193.5	353 (M^+)	3370 3200	1765 1625	1580
1c	*p*-$CH_3C_6H_4$	C_6H_5	74	185.5—186	322 (M^+)	3390 3295	1765 1630	1600
1d	*p*-$CH_3C_6H_4$	*p*-$NO_2C_6H_4$	71	193—194.5	366 (M^+)	3400 3225	1755 1625	1625 1590
1e	C_6H_5		48	228.5—229	—[a]	3400 3270	1780, 1765 1610	1570

a) No molecular ion was observed.

TABLE 2. PHYSICAL PROPERTIES AND SPECTRAL DATA OF 2

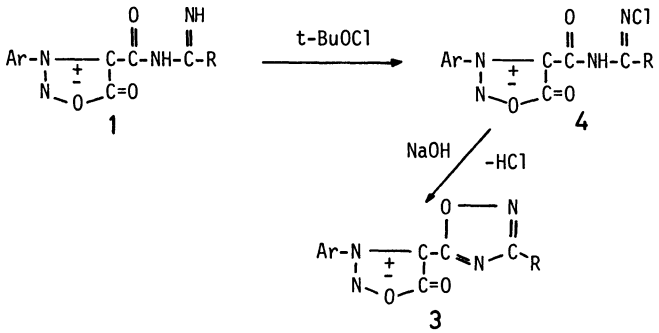
Sydnone compd	Yield	Mp	MS	^{1}H NMR (DMSO-d_6) δ			
	%	θ_m/°C	(*m/e*)	$(CH_3)_2N$	Ar-H	$CH_3C_6H_4$	-N=CH-
2a	100	192—193.5	260 (M^+)	2.60 (s, 3H) 3.10 (s, 3H)	7.72 (s, 5H)	—	8.43 (s, 1H)
2b	97	175—176	274 (M^+)	2.64 (s, 3H) 3.13 (s, 3H)	7.41 (d, 2H) 7.63 (d, 2H)	2.47 (s, 3H)	8.40 (s, 1H)
2c	100	146.5—147	—[a]	2.67 (s, 3H) 3.03 (s, 3H)	7.53 (s, 5H)	—	8.32 (s, 1H)

a) No molecular ion was observed.

TABLE 3. SYNTHETIC RESULTS OF SYDNONE COMPOUNDS (3) FROM 1

	Sydnone compd		Yield	Mp	IR (KBr)	
	Ar	R	%	θ_m/°C	ν_{ring}/cm^{-1}	$\nu_{C=O}$/cm^{-1}
3a	C_6H_5	C_6H_5	75	168.5—170	1600	1790
3b	C_6H_5	*p*-$NO_2C_6H_4$	92	204.5—205.5	1620 1600	1795
3c	*p*-$CH_3C_6H_4$	C_6H_5	89	169—171	1600	1790
3d	*p*-$CH_3C_6H_4$	*p*-$NO_2C_6H_4$	89	192—192.5	1610	1800
3e	C_6H_5		0	—	—	—

conversion of **1** into **3**, as shown in Scheme 3. The cyclization was found to proceed in DMF only when accurately equivalent amounts of both *t*-butyl hypochlorite and sodium hydroxide were used. When either reagent was used in excess, no sydnone derivatives having 1,2,4-oxadiazol-5-yl group (**3**) were obtained because the sydnone ring is very unstable to oxidation and alkali. In this reaction, attempts to isolate *N*-chloro intermediate (**4**) failed because of its instability. As shown in Table 3, **3** was thus prepared from **1** in excellent yields except for **3e**.



Scheme 3.

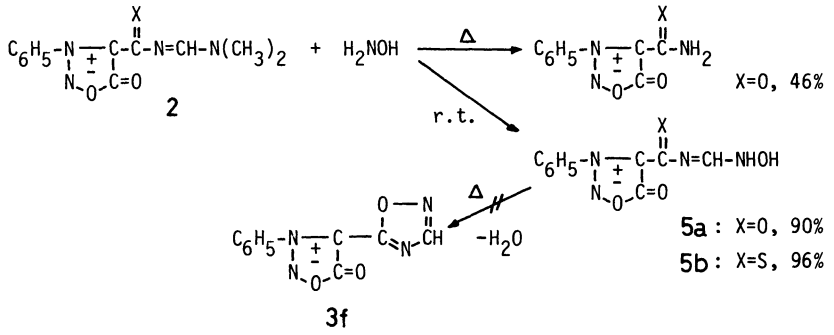
The cyclization seems to proceed *via* a nitrene intermediate as proposed previously by us.[7,8,10]

Attempts to Synthesize Sydnone Derivatives (3) Having 1,2,4-Oxadiazol-5-yl Group from 2: Recently Lin *et al.*[9] have reported a facile synthesis of 1,2,4-oxadiazoles and 1,2,4-triazoles by the reaction of N^2-acyl-N^1,N^1-dimethylamidines with hydroxylamine and hydrazine. Using their procedure, the cyclization of **2** to the corresponding (1,2,4-oxadiazol-5-yl)sydnone was attempted. However, when heated **2a** with hydroxylamine in an aq acetic acid solution, 4-carbamoylsydnone was formed instead of desired **3f**.

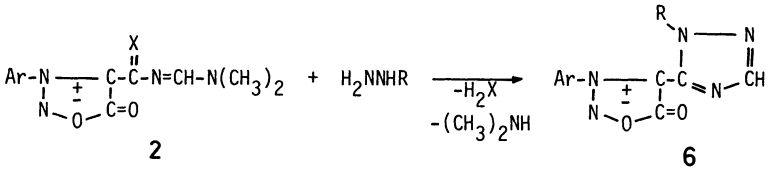
On the other hand this reaction was carried out at room temperature to give an open-chain intermediate (**5a**) in 90% yield. The cyclization was attempted by heating **5a** at 100 °C for 1 h in acetic acid, at 90 °C for 1 h in a mixed solution of acetic acid and dioxane (1 : 1), and for 2 h in boiling toluene, respectively. However all our

attempts failed and the starting material was recovered. The reaction seemed quite different from that of ordinary *N*-acylamidines with hydroxylamine. In a manner similar to the preparation of **5a**, **5b** was obtained in a high yield. When **5b** was heated in acetic acid at 90 °C, evolution of hydrogen sulfide was observed. However, **3b** expected could not be isolated.

Synthesis of Sydnone Derivatives (6) Having 1,2,4-Triazol-5-yl Groups from 2: Sydnone compounds (**6**) could be obtained in good yields by heating **2** and hydrazine hydrate in acetic acid at 90—100 °C for 1 h, as shown in Table 4.



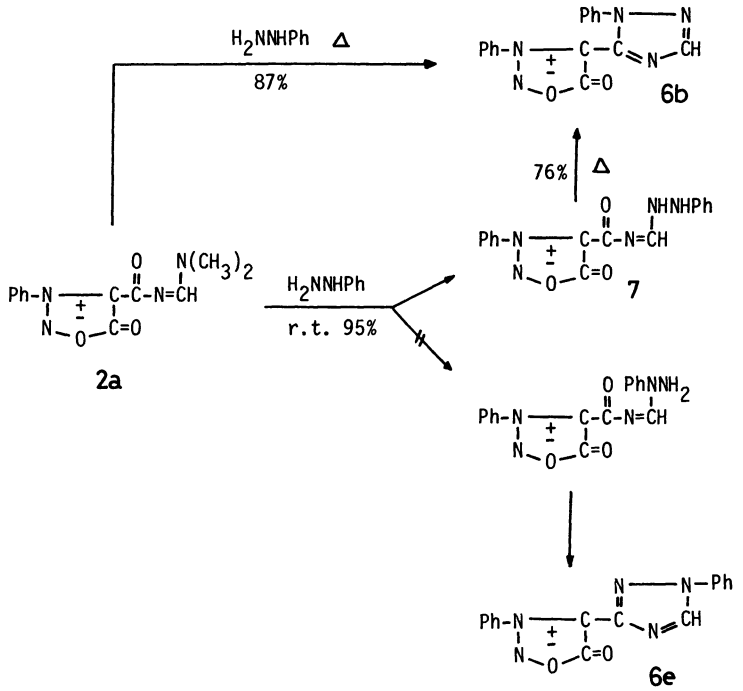
Scheme 4.



Scheme 5.

Table 4. Synthesis of sydnone compounds (**6**) from **2**

	Sydnone		Hydrazine	Product	Yield	Mp	IR (KBr)
	Ar	X	R		%	θ_m/°C	$\nu_{C=N}$/cm^{-1}
2a	C_6H_5	O	H	**6a**	85	268—269	1565
2c	C_6H_5	S	H	**6a**	88	268—269	1565
2a	C_6H_5	O	C_6H_5	**6b**	87	161—162.5	1560
2b	*p*-$CH_3C_6H_4$	O	H	**6c**	88	278—279	1570
2b	*p*-$CH_3C_6H_4$	O	C_6H_5	**6d**	82	193—194	1570

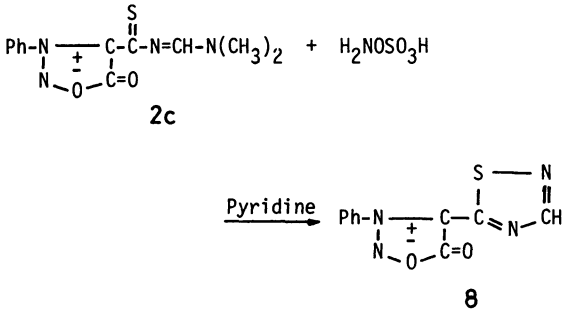


Scheme 6.

Since **2c** provided **6a** in an approximately same yield as **2a**, no remarkable difference in the reactivity was observed between the carbonyl and thiocarbonyl groups of **2**.

A sole product, **6b** was obtained in a good yield by heating **2** and phenylhydrazine although two possible products (**6b** and **6e**) were expected to be formed as shown in Scheme 6. The structure of **6b** was established by the NMR spectral study of an open-chain intermediate (**7**) which was obtained by the same reaction at room temperature. The proton NMR spectrum (DMSO-d_6) of the intermediate shows two doublets (C<u>H</u> and N<u>H</u>) at 8.25 and 9.55 ppm and one singlet (N<u>H</u>C_6H_5) at 9.81 ppm. The latter two signals disappeared while the former did not and changed to singlet by addition of deuterium oxide. On this bases, the structure of the open-chain intermediate was identified as **7**. When heated, **7** cyclized to give **6b**.

Synthesis of a Sydnone Derivative (8) Having 1,2,4-Thiadiazol-5-yl Group from 4-(Dimethylaminomethylenethiocarbonyl)-3-phenylsydnone (2c). Most recently, N^2-arylthiocarbonyl-N^1,N^1-dimethylamidines have been found to be transformed to 1,2,4-thiadiazoles by treatment with hydroxylamine-*O*-sulfonic acid in the presence of pyridine.[11] Using this new cyclization method, the transformation of **2c** to **8** was attempted. According to recommendation of the literature,[11] the reaction of **2c** was first run in a dichloromethane-ethanol mixture at room temperature, but the desired **8** was not formed and the starting **2c** was almost completely recovered. The reaction then was run under refluxing conditions to afford the formation **8** in a low yield as 35%. In this case, the starting **2c** still remained unreacted and 3-phenyl-4-thiocarbamoylsydnone was found to be formed. These results indicate that the thiocarbonyl group of **2c** is fairly less reactive than that of ordinary aromatic compounds.



Scheme 7.

The new types of sydnone compounds thus prepared are expected to be pharmacologically active and screening tests of several biological activities of these sydnones are currently under investigation.

Experimental

^{1}H NMR spectra were recorded at 60 MHz on a Hitachi R24B spectrometer using DMSO-d_6 and Me_4Si as solvent and an internal standard, respectively. IR spectra were obtained on a Hitachi 295 infrared spectrometer. Electron impact mass spectra were determined at 30 eV on a JEOL JMS-D100 mass spectrometer by direct introduction *via* solid probe.

3-Phenyl-4-thiocarbamoylsydnone was prepared as follows: Hydrogen sulfide was passed into the solution of 4-cyano-3-phenylsydnone (2.20 g, 11.8 mmol) and triethylamine (1.44 g, 14.3 mmol) in 50 ml of ethanol at 0 °C for 1 h. The precipitating yellow solid was collected by filtration and washed with ether. The yield was 1.23 g (47%); mp 161 °C. Recrystallization from ethanol provided 0.96 g (37%) of the pure thiocarbamoylsydnone as orange-yellow needles; mp 161 °C (decomp). (Ref,[12] 133 °C).

4-Benzimidoylcarbamoyl-3-phenylsydnone (1a). To a stirred solution of benzamidine hydrochloride (0.44 g, 2.3 mmol) and triethylamine (0.73 g, 7.2 mmol) in 10 ml of DMF, gradually added a solution of 4-chloroformyl-3-phenylsydnone[13] (0.50 g 2.2 mmol) in 2 ml of DMF at 0 °C. After addition, the reaction mixture was stirred for 1.5 h at room temperature and was poured into about 100 ml of ice-water. The precipitates were collected by filtration. The yield was 0.51 g; mp 192—194 °C (decomp). Recrystallization from methanol provided 0.40 g (58%) of pure **1a** as a white solid. ^{1}H NMR δ=7.12—7.97 (m, 10H, C_6<u>H</u>$_5$), 9.36 (br s, 1H, N<u>H</u>), and 9.89 (br s, 1H, N<u>H</u>). Found: C, 62.28; H, 3.65; N, 18.04%. Calcd for $C_{16}H_{12}N_4O_3$: C, 62.34; H, 3.92; N, 18.17%.

4-(p-Nitrobenzimidoyl)-3-phenylsydnone (1b). Using the same procedure, the crude product was obtained; mp 169.5 —171.5 °C (decomp). Recrystallization from methanol provided pure **1b** (38%) as white needles. ^{1}H NMR δ=7.78—8.65 (m, 9H, Ar-<u>H</u>) and 10.05 (br s, 2H, N<u>H</u>). Found: C, 54.24; H, 3.49; N, 19.68%. Calcd for $C_{16}H_{11}N_5O_5$: C, 54.40; H, 3.14: N, 19.82%.

4-Benzimidoylcarbamoyl-3-(p-tolyl)sydhone (1c). Using the same procedure, the crude product was obtained from benzamidine and 4-chloroformyl-3-(*p*-tolyl)sydnone:[3e] mp 184—185 °C (decomp). Recrystallization from methanol provided pure **1c** (45%) as white needles. ^{1}H NMR δ=2.48 (s, 3H, C<u>H</u>$_3$), 7.40—7.80 (m, 9H, Ar-<u>H</u>), 9.42 (br s, 1H, N<u>H</u>), and 9.85 (br s, 1H, N<u>H</u>). Found: C, 63.13; H, 4.44; N, 17.08%. Calcd for $C_{17}H_{14}N_4O_3$: C, 63.35; H, 4.38; N, 17.38%.

4-(p-Nitrobenzimidoylcarbamoyl)-3-(p-tolyl)sydnone (1d). By the similar procedure, pure **1d** was obtained as white needles after recrystallization from methanol. ^{1}H NMR δ=2.30 (s, 3H, C<u>H</u>$_3$), 7.36 (d, 2H, J=8.4 Hz, Ar-<u>H</u>), 7.72 (d, 2H, J=8.4 Hz, Ar-<u>H</u>), 7.95 (d, 2H, J=11.4 Hz, Ar-<u>H</u>), 8.28 (d, 2H, J=11.4 Hz, Ar-<u>H</u>), and 9.75 (br s, 2H, N<u>H</u>). Found: C, 55.90; H, 3.46; N, 19.08%. Calcd for $C_{17}H_{13}N_5O_5$: C, 55.59; H, 3.57; N, 19.07%.

3-Phenyl-4-(piperidinocarbonimidoylcarbamoyl)sydnone (1e). By the similar method, pure **1e** was obtained as white needles after recrystallization from aq methanol. ^{1}H NMR δ=1.38 (br s, 6H, C<u>H</u>$_2$), 3.13 (br s, 4H, C<u>H</u>$_2$), 7.62 (s, 5H, C_6H_5), and 8.27 (br s, 2H, N<u>H</u>). Found: C, 57.27; H, 5.37; N, 22.30%. Calcd for $C_{15}H_{17}N_5O_3$: C, 57.14; H, 5.43; N, 22.21%.

4-(Dimethylaminomethylenecarbamoyl)-3-phenylsydnone (2a). A suspension of 4-carbamoyl-3-phenylsydnone[13] (4.07 g, 19.9 mmol) in *N*,*N*-dimethylformamide dimethyl acetal (4.68 g, 37.3 mmol) was heated at 110—120 °C for 1 h. After evaporation under reduced pressure, 5.16 g of a white solid was obtained. Recrystallization from ethanol provided 4.08 g (79%) of pure **2a** as white prisms. Found: C, 55.43; H, 4.49; N, 21.76%. Calcd for $C_{12}H_{12}N_4O_3$: C, 55.38; H, 4.65; N, 21.53%.

4-(Dimethylaminomethylenecarbamoyl)-3-(p-tolyl)sydnone (2b). Using the same procedure, the crude product was obtained; mp 175—176 °C. Recrystallization from ethanol provided pure **2b** as white prisms. Found: C, 56.67; H, 4.78; N, 20.15%. Calcd for $C_{13}H_{14}N_4O_3$: C, 56.93; H, 5.15; N, 20.43%.

4-(Dimethylaminomethylenethiocarbamoyl)-3-phenylsydnone (2c). A suspension of 3-phenyl-4-thiocarbamoylsydnone (1.00 g, 4.52 mmol) in *N*,*N*-dimethylformamide dimethyl acetal (0.68 g, 5.4 mmol) was allowed to stand at room

temperature for 1 h. Evaporation under reduced pressure provided 1.25 g of a reddish solid, mp 147 °C (decomp). Recrystallization from methanol gave 0.94 g (75%) of pure **2c** as reddish prisms. Found: C, 52.49; H, 4.45; N, 20.36; S, 11.56%. Calcd for $C_{12}H_{12}N_4O_2S$: C, 52.16; H, 4.38; N, 20.28; S, 11.60%.

*3-Phenyl-4-(3-phenyl-1,2,4-oxadiazol-5-yl)sydnone (**3a**).* To a stirred solution of **1a** (0.50 g, 1.61 mmol) in 20 ml of DMF was gradually added a solution of *t*-butyl hypochlorite (0.17 g, 1.60 mmol) in 5 ml of DMF at 0 °C. The color of the solution gradually changed to yellow. After the mixture had been stirred at the same temperature for 1 h, 1.6 ml of 1 M sodium hydroxide was added and the solution was stirred for additional 1 h. After the mixture had been warmed at 70—80 °C for 30 min, it was poured into about 100 ml of ice-water. After cooling the precipitates were separated by filtration and washed with water. The yield was 0.37 g, mp 163—166 °C (decomp). Recrystallization from dichloromethane-hexane provided pure **3a** as white needles. ^{1}H NMR δ=7.78—8.33 (m, 10H, C_6H_5). *m/e* 306 (M^+) and 248 (M^+—NO—CO). Found: C, 62.73; H, 3.02; N, 18.12%. Calcd for $C_{16}H_{10}N_4O_3$: C, 62.75; H, 3.29; N, 18.29%.

*4-[3-(p-Nitrophenyl)-1,2,4-oxadiazol-5-yl]-3-phenylsydnone (**3b**).* By the same procedure, the crude product was obtained; mp 205—206 °C (decomp). Recrystallization from dichloromethane-ether provided pure **3b** as white needles. ^{1}H NMR δ=7.85—8.53 (m, 9H, Ar-H). *m/e* 351 (M^+) and 293 (M^+—NO—CO). Found: C, 54.61; H, 2.47; N, 19.89%. Calcd for $C_{16}H_9N_5O_5$: C, 54.71; H, 2.58; N, 19.94%.

*4-(3-Phenyl-1,2,4-oxadiazol-5-yl)-3-(p-tolyl)sydnone (**3c**).* By the same procedure, the crude product was obtained; mp 159—163 °C (decomp). Recrystallization from dichloromethane-hexane provided pure **3c** as white needles in 60% yield. ^{1}H NMR δ=2.53 (s, 3H, CH_3), 7.52—7.95 (m, 9H, Ar-H). *m/e* 320 (M^+) and 262 (M^+—NO—CO). Found: C, 63.49; H, 3.68; N, 17.23%. Calcd for $C_{17}H_{12}N_4O_3$: C, 63.75; H, 3.78; N, 17.49%.

*4-[3-(p-Nitrophenyl)-1,2,4-oxadiazol-5-yl]-3-(p-tolyl)sydnone (**3d**).* By the same procedure, the crude product was obtained; mp 186—186.5 °C (decomp). Recrystallization from dichloromethane-ether provided pure **3d** as white needles. ^{1}H NMR δ=2.30 (s, 3H, CH_3), 7.63 (d, 2H, J=9.0 Hz, Ar-H), 7.93 (d, 2H, J=9.0 Hz, Ar-H), 8.15 (d, 2H, J=9.0 Hz, Ar-H), and 8.48 (d, 2H, J=9.0 Hz, Ar-H). *m/e* 365 (M^+) and 307 (M^+—NO—CO). Found: C, 55.82; H, 2.79; N, 19.04%. Calcd for $C_{17}H_{11}N_5O_5$: C, 55.90; H, 3.04; N, 19.17%.

*4-Hydroxyaminomethylenecarbamoyl-3-phenylsydnone (**5a**).* To a stirred solution of 0.30 g (4.3 mmol) of hydroxylamine hydrochloride, 10 ml of acetic acid, and 4.4 ml of 1 M sodium hydroxide was added **2a** (1.10 g, 4.2 mmol) and the mixture was stirred at room temperature for 1 h. The yellow precipitates were separated by filtration and washed with water. The yield was 0.94 g (90%), mp 180.5—182 °C (decomp). Recrystallization from ethanol provided pure **5a**; mp 180.5—182 °C (decomp). IR (KBr) 1775, 1695 (C=O), and 1660 cm^{-1} (C=N). ^{1}H NMR δ=7.61 (d, 1H, J=10.2 Hz, Ar-CH), and 7.75 (s, 5H, C_6H_5), 10.14 (d, 1H, J=10.2 Hz, NH), and 11.11 (s, 1H, OH). *m/e* 248 (M^+) and 190 (M^+—NO—CO). Found: C, 48.65; H, 3.18; N, 22.32%. Calcd for $C_{10}H_8N_4O_4$: C, 48.39; H, 3.25; N, 22.57%.

*4-Hydroxyaminomethylenethiocarbamoyl-3-phenylsydnone (**5b**).* The mixture of hydroxylamine hydrochloride (0.27 g, 3.9 mmol) and **2c** (1.00 g, 3.6 mmol) in 10 ml of acetic acid and 3.6 ml of 1 M sodium hydroxide was stirred at room temperature for 1 h. The resulting solid was separated by filtration and washed with ethanol to provide 0.79 g (83%) of a crude product, mp 142—145 °C (decomp). After addition of about 100 ml of water to the filtrate, the resulting precipitates were collected by filtration and washed with ethanol to provide the additional product, 0.12 g (13%); mp 141—143 °C (decomp). Recrystallization from aq acetone provided pure **5b** as orange needles; mp 142—144 °C (decomp). IR (KBr) 1755 (C=O), and 1655 cm^{-1} (C=N). ^{1}H NMR δ=7.68 (s, 5H, C_6H_5), 8.14 (d, 1H, J=8.4 Hz, CH), 11.55 (s, 1H, OH), and 11.78 (d, 1H, J=8.4 Hz, NH). *m/e* 264 (M^+), 246 (M^+—H_2S—NO—CO). Found: C, 45.85; H, 3.20; N, 21.02%; S, 12.15%. Calcd for $C_{10}H_8N_4O_3S$: C, 45.45; H, 3.05; N, 21.20; S, 12.13%.

*3-Phenyl-4-(1,2,4-triazol-3-yl)sydnone (**6a**). Synthesis of **6a** from **2a**:* The mixture of **2a** (1.00 g, 3.8 mmol) and hydrazine hydrate (0.20 g, 3.9 mmol) in 10 ml of acetic acid was heated at 90—100 °C for 1 h. After cooling, water was added to the reaction mixture. The precipitates were separated by fitration and washed with water. The yield was 0.75 g; mp 269—269.5 °C (decomp). Recrystallization from ethanol provided pure **6a** as white needles. IR (KBr) 1760 cm^{-1} (C=O). ^{1}H NMR δ=7.71 (s, 5H, C_6H_5), 8.52 (s, 1H, triazole C-H), and 14.36 (br s, 1H, NH). *m/e* 229 (M^+) and 171 (M^+—NO—CO). Found: C, 52.62; H, 2.85; N, 30.42%. Calcd for $C_{10}H_7N_5O_2$: C, 52.40; H, 3.80; N, 30.56%.

*Synthesis of **6a** from **2c***: The mixture of hydrazine hydrate (0.60 g, 1.1 mmol) and **2c** (0.30 g, 1.1 mmol) in 2 ml of acetic acid was heated at 90—100 °C for 1 h. After cooling about 50 ml of water was added to the reaction mixture. The needle precipitates were separated by filtration and washed with ethanol. The yield of **6a** was 0.22 g

*3-Phenyl-4-(1-phenyl-1,2,4-triazol-5-yl)sydnone (**6b**).* To a stirred solution of phenylhydrazine (0.13 g, 1.2 mmol) in 3 ml of acetic acid was added **2a** (0.30 g, 1.2 mmol). The color of the mixture changed to red and precipitates began to appear. Then, the mixture was heated at 90—100 °C for 1 h. The color gradually changed to yellow. About 100 ml of water was added to the reaction mixture and the resulting precipitates were separated and washed with ethanol. The yield was 0.31 g; mp 160.5—162 °C. Recrystallization from ethanol provided pure **6b** as pale yellow needles. IR (KBr) 1790 and 1780 cm^{-1} (C=O). ^{1}H NMR δ=7.56 (s, 5H, C_6H_5), 7.66 (s, 5H, C_6H_5), and 8.39 (s, 1H, triazole C-H). *m/e* 305 (M^+) and 247 (M^+—NO—CO). Found:, 63.20; H, 3.50; N, 23.20%. Calcd for $C_{16}H_{11}N_5O_2$: C, 62.95; H, 3.63; N, 22.94%.

*3-(p-Tolyl)-4-(1,2,4-triazol-3-yl)sydnone (**6c**).* Using the same procedure, the crude product was obtained; mp 278—279.5 °C (decomp). Recrystallization from ethanol provided pure **6c** as white needles. IR (KBr) 1775 cm^{-1} (C=O). ^{1}H NMR δ=2.45 (s, 3H, CH_3), 7.51 (d, 2H, J=9.0 Hz, tolyl CH), 7.74 (d, 2H, J=9.0 Hz, tolyl C-H), 8.70 (s, 1H, CH), and 14.74 (br s, 1H, NH). Found: C, 54.37; H, 3.57; N, 28.77%. Calcd for $C_{11}H_9N_5O_2$: C, 54.32; H, 3.73; N, 28.79%.

*4-(1-Phenyl-1,2,4-triazol-5-yl)-3-(p-tolyl)sydnone (**6d**).* Using the same prcedure, the crude product was obtained; mp 185—187 °C. Recrystallization from ethanol provided pure **6d** as white needles. IR (KBr) 1785 cm^{-1} (C=O). ^{1}H NMR δ=2.43 (s, 3H, CH_3), 7.48, 7.58 (two s, 9H, Ar-H), and 8.41 (s, 1H, triazol C-H). *m/e* 319 (M^+) and 261 (M^+—NO—CO) Found: C, 64.16; H, 3.98; N, 21.76%. Calcd for $C_{17}H_{13}N_5O_2$: C, 63.94; H, 4.10; N, 21.93%.

*3-Phenyl-4-(phenylhydrazinomethylenecarbamoyl)sydnone (**7**).* The mixture of phenylhydrazine (0.13 g, 1.2 mmol) and **2a** (0.30 g, 1.2 mmol) in 3 ml of acetic acid was allowed to stand at room temperature for 5 min. The resulting precipitates were separated by filtration and washed with ethanol. The yield was 0.34 g (90%); mp 182.5—184.5 °C. Recrystallization from acetone-hexane provided pure **7** as orange needles; mp 183—184.5 °C. IR (KBr) 1760 and 1675 cm^{-1} (C=O). ^{1}H NMR δ=6.56—7.30 (m, 5H, C_6H_5), 7.75 (s, 5H, C_6H_5) 8.25 (d, 1H, J=8.4 Hz, CH), 9.55 (d, 1H, J=8.4 Hz, NH), and 9.81 (s, 1H, NHC_6H_5). *m/e* 323 (M^+), 305 (M^+—H_2O) and 247 (M^+—H_2O—NO—CO). Found: C, 59.43; H, 3.99; N, 21.81%.

Calcd for $C_{16}H_{13}N_5O_3$: C, 59.44; H, 4.05; N, 21.66%.

Cyclization of **7** *to* ***6b***. A mixture of **7** (84 mg, 0.26 mmol) in 1 ml of acetic acid was heated at 90—100 °C for 20 min. After cooling, about 100 ml of water was added to the reaction mixture. The resulting pale yellow precipitatees (60 mg, 76%) were separated by filtration. The product was identified as **6b** by comparison with IR spectrum.

3-Penyl-4-(1,2,4-thiadiazol-5-yl)sydnone (8). To a solution of **2c** (0.76 g, 2.8 mmol) and pyridine (0.49 g, 6.1 mmol) in 15 ml of dry dichloromethane was added a solution of hydroxylamine-*O*-sulfonic acid (0.35 g, 3.1 mmol) in 5 ml of absolute methanol. The reaction mixture was refluxed for 5 h. After cooling, about 30 ml of dichloromethane was added and the dichloromethane solution was washed with 2 M hydrochloric acid (50 ml×2), and water (50 ml), and then dried over sodium sulfate. After removal of the dichloromethane, the residue was chromatographed on silica gel (70—230 mesh). Elution with dichloromethane provided 0.24 g (35%) of the crude product. Recrystallization from dichloromethane-hexane provided 0.13 g (19%) of pure **8** as white needles, mp 144—145 °C. IR (KBr) 1775 cm^{-1} (C=O). ^1H NMR δ=7.73 (s, 5H, $C_6\underline{H}_5$) and 8.17 (s, 1H, thiazole C-$\underline{H}$). *m/e* 246 (M^+) and 188 ($M^+ -NO-CO$). Found: C, 48.68; H, 2.25; N, 22.57; S, 13.02%. Calcd for $C_{10}H_6N_4O_2S$: C, 48.78; H, 2.46; N, 22.75; S, 13.02%.

References

1) A Part of this work is "Organic *N*-Halogeno Compounds. Part 15." Part 14: T. Fuchigami and T. Nonaka, *J. Org. Chem.*, **46**, 5215 (1981).

2) M. Ohta and H. Kato, "Non-benzenoid Aromatics," Academic Press, New York, N. Y. (1969), Vol. 1, Chap. 4.

3) F. H. C. Stewart, *Chem. Rev.*, **64** 129 (1964).

4) a) L. B. Kier and E. B. Roche., *J. Pharm. Sci.*, **56**, 149 (1967); b) L. B. Kier, D. Dhawan, and M. J. Flegry, *ibid.*, **53**, 677 (1964); c) S. G. Boots and C. C. Cheng, *J. Heterocycl. Chem.*, **4**, 272 (1967); d) T. Bruzzese, S. Casadio, E. Marazzi-Uberti, and C. Turba, *J. Pharm. Sci.*, **54**, 1041 (1965); e) L. B. Kier, A. Al-shama, D. Campbell, P. Patil, and A. Tye, *Nature*, **210**, 742 (1966); f) T. Naito, S. Nakagawa, T. Takahashi, and K. Masuko, *J. Antibiot. (Tokyo)*, **21**, 290 (1968); g) H. Wagner and J. B. Hill, *J. Med. Chem.*, **17**, 1337 (1974).

5) a) H. Kato and M. Ota, *Bull. Chem. Soc. Jpn.*, **32**, 282 (1959); b) M. Hashimoto, Dr. Dissertation, Tokyo Institute of Technology, 1969; c) H.-J. Tien *Cheng-kung Ta Hsueh Pao*, **14**, 19 (1979); *Chem. Abstr.*, **92**, 181090x (1980); d) M.-Y. Yen, H.-J. Tien, and T. Nonaka, *J. Org. Chem.*, **48**, 1382 (1983).

6) M.-Y. Yeh, T. Nonaka, T. Goto, M.-C. Hsu, T. Fuchigami, and H.-J. Tien, *Bull. Chem. Soc. Jpn.*, **56**, 3535 (1983).

7) T. Fuchigami and K. Odo, *Chem. Lett.*, **1974**, 1139.

8) T. Fuchigami and K. Odo, *Bull. Chem. Soc. Jpn.*, **49**, 3607 (1976).

9) Y. Lin, S. A. Lang, Jr., M. F. Lovell, and N. A. Perkinson, *J. Org. Chem.*, **44**, 4160 (1979)

10) T. Fuchigami and K. Odo, *Bull. Chem. Soc. Jpn.*, **50**, 1739 (1977).

11) Y. Lin, S. A. Lang, Jr., and S. R. Petty, *J. Org. Chem.*, **45**, 3750 (1980).

12) S. A. Zotova and V. G. Yashunskii, *Zh. Org. Khim.*, **1**, 2218 (1965).

13) K. Kishimoto and M. Ota, *Nippon Kagaku Zasshi*, **83**, 833 (1962).