  Bull. Chem. Soc. Jpn., 55, 1183—1187 (1982)

The Thermal Decomposition of *N,O*-Diacyl-*N*-*t*-butylhydroxylamines. III. Novel Routes to 2-Substituted 1,2-Benzisothiazol-3-(2*H*)-ones[1]

Yuzuru UCHIDA* and Seizi KOZUKA†

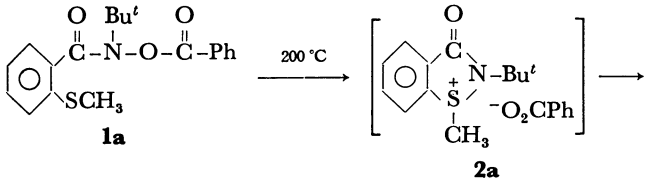
Department of Applied Chemistry, Osaka Institute of Technology, Asahi-ku, Osaka 535
†*Department of Applied Chemistry, Faculty of Engineering, Osaka City University, Sumiyoshi-ku, Osaka 558*

(Received September 1, 1981)

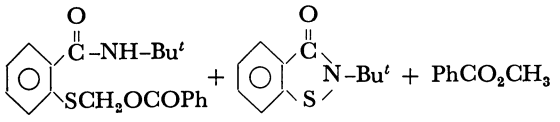
The reactions of *N*-alkyl- and *N*-aryl-2-(methylsulfinyl)benzamides and *N*-[2-(methylthio)benzoyl]-*N*-alkylhydroxylamines with thionyl chloride have been found to give 2-substituted 1,2-benzisothiazol-3(2*H*)-ones in nearly quantitative yields. The reactions of *N*-[2-(methylthio)benzoyl]-*N*-arylhydroxylamines with thionyl chloride gave chlorinated anilides as the major products.

2-Substituted 1,2-benzisothiazol-3(2*H*)-ones (**4**) have received much attention in recent years because of their antibacterial and antifungal properties.[2-5] The 2-substituted 1,2-benzisothiazol-3(2*H*)-ones have been synthesized by the reaction of 2-(chlorothio)benzoyl chloride with appropriate amines,[3] cyclization of 2-carbamoylbenzenesulfenyl halides with amines,[4] reaction of bis(2-carbamoylphenyl) disulfides with thionyl chloride,[5] and catalytic cyclization of *N*-substituted 2-(methoxycarbonyl) benzenesulfenamides by strong base.[6]

On the other hand, we have studied the thermal decompositions of *O*-acyl-*N*-[2-(methylthio)benzoyl]-*N*-*t*-butylhydroxylamines (**1**) and found that 2-*t*-butyl-1,2-benzisothiazol-3(2*H*)-one (**4a**) was formed in moderate yield as one of the products.[7] Acylaminosulfonium salt

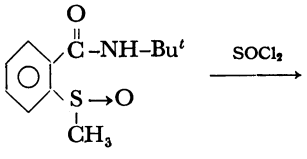


1a **2a**

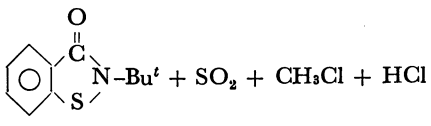


3 **4a**

(**2a**) has been suggested as the intermediate for the thermolysis. In order to prove the intermediacy of **2**, Pummerer reactions of *N*-*t*-butyl-2-(methylsulfinyl)-benzamide (**5a**) with either benzoic anhydride or thionyl chloride were tried; a facile formation of **4a**, by the reaction with thionyl chloride, was found.[7] This reaction would provide a novel and general route to prepare **4**, since a variety of *N*-substituted 2-(methylsulfinyl)benzamides (**5**) can easily be prepared from the corresponding sulfides. Thus, several *N*-alkyl- and *N*-arylbenzamides **5** were prepared and their reactions with thionyl chloride were examined.

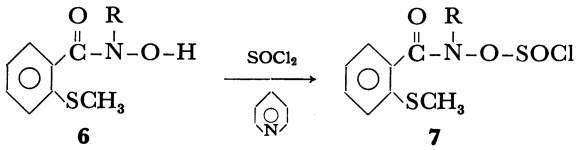


5a



4a

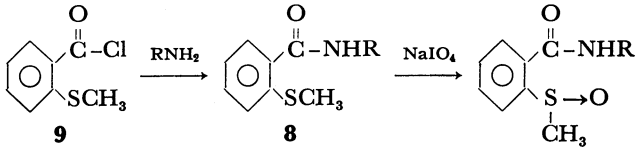
In the thermal decomposition of **1**, the mechanism of the formation of acylaminosulfonium salt (**2**) involves nucleophilic attack of the sulfur atom on the nitrogen atom. A better leaving group would facilitate the formation of **2**. Thus, the reaction of *N*-[2-(methylthio)-benzoyl]-*N*-alkylhydroxylamines (**6**) with thionyl chloride was examined, expecting the formation of the corresponding *N*-chlorosulfinyloxy-2-(methylthio)benzamide (**7**) as the transient product of the reaction. The transient products (**7**) would undergo a subsequent cyclization reaction, since the chlorosulfinate ion would be a better leaving group than the benzoate ion for the nucleophilic attack of the methylthio-sulfur atom on the nitrogen atom.



6 **7**

Results and Discussion

Reactions of N-*Alkyl- and* N-*Aryl-(2-methylsulfinyl)-benzamides with Thionyl Chloride.* Several *N*-substituted 2-(methylthio)benzamides (**8a—j**) were prepared from 2-(methylthio)benzoyl chloride (**9**) with appropriate alkyl- and arylamines. The corresponding sulfoxides (**5a—j**) were obtained by periodate oxidation of the sulfides (**8**) in good yields. The reaction of **5**



9 **8** **5**

with thionyl chloride was carried out in refluxing dichloromethane or chloroform. Evolution of hydrogen chloride and sulfur dioxide was found during the reaction and the reaction was completed within 30 min. 2-Substituted 1,2-benzisothiazol-3(2*H*)-eones were isolated by chromatographic separation with an alumina column in good yields. The results are given in Table 1. The structures of the products were established by elemental and spectral analyses.

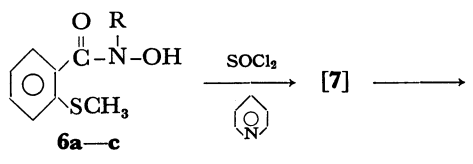
TABLE 1. PREPARATION OF 2-SUBSTITUTED 1,2-BENZISOTHIAZOL-3(2*H*)-ONES (**4**) BY THE REACTIONS OF 2-MeS(O)C_6H_4CONHR (**5**) AND 2-MeSC_6H_4CONROH (**6**) WITH $SOCl_2$

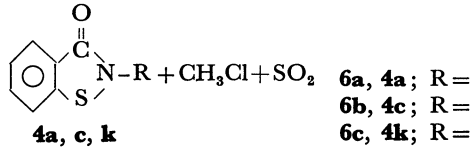
Compd	R	Solvent	Reaction conditions	Product	Yield[a] %
5a	*t*-C_4H_9	CH_2Cl_2	Reflux 10 min	**4a**	92
5b	C_2H_5	CH_2Cl_2	Reflux 10 min	**4b**	96
5c	$(CH_3)_2CH$	CH_2Cl_2	Reflux 10 min	**4c**	97
5d	cyclo-C_6H_{11}	CH_2Cl_2	Reflux 10 min	**4d**	98
5e	$C_6H_5CH_2$	CH_2Cl_2	Reflux 10 min	**4e**	98
5f	C_6H_5	CH_2Cl_2	Reflux 10 min	**4f**	98
5g	*p*-$CH_3C_6H_4$	CH_2Cl_2	Reflux 10 min	**4g**	98
5h	*p*-$CH_3OC_6H_4$	$CHCl_3$	Reflux 30 min	**4h**	84
5i	*p*-$NO_2C_6H_4$	CH_2Cl_2	Reflux 10 min	**4i**	97
5j	1-Naphthyl	CH_2Cl_2	Reflux 30 min	**4j**	98
6a	*t*-C_4H_9	CCl_4	Pyridine, 55 °C, 3 h	**4a**	92
6b	$(CH_3)_2CH$	CCl_4	Pyridine, 55 °C, 3 h	**4c**	81
6c	C_3H_7	CCl_4	Pyridine, 55 °C, 3 h	**4k**	80
6d	C_6H_5	CH_2Cl_2	Pyridine, 30 °C, 3 h	**4f**	Trace[b]
				10a	59[b]
				11	8[b]
				8f	20[b]
6e	*p*-$CH_3C_6H_4$	CH_2Cl_2	Pyridine, 30 °C, 3 h	**5g**	Trace[b]
				10b	66[b]
				8g	8[b]

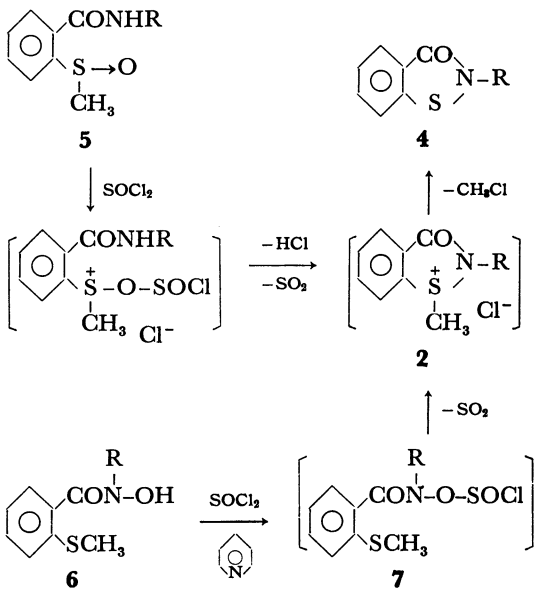
a) Isolated yields following chromatographic separation. b) The yields were estimated by GLC.

Reactions of N-*Alkyl- or* N-*Aryl*-N-[*2-(methylthio)benzoyl*]*hydroxylamines with Thionyl Chloride.* *N*-[2-(Methylthio)benzoyl]-*N*-*t*-butylhydroxylamine (**6a**) was prepared by alkaline hydrolysis of *N*-[2-(methylthio)-benzoyl]-*O*-benzoyl-*N*-*t*-butylhydroxylamine (**1a**).[7] *N*-Isopropyl (**6b**), *N*-propyl (**6c**), *N*-phenyl (**6d**), and *N*-(4-methylphenyl) derivatives (**6e**) were prepared by the reactions of 2-(methylthio)benzoyl chloride with the corresponding *N*-alkyl- and *N*-arylhydroxylamines.

The reaction of **6a** with thionyl chloride was carried out in carbon tetrachloride at 55 °C in the presence of pyridine. The reaction was monitored by following NMR signals of the *t*-butyl protons. After about 3 h, the spectrum showed the signals of **4a** together with chloromethane (δ, 2.99, s).[7] Although the signal due to **7** was not detected during the reactions, **7** would be the intermediate of the reaction. Similarly, **6b** and **6c** gave **4c** and **4k** by the reactions with thionyl chloride in good yields, respectively. The results are summarized in Table 1. The results show that the reactions of *N*-[2-(methylthio)benzoyl]-*N*-alkylhydroxylamines with thionyl chloride are applicable to syntheses of 2-alkyl-1,2-benzisothiazol-3(2*H*)-ones (**4**). The reaction of **6** with thionyl chloride required somewhat longer heating than that of **5**, but proceeded at much lower temperature than that employed for the thermolysis of **1** (200 °C),[7] as expected from the ability of the leaving groups. Accordingly, the present results also support the mechanism involving the nucleophilic attack of the sulfur atom on the nitrogen which has been suggested as the initial step for the thermolysis of **1**.[7]





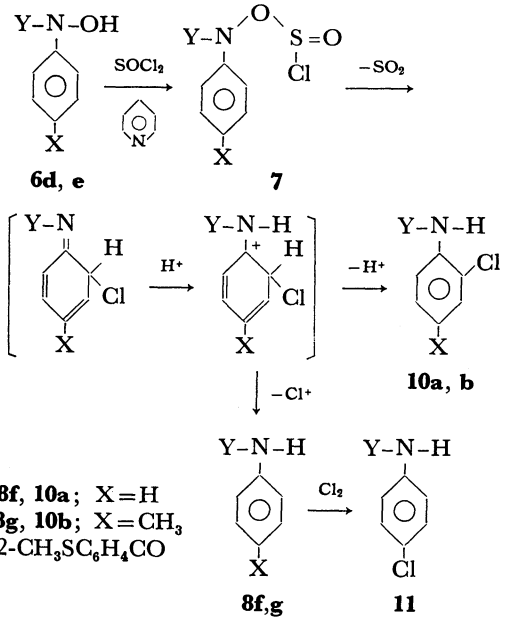


Scheme 1.

Both the reactions examined here appear to be novel and convenient routes to prepare **4**. The probable mechanisms for these reactions are shown in Scheme 1. The acylaminosulfonium salt **2** is involved as the key intermediate of the reactions. The final step of the

reactions would be the nucleophilic attack of the chloride ion on the methyl carbon of the sulfonium ion, since chloromethane was detected as an alternative product.

On the other hand, the reactions of *N*-arylhydroxylamine derivatives (**6d**) and (**6e**) with thionyl chloride gave only trace amounts of **4f** and **4g**, respectively. When the reaction of *N*-[2-(methylthio)benzoyl]-*N*-phenylhydroxylamine (**6d**) with thionyl chloride was carried out in the presence of pyridine, 2'-chloro-2-(methylthio)benzanilide (**10a**), 4'-chloro-2-(methylthio)-benzanilide (**11**), and 2-(methylthio)benzanilide (**8f**) were obtained as the major products. These products were isolated from the reaction products by chromatographic separation and identified by comparison of their physical properties with those of the authentic samples. Similarly, **6e** gave 2'-chloro-4'-methyl-2-(methylthio)-benzanilide (**10b**) and 4'-methyl-2-(methylthio)benzanilide (**8g**). The yields of products were estimated by GLC analysis and the results are summarized in Table 1. A possible mechanism leading to these products involving **7** as the intermediate is shown in Scheme 2.



Scheme 2.

Experimental

All the melting points and the boiling points are uncorrected. The IR spectra were recorded on a Shimadzu IR 430 infrared spectrometer. The NMR spectra were recorded on a Varian EM-360 spectrometer using TMS as the internal standard.

Preparation of N-*Alkyl- and* N-*Aryl-2-(methylthio)benzamides (8).* Typical procedures were as follows: (*a*) A solution of 2-(methylthio)benzoyl chloride (9.3 g, 50 mmol) in benzene (50 cm³) was added to a solution of isopropylamine (6.0 g, 102 mmol) in benzene (100 cm³) with stirring. The mixture was heated at 60 °C for 30 min. The reaction mixture was washed with dil HCl, aqueous Na_2CO_3, and water, then the solvent was evaporated. The residue was recrystallized from benzene–ether to give **8c** (7.1 g, 68%); mp 87.5—88.5 °C. IR (KBr): 3400, 3350 (N-H), and 1625 cm^{-1} (C=O). Found: C, 63.10; H, 7.49; N, 6.44%. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69%.

By the same procedure, amides **8a**, **8b**, and **8d—f** were prepared by the reaction of 2-(methylthio)benzoyl chloride with appropriate amines. Amides **8g**, **8h**, and **8j** were prepared by the reaction of 2-(methylthio)benzoyl chloride and an equivalent of amines in the presence of an equivalent of pyridine in benzene. The yields and the physical properties of the amides were as follows: **8a**, 85%; mp 133—134 °C.[7] **8b**, 62%, mp 90.5—91.5 °C. IR (KBr): 3300 (N-H) and 1630 cm^{-1} (C=O). Found: C, 61.73; H, 6.78; N, 7.06%. Calcd for $C_{10}H_{13}NOS$: C, 61.50; H, 6.71; N, 7.17%. **8d**, 79%; mp 138—139 °C. IR (KBr): 3300 (N-H) and 1630 cm^{-1} (C=O). Found: C, 67.30; H, 7.75; N, 5.57%. Calcd for $C_{14}H_{19}NOS$: C, 67.43; H, 7.68; N, 5.62%. **8e**, 98%; mp 131—132 °C. IR (KBr): 3270 (N-H) and 1640 cm^{-1} (C=O). Found: C, 70.10; H, 5.78; N, 5.15%. Calcd for $C_{15}H_{15}NOS$: C, 70.00; H, 5.88; N, 5.44%. **8f**, 98%; mp 148—149 °C. IR (KBr): 3300 (N-H) and 1645 cm^{-1} (C=O). Found: C, 69.04; H, 5.11; N, 5.53%. Calcd for $C_{14}H_{13}NOS$: C, 69.10; H, 5.39; N, 5.76%. **8g**, 93%; mp 145—146 °C. IR (KBr): 3280 (N-H) and 1645 cm^{-1} (C=O). Found: C, 70.15; H, 5.87; N, 5.28%. Calcd for $C_{15}H_{15}NOS$: C, 70.00; H, 5.88; N, 5.44%. **8h**, 91%; mp 137—138 °C. IR (KBr): 3250 (N-H) and 1650 cm^{-1} (C=O). Found: C, 65.99; H, 5.25; N, 5.13%. Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12%. **8j**, 96%; mp 130.5—131.5 °C. IR (KBr): 3250 (N-H) and 1640 cm^{-1} (C=O). Found: C, 73.62; H, 4.87; N, 4.52%. Calcd for $C_{18}H_{15}NOS$: C, 73.69; H, 5.15; N, 4.77%.

(*b*) A mixture of 2-(methylthio)benzoyl chloride (9.3 g, 50 mmol), *p*-nitroaniline (8.0 g, 58 mmol), and pyridine (20 cm³) was heated under refluxing for 5 h. The reaction mixture was poured into dil HCl (5%, 500 cm³) with stirring. The precipitate was collected by filtration and washed with hot dil HCl, aqueous $NaHCO_3$, and water, then dried. The crude amide (**8i**) was recrystallized from acetone (11.9 g, 83%); mp 165.5—166.5 °C. IR (KBr): 3300 (N-H) and 1655 cm^{-1} (C=O). Found: C, 58.58; H, 3.97; N, 9.86%. Calcd for $C_{14}H_{12}N_2O_3S$: C, 58.32; H, 4.20; N, 9.72%.

Preparation of N-*Alkyl- and* N-*Aryl-2-(methylsulfinyl)benzamides (5).* A typical run was as follows: A solution of sodium periodate (8.6 g, 40 mmol) in water (50 cm³) was added to a solution of **8f** (9.7 g, 37 mmol) in methnoal (300 cm³) with stirring. The mixture was stirred for 2 h at 50 °C. The solvent was evaporated and the residue was washed with water. The residue was crude **5f**, which was recrystallized from methanol–dichloromethane (9.0 g, 94%); mp 194—195 °C. IR (KBr): 3280 (N-H), 1660 (C=O), and 1010 cm^{-1} (S-O). Found: C, 64.86; H, 4.90; N, 5.22%. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40%.

Benzamides (**5a—e**) and (**5g—j**) were prepared by the same procedure. The results were as follows: **5a**: 92%; mp 150—151 °C.[7] **5b**, 81%; mp 157—158 °C. IR (KBr): 1640 (C=O) and 1010 cm^{-1} (S-O). Found: C, 56.60; H, 6.08; N, 6.50%. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.20; N, 6.63%. **5c**, 92%; mp 158—159 °C. IR (KBr): 1635 (C=O) and 1010 cm^{-1} (S-O). Found: C, 58.56; H, 6.79; N, 6.12%. Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71; N, 6.22%. **5d**, 83%; mp 138.5—139.5 °C. IR (KBr): 1640 (C=O) and 1010 cm^{-1} (S-O). Found: C, 63.32; H, 7.21; N, 5.07%. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28%. **5e**, 82%; mp 142—143 °C. IR (KBr): 1645 (C=O) and 1030 cm^{-1} (S-O). Found: C, 65.85; H, 5.43; N, 5.01%. Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12%. **5g**, 94%; mp 180.5—181.5 °C. IR (KBr): 1660 (C=O) and 1010 cm^{-1} (S-O). Found: C, 65.79; H, 5.54; N, 5.14%. Calcd

for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12%. **5h**, 99%; mp 176—177 °C. IR (KBr): 1650 (C=O) and 1010 cm^{-1} (S–O). Found: C, 62.34; H, 5.08; N, 4.73%. Calcd for $C_{15}H_{15}NO_3S$: C, 62.26; H, 5.23; N, 4.84%. **5i**, 99%, mp 244—245 °C (dec). IR (KBr); 1670 (C=O) and 1020 cm^{-1} (S–O). Found: C, 55.49; H, 3.99; N, 8.95%. Calcd for $C_{14}H_{12}N_2O_4S$: C, 55.25; H, 3.97; N, 9.21%. **5j**, 96%; mp 213—214 °C (dec). IR (KBr): 1670 (C=O) and 1020 cm^{-1} (S–O). Found: C, 69.83; H, 5.05; N, 4.37%. Calcd for $C_{18}H_{15}NO_2S$: C, 69.88; H, 4.89; N, 4.53%.

Reactions of N-*Alkyl- and* N-*Aryl-2-(methylsulfinyl)benzamides (***5***) with Thionyl Chloride.* A typical run was as follows: Thionyl chloride (1.50 g, 13 mmol) was added to a stirred suspension of **5f** (2.59 g, 10 mmol) in dry dichloromethane (20 cm^3). The reaction mixture was refluxed for 10 min; then the solvent and the excess of thionyl chloride were removed by distillation under reduced pressure. The residue was chromatographed on alumina with dichloromethane as the eluent to give **4f** (2.34 g, 98%), which was recrystallized from carbon tetrachloride–dichloromethane; mp 140.5—141.5 °C (lit,[5a] 140—141 °C). IR (KBr): 1660 cm^{-1} (C=O). By the same procedure, **4a—e** and **4g—j** were prepared, and the results are given in Table 1. **4a**; mp 57—58 °C. IR (KBr): 1650 cm^{-1} (C=O).[7] **4b**; bp 132 °C/2.5 Torr.†† IR (neat): 1650 cm^{-1} (C=O). NMR (δ, $CDCl_3$): 1.36 (3H, t, J=7 Hz), 3.93 (2H, q, J=7 Hz), and 7.2—8.2 (4H, m). Found: C, 58.64; H, 4.68; N, 7.29%.[8] Calcd for C_9H_9NOS: C, 60.31; H, 5.06; N, 7.82%. **4c**; bp 128 °C/2 Torr. IR (neat): 1650 cm^{-1} (C=O). NMR (δ, $CDCl_3$): 1.33 (6H, d, J=7 Hz), 4.93 (1H, m), and 7.1—8.1 (4H, m). Found: C, 61.12; H, 5.37; N, 6.75%.[8] Calcd for $C_{10}H_{11}NOS$: C, 62.14; H, 5.74; N, 7.25%. **4d**; mp 87—88 °C (lit,[5a] mp 87—88 °C). IR (KBr): 1635 cm^{-1} (C=O). NMR (δ, $CDCl_3$): 1.0—2.3 (10H, broad), 4.6 (1H, broad), and 7.2—8.2 (4H, m). **4e**; mp 87.5—88.5 °C (lit,[5a] mp 88 °C). IR (KBr): 1665 cm^{-1} (C=O). NMR (δ, $CDCl_3$): 5.03 (2H, s) and 7.0—8.2 (9H, m). **4g**; mp 135.5—136.5 °C (lit,[5a] mp 136—137 °C). IR (KBr); 1640 cm^{-1} (C=O). NMR (δ, $CDCl_3$): 2.37 (3H, s) and 7.1—8.2 (8H, m). **4h**; mp 147—148 °C (lit,[6] 147—149 °C). IR (KBr): 1660 cm^{-1} (C=O). NMR (δ, $CDCl_3$): 3.83 (3H, s) and 6.8—8.2 (8H, m). **4i**; mp 238—239 °C. IR (KBr): 1680 cm^{-1} (C=O). Found: C, 57.39; H, 2.68; N, 10.39%. Calcd for $C_{13}H_8N_2O_3S$: C, 57,34; H, 2.96; N, 10.29%. **4j**; mp 154—155 °C. IR (KBr): 1645 cm^{-1} (C=O). Found: C, 73.77; H, 3.75; N, 4.89%. Calcd for $C_{17}H_{11}NOS$: C, 73.62; H, 4.00; N, 5.05%.

Preparation of N-[*2-(Methylthio)benzoyl*]-N-t-*butylhydroxylamine (**6a**).* This compound was prepared by alkaline hydrolysis of *N*-[2-(methylthio)benzoyl]-*O*-benzoyl-*N*-*t*-butylhydroxylamine as described in the previous paper;[7] mp 145—146 °C.

Preparation of N-[*2-(methylthio)benzoyl*]-N-*isopropylhydroxylamine (**6b**).* Aluminium foil (10.5 g) was amalgamated by immersing it in a solution of mercury(II) chloride (3.0 g) in water (200 cm^3). The amalgamated aluminium was washed with water and added to a mixture of ether (500 cm^3) and water (5 cm^3). A solution of 2-nitropropane (18.0 g, 202 mmol) in ether (50 cm^3) was added dropwise into the mixture with stirring under refluxing. After addition of the 2-nitropropane was completed, the reaction mixture was refluxed for 30 min, and then cooled with ice-water. A solution of NaOH (10.0 g) in water (30 cm^3) was added to the mixture with stirring. The ether layer was separated and dried over Na_2SO_4. Into the solution which contained *N*-isopropylhydroxylamine, a solution of 2-(methylthio)benzoyl chloride (9.3 g, 50 mmol) in ether (100 cm^3) was added with stirring. After stirring for 1 h, the reaction mixture was washed with dil HCl and water, and then extracted with aqueous NaOH (5%, 200 cm^3). The extract was acidified with HCl. The crude *N*-[2-(methylthio)benzoyl]-*N*-isopropylhydroxylamine (**6b**) was collected by filtration (6.3 g, 56%), and then recrystallized from dichloromethane–petroleum ether; mp 100.5—101.5 °C. IR (KBr): 3200 (O–H) and 1610 cm^{-1} (C=O). NMR (δ, $CDCl_3$): 1.28 (6H, d, J=7 Hz), 2.47 (3H, s), 3.9 (1H, m), 7.0—7.6 (4H, m), and 8.8 (1H, broad). Found: C, 58.56; H, 6.92; N, 5.69%. Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71; N, 6.22%.

Preparation of N-[*2-(Methylthio)benzoyl*]-N-*propylhydroxylamine (**6c**).* Into an ethereal solution of *N*-propylhydroxylamine which was prepared from 1-nitropropane (18.0 g, 202 mmol) by the procedure described above, pyridine (15.0 g) and a solution of 2-(methylthio)benzoyl chloride (15.0 g, 81 mmol) in ether (100 cm^3) were added with stirring. After the reaction, the mixture was washed with dil HCl and water, and then extracted with aqueous NaOH (5%, 200 cm^3). The extract was acidified with HCl, and the crude *N*-[2-(methylthio)benzoyl]-*N*-propylhydroxylamine (**6c**) was collected by filtration (12.5 g, 69%), and then recrystallized from benzene–petroleum ether; mp 89.5—90.5 °C. IR (KBr): 3100 (O–H) and 1605 cm^{-1} (C=O). NMR (δ, $CDCl_3$) 0.85 (3H, t, J=7 Hz), 1.73 (2H, m, J=7 Hz), 2.50 (3H, s), 3.47 (2H, t, J=7 Hz), 7.0—7.7 (4H, m) and 8.5 (1H, broad s). Found: C, 58.70; H, 6.86; N, 6.04%. Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71; N, 6.22%.

Preparation of N-[*2-(Methylthio)benzoyl*]-N-*arylhydroxylamines (**6d—e**).* A solution of 2-(methylthio)benzoyl chloride (5.6 g, 30 mmol) in ether (50 cm^3) was added to a mixture of *N*-phenylhydroxylamine (3.3 g, 30 mmol), pyridine (3.0 g, 38 mmol), and ether (150 cm^3) with stirring. The reaction mixture was refluxed for 30 min, washed with dil HCl, and water, and then extracted with aqueous NaOH (5%, 100 cm^3). The extract was acidified with HCl, and the crude *N*-[2-(methylthio)benzoyl]-*N*-phenylhydroxylamine (**6d**) was collected by filtration (5.6 g, 71%), and then recrystallized from methanol; mp 141.5—142.5 °C. IR (KBr): 3120 (O–H) and 1630 cm^{-1} (C=O). NMR (δ, $CDCl_3$): 2.40 (3H, s), 6.8—7.5 (9H, m), and 9.3 (1H, broad s). Found: C, 64.80; H, 4.83; N, 5.39%. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40%.

N-[2-(Methylthio)benzoyl]-*N*-(4-methylphenyl)hydroxylamine (**6e**) was prepared similarly by the reaction of *N*-(4-methylphenyl)hydroxylamine and 2-(methylthio)benzoyl chloride in 80% yield; mp 169—170 °C (decomp). IR (KBr): 3230 (O–H) and 1615 cm^{-1} (C–O). NMR (δ, $CDCl_3$): 2.30 (3H, s), 2.43 (3H, s), 6.8—7.6 (8H, m), and 9.1 (1H, broad). Found: C, 65.86; H, 5.44; N, 4.91%. Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.53; N, 5.12%.

Reaction of N-[*2-(Methylthio) benzoyl*]-N-*alkylhydroxylamines (**6a—c**) with Thionyl Chloride.* Typical procedure was as follows: Thionyl chloride (1.50 g, 13 mmol) was added to a mixture of **6c** (2.25 g, 10 mmol) and pyridine (1.00 g, 13 mmol) in carbon tetrachloride (100 cm^3). The mixture was stirred for 3 h at 55 °C. The reaction mixture was washed with dil HCl and water, and dried over $CaCl_2$. After evaporation of the solvent, the residue was chromatographed on alumina with dichloromethane as the eluent to give **4k** (1.56 g, 80%), which was distilled under reduced pressure; bp 140 °C/2 Torr (lit,[6] 126—128 °C/0.2 Torr). IR (neat): 1650 cm^{-1} (C=O), NMR (δ, $CDCl_3$): 0.97 (3H, t, J=7 Hz), 1.80 (2H, m), 3.87 (2H, t, J=7 Hz), and 7.2—8.2 (4H, m). By the same procedure, **4a** and **4c** were prepared by the reactions of **6a** and **6b** with thionyl chloride, respectively. The results

†† 1 Torr≈133.322 Pa.

are given in Table 1.

Reactions of N-[*2-(Methylthio)benzoyl*]-N-*arylhydroxylamines (6d and 6e) with Thionyl Chloride.* A solution of thionyl chloride (0.70 g, 6 mmol) in dichloromethane (10 cm^3) was added to a mixture of *N*-[2-(methylthio)benzoyl]-*N*-phenylhydroxylamine (**6d**) (1.176 g, 5 mmol), pyridine (0.80 g, 10 mmol), and dichloromethane (40 cm^3) with stirring. After the reaction for 3 h at room temperature, the reaction mixture was washed with dil HCl, aqueous $NaHCO_3$, and water, then the solvent was removed by distillation under reduced pressure. The residue was subjected to GLC analysis, and the remainder was chromatographed on silica gel to isolate the products. The results are given in Table 1. The reaction of **6e** (1.372 g, 5 mmol) with thionyl chloride (0.70 g) in the presence of pyridine (0.80 g) was carried out in dichloromethane (50 cm^3) by the same procedure. **10a**; mp 93—94 °C. IR (KBr): 3200 (N–H) and 1640 cm^{-1} (C=O). NMR (δ, $CHCl_3$): 2.50 (3H, s), 6.9—8.7 (8H, m), and 8.7 (1H, broad). Found: C, 60.59; H, 4.27; N, 5.00%. Calcd for $C_{14}H_{12}ClNOS$: C, 60.53; H, 4.35; N, 5.04%. **10b**; mp 92.5—93.5 °C. IR (KBr): 3400 (N–H) and 1670 cm^{-1} (C=O). NMR (δ, $CDCl_3$): 2.38 (3H, s), 2.53 (3H, s), 7.0—8.6 (7H, m), and 8.6 (1H, broad). Found: C, 61.54; H, 4.73; N, 4.61%. Calcd for $C_{15}H_{14}ClNOS$: C, 61.74, H, 4.84; N, 4.80%. **11**; mp 137—138 °C. IR (KBr): 3300 (N–H) and 1660 cm^{-1} (C=O). NMR (δ, $CDCl_3$): 2.47 (3H, s), 7.0—7.8 (8H, m), and 8.5 (1H, broad). Found: C, 60.25, H, 4.14; N, 4.97%. Calcd for $C_{14}H_{12}ClNOS$: C, 60.53; H, 4.35; N, 5.04%.

References

1) Preliminary results have been reported. Y. Uchida and S. Kozuka, *J. Chem. Soc., Chem. Commun.*, **1981**, 510.

2) F. Gialdi, R. Ponci, and P. Caccialanza, *Mycopathol. Mycol. Appl.*, **24**, 163 (1964); *Chem. Abstr.*, **63**, 429e (1965).

3) F. Gialdi, R. Ponci, and A. Baruffini, *Farmaco, Ed. Sci.*, **16**, 509 (1961); *Chem. Abstr.*, **60**, 512 (1964); R. Ponci, F. Gialdi, and A. Baruffini, *Farmaco, Ed. Sci.*, **19**, 254 (1964); *Chem. Abstr.*, **61**, 3088e (1964); R. Ponci, T. Vitali, L. Amoretti, and F. Mossini, *Farmaco, Ed. Sci.*, **22**, 935, 999 (1968); *Chem. Abstr.*, **68**, 105078p, 114493x (1968); J. C. Grivas, U. S. Patent, 3761489 (1973); *Chem. Abstr.*, **79**, 137126 (1973).

4) J. S. Morley, Brit. Patent 848130 (1960); *Chem. Abstr.*, **55**, 9430c (1961); R. Ponci, A. Baruffini, M. Croci, and F. Gialdi, *Farmaco, Ed. Sci.*, **18**, 732 (1963); *Chem. Abstr.*, **60**, 2919h (1964); R. Ponci, T. Vitali, F. Mossini, and L. Amoretti, *Farmaco, Ed. Sci.*, **22**, 989 (1967); *Chem. Abstr.*, **69**, 27322t (1968); T. Vitali, L. Amoretti, and F. Mossini, *Farmaco, Ed. Sci.*, **23**, 468 (1968); *Chem. Abstr.*, **69**, 59147f (1968).

5) T. Vitali. L. Amoretti, and V. Plazzi, *Farmaco, Ed. Sci.*, **23**, 1075 (1967); *Chem. Abstr.*, **70**, 37701a (1969); A. Bellotti, E. Coghi, and O. Sgorbati, *Ateneo Parmense, Sez.*, *2*, **7**, 127 (1972); *Chem. Abstr.*, **77**, 48319c (1972).

6) J. C. Grivas, *J. Org. Chem.*, **40**, 2029 (1975).

7) Y. Uchida, Y. Kobayashi, and S. Kozuka, *Bull. Chem. Soc. Jpn.*, **54**, 1781 (1981).

8) The analytical values were lower than the calculated ones, which might be due to evaporation of the liquid samples.