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Received September 28, 1995
Revised July 18, 1996

2-Aroyl-5-aroylamino-1,2,4-thiadiazolin-3-ones **2** have been synthesized through aroylation of 5-amino-2*H*-1,2,4-thiadiazolin-3-one (**1**) as an analog of cytosine. The aroylation was carried out with a substituted aroyl chloride in pyridine at 56~58°. It has been established that the intermediates of the reactions are 2-aroyl-5-amino-1,2,4-thiadiazolin-3-ones **3** on the basis of the spectral data, additional experimental information and *ab initio* molecular orbital calculations.

J. Heterocyclic Chem., **33**, 1823 (1996).

Our interest in 5-amino-2*H*-1,2,4-thiadiazolin-3-one (**1**) [1-4] is because it can be considered an analog of cytosine. 5-Amino-2*H*-1,2,4-thiadiazolin-3-one is the compound that the carbon-carbon double bond of cytosine is replaced by a divalent sulfur. Analogy between -HC=CH- of benzenoid hydrocarbons (cytosine) and the divalent -S- in their sulfur-containing counterparts is a well-known chemistry. The derivatives of compound **1** were reported as antimicrobal agents [5]. Thus most studies on 5-amino-2*H*-1,2,4-thiadiazoline-3-one have been devoted to their synthesis [5-9] while very little is known about their reactivity [10,11]. Like cytosine, 5-amino-2*H*-1,2,4-thiadiazolin-3-one can exist in two stable tautomeric forms: lactam (oxo) and lactim (enol). Investigation of the relative stability of tautomers in biologically active compounds is important for understanding the relationships of structure-biological activity.

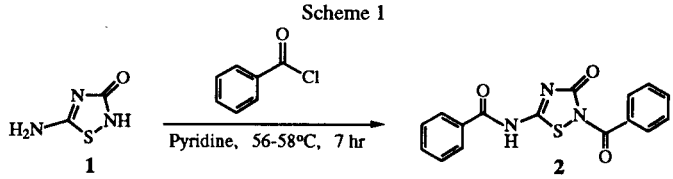
Thus we have studied the tautomerism and selective alkylation at N(2) of 5-amino-2*H*-1,2,4-thiadiazolin-3-one [1,4]. 5-Aroylamino-2*H*-1,2,4-thiadiazolin-3-ones have been synthesized by an oxidative cyclization of 5-aroyl-2-thiobiurets and their tautomerism has also been examined [2,3]. It was proven that 5-amino-2*H*-1,2,4-thiadiazolin-3-one [4] and 5-aroylamino-2*H*-1,2,4-thiadiazolin-3-one [3] exist in their lactam form rather than a lactim form from the results of their ^{13}C nmr and ^{1}H nmr, ir spectra and *ab initio* molecular orbital calculations.

However, the acylation of 5-*N,N*-dimethyl-2*H*-1,2,4-thiadiazolin-3-one with *N,N*-dimethylcarbamoyl chloride was reported to give a mixture of *O*-acyl and *N*-acyl derivatives [10]. In the same way the methylation of 5-phenyl-2*H*-1,2,4-thiadiazolin-3-one with dimethyl sulfate led to *O*-methyl and *N*-methyl products [11]. In contrast to our results [4], these reactions indicate that derivatives of 2*H*-1,2,4-thiadiazolin-3-one react in an equilibrium state between the two forms: a keto form and an enol form depending upon the reaction conditions. To conform the stable structure of 5-amino-2*H*-1,2,4-thiadiazolin-3-one by a synthetic experiment, the aroylation of 5-amino-2*H*-1,2,4-thiadiazolin-3-one was examined from the point of view of the relationship between the structure and its reactivity of compound **1**.

Results and Discussion

The new 2-aroyl-5-aroylamino-1,2,4-thiadiazolin-3-ones **2** were synthesized as shown in Scheme 1.

Scheme 1

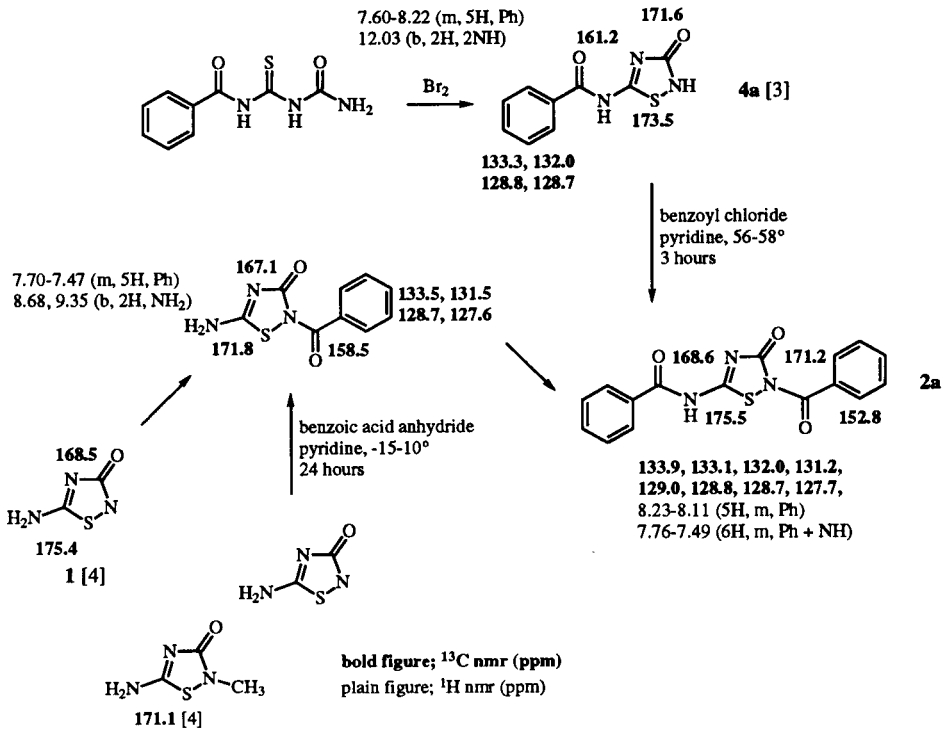


1 **2**

R, **a** = H **d** = *p*-Cl **g** = *m*-NO_2 **j** = *o*-NO_2
b = *p*-CH_3 **e** = *p*-NO_2 **h** = *o*-CH_3
c = *p*-OCH_3 **f** = *m*-OCH_3 **i** = *o*-Cl

The starting compound, 5-amino-2*H*-1,2,4-thiadiazolin-3-one (**1**) was prepared by the published procedure in the literature [1,4]. When compound **1** was aroylated with a substituted aroyl chloride at 56-58° in pyridine for 7 hours, only 2-aroyl-5-aroylamino-1,2,4-thiadiazolin-3-ones **2** were obtained in high yields. Especially with *p*-nitrobenzoyl chloride compound **2** was produced quantitatively. In contrast with the acylation of 5-*N,N*-dimethyl-2*H*-1,2,4-thiadiazolin-3-one [10] and the methylation of 5-phenyl-2*H*-1,2,4-thiadiazolin-3-one [11], either *O*(3)-aroylated, 5-amino-3-aroyloxy-1,2,4-thiadiazoles, or *N*(5)-aroylated, 5-aroylamino-2*H*-1,2,4-thiadiazolin-3-ones were not detected. During the reactions tlc was followed for observation of the intermediates. In the case of the reaction of **1** with benzoyl chloride, the R_F value of the reaction intermediate **3a** was characterized as 0.31 on silica gel tlc with *n*-hexane, ethyl acetate and acetic acid (4:8:1 v/v) as the eluent. One possible intermediate of this reaction is 5-benzoylamino-2*H*-1,2,4-thiadiazolin-3-one (**4a**). Authentic **4a** was prepared by the oxidative cylization of 1-benzoyl-2-thiobiuret. To our surprise, the R_F value of **4a**, was characterized as 0.16. For the identification of **3a** the compound was prepared *via* the reaction of **1** with benzoic anhydride at -15~-10°, which is less reactive than benzoyl chloride (see Experimental). The product of this reaction was identical with **3a**.

Scheme 2



The structure of **3a** was verified as 5-amino-2-benzoyl-1,2,4-thiadiazolin-3-one and supported by ^{1}H nmr, ^{13}C nmr, ir and high resolution mass spectroscopy. In the ir spectrum, the carbonyl groups are indicated as strong bands at 1700 and 1670 cm^{-1} and the C=N bond as a weak absorption at 1530 cm^{-1}. If **3a** is the *O*(3)-aroylated compound, the carbonyl band of the ester should appear at 1730~1750 cm^{-1} instead of 1700 and 1670 cm^{-1}. The ^{1}H nmr indicates the presence of the amino group at 9.35 and 8.68 ppm and the phenyl group at 7.47~7.70 ppm for compound **3a**. To confirm the structure of **3a** the ^{13}C nmr was compared with that of 5-amino-2-methyl-1,2,4-thiadiazolin-3-one (Scheme 2). The chemical shifts of the ring carbons in the two spectra are nicely matched with each other. Compound **3a** also gave a satisfactory high resolution mass spectrum.

For the preparation of **2**, the optimum mole ratio of compound **1** and a substituted aroyl chloride was 1:2.3. The aroyl chloride was added all at once to the suspended mixture of compound **1** in pyridine at 56~58°. During the progress of the reaction, the reaction mixture became a solution for a while and then the product was isolated as a precipitate. The effects of the reaction temperature and the substituents of aroyl chlorides on the yields of compounds **2** are summarized in Tables I and II respectively.

The yields of **2** vary from 61 to 98% depending on the substituents on the aroyl chlorides. The steric and inductive effects of aroyl chloride in this aroylation are nicely followed as shown in the esterification with benzoyl chloride [12]. At high reaction temperature compound **1** was decomposed to tar, thus the yield was low. At low temperature compound **1** was reacted to form 2-aroyl-5-aroylamino-1,2,4-thiadiazolin-3-ones along with 2-aroyl-5-amino-1,2,4-thiadiazolin-3-ones. The optimum reaction temperature for the formation of compounds **2** is at 56~58°. 2-Aroyl-5-aroylamino-1,2,4-thiadiazolin-3-ones **2** are colorless solids.

Table I
The Effect of Reaction Temperature and Reaction Time on the 2,5-Diaroylation [a] of 5-Amino-2*H*-1,2,4-iadiazolin-3-one, **1**

Run No.	Reaction Temperature (°C)	Reaction Time (hours)	Yield (%)	HPLC Purity (%)
1	110 ~ 120	9	13	–
2	110	1	25	–
3	65 ~ 70	2.5	75	–
4	65 ~ 70	3	83	99.0
5	56 ~ 58	4	80	–
6	56 ~ 58	7	98	–
7	50 ~ 55	24	74	98.8
8	45 ~ 50	20	76	98.7
9	35 ~ 40	40	82	98.6
10	30 ~ 40	50	71	97.1
11	0 ~ -5	6	50	14.4

[a] The aroyltion of 5-amino-2*H*-1,2,4-thiadiazolin-3 one, **1**, (5.1 mmoles) was carrieded out with *p*-toluoyl chloride (11.8 mmoles) in pyridine.

The structures of the new compounds **2** were established on the basis of their elemental analysis, ^{1}H nmr,

Table II
Synthesized 2-Aroyl-5-aroylamino-1,2,4-thiadiazolin-3-ones, **2**

Compound No.	R	Rex. time hour	Yield (%)	Mp °C [a]	Molecular Formula (mole wt)	Analysis Calcd./Found% C	H	N
2a	H	6	94	234 ~ 237	$C_{16}H_{11}N_3SO_3$	59.07	3.41	12.92
					(325.34)	58.99	3.37	12.98
2b	*p*-Me	7	98	241 ~ 244	$C_{18}H_{15}N_3SO_3$	61.18	4.28	11.89
					(353.40)	61.32	4.15	11.84
2c	*p*-OMe	7	93	232 ~ 234	$C_{18}H_{15}N_3SO_5$	56.10	3.92	10.90
					(385.40)	55.20 [b]	4.03	10.70
2d	*p*-Cl	0.1	85	256 ~ 257	$C_{16}H_9N_3SO_3Cl_2$	48.75	2.30	10.66
					(394.23)	48.79	2.29	10.60
2e	*p*-NO_2	1	98	253 ~ 254	$C_{16}H_9N_3SO_7$	46.27	2.18	16.86
					(415.34)	46.44	2.12	16.83
2f	*m*-OMe	4	75	190 ~ 192	$C_{18}H_{15}N_3SO_5$	56.10	3.92	10.90
					(385.40)	55.30 [b]	3.81	11.00
2g	*m*-NO_2	0.5	97	222 ~ 124	$C_{16}H_9N_3SO_7$	46.27	2.18	16.86
					(415.34)	46.58	2.14	16.75
2h	*o*-Me	7	59	196 ~ 199	$C_{18}H_{15}N_3SO_3$	61.18	4.28	11.89
					(353.40)	61.71 [b]	4.22	11.85
2i	*o*-Cl	2	61	193 ~ 195	$C_{16}H_9N_3SO_3Cl_2$	48.75	2.30	10.66
					(394.23)	48.95	2.34	10.57
2j	*o*-NO_2	4	91	242 ~ 244	$C_{16}H_9N_5SO_7$	46.27	2.18	16.86
					(415.34)	46.42	2.13	16.82

[a] All compounds were recrystallized from DMF ethanol (5:1). [b] After repeated analyses, more satisfactory values could not be obtained.

^{13}C nmr, and ir spectra. The elemental analyses and melting points of compounds **2** which were synthesized are shown in Table II. Table III contains the ir, ^1H nmr and ^{13}C nmr spectra of compounds **2**.

In the ^1H nmr spectra, the disappearance of NH_2 (8.0 ppm) present in the original 5-amino-2*H*-1,2,4-thiadiazolin-3-one (**1**) and the appearance of amide NH at 6.93 ~10.5 ppm and two phenyl groups at 6.93~8.91 ppm can serve as supporting evidence for the diaroylation of **1** to **2**. Along with ^1H nmr, carbonyl functional groups of an amide and a lactam clearly appear in the ir spectra at 1760~1700 and 1620~1680 cm^{-1} respectively. The C=N stretching band also is present at 1500~1550 cm^{-1}. To confirm the structure of **2** the ^{13}C chemical shifts for these compounds were compared with those of 5-amino-2-aroyl-1,2,4-thiadiazolin-3-ones **3** and authentic 5-aroylamino-2*H*-1,2,4-thiadiazolin-3-ones **4** [3]. In the case of 2-benzoyl-5-benzoylamino-1,2,4-thiadiazolin-3-one, the chemical shifts were identified as follows (see Scheme 2). The chemical shifts of carbon atoms in the phenyl ring were very satisfactorily correlated with the calculated values obtained using the substituent parameters [13] of monosubstituted benzenes, which the C=O(NH) group approximated C=O(NH_2) (Scheme 2). The chemical shifts of 2-benzoyl-5-benzoylamino-1,2,4-thiadiazolin-3-one are additively matched with those of 5-benzoylamino-2*H*-1,2,4-thiadiazolin-3-one and 5-amino-2-benzoyl-1,2,4-thiadiazolin-3-one. 5-Benzoylamino-2*H*-1,2,4-thiadiazolin-3-one (**4a**) [3] was also aroylated to **2a** with benzoyl chloride in pyridine at 56~58°. Its melting point and other physical constants were in agreement with those of an authentic sample of **2a** prepared by the method of diaroylation of compound **1**. All these spectral and experimental data support the structures of 2-aroyl-5-aroylamino-1,2,4-thiadiazolin-3-ones. Furthermore, the elemental analyses of the new compounds **2** were in a good agreement with the proposed structures (Table II).

The aroylation of **1** is particularly compared with those of other 5-aminothiadiazolines. For example, 5-amino-3*H*-1,3,4-thiadiazolin-2-thione is aroylated to 5-aroylamino-3*H*-1,2,4-thiadiazoline-2-thione [14-16]. However

Scheme 3
Optimized bond lengths and angles for 1-1 and 1-2 at the HF/3-21G* level.
Bond lengths are in angstoms and angles in degrees

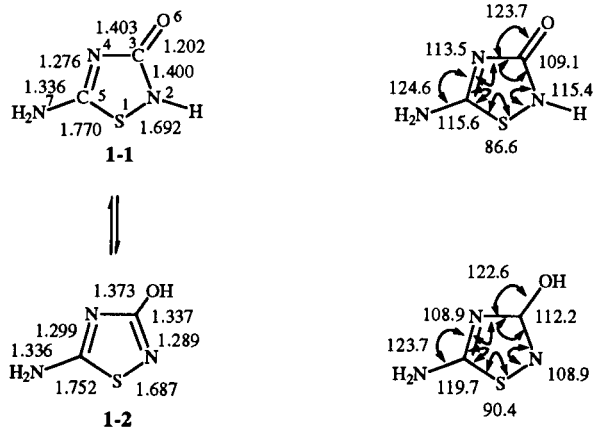


Table III
Spectral Data for 2-Aroyl-5-aroylamino-1,2,4 thiadiazolin-3-ones, **2**

Compound No.	R	IR Spectra cm^{-1} (potassium bromide) ^1H NMR (ppm, DMSO-d_6) ^{13}C NMR (ppm, DMSO d_6)
2a	H	3125 (NH), 3050 (CH), 1700, 1660 (C=O), 1540 (C=N) 8.23~8.11 (5H, m, Ph), 7.76~7.49 (6H, m, Ph + NH) 175.5 (C=N), 171.2 (C=O), 168.6, 15:2.8 (amide), 133.9, 133.1, 132.0, 131.2, 129.0, 128.8, 128.7, 127.7 (2Ph)
2b	*p*-Me	3125 (NH), 3050, 2950, 2900 (CH), 1700, 1650 (C=O), 1540 (C=N) 8.1, 8.0, 7.7, 7.6 (4H, dd, Ph), 7.6, 7.3, 7.2 (5H, dd, Ph + NH), 2.41 (3H, s, Me), 2.38 (3H, s, Me) 172.2 (C=N), 168.8, 167.0 (amide), 144.3, 142.5, 131.6, 130.6, 129.5, 129.2, 128.7, 128.3 (2Ph), 21.3 (Me), 21.1 (Me)
2c	*p*-OMe	3200 (NH), 3050, 2950 (CH), 1680, 1655 (C=O), 1540 (C=N) 8.19, 8.08, 7.78, 7.67 (4H, dd, Ph), 7.15, 7.04, 6.93 (5H, dd, Ph + NH), 3.85 (OMe, s, 3H), 3.83 (OMe, s, 3H) 170.8 (C=N), 168.0 (C=O), 163.9 (amide), 162.8, 131.9 131.5, 124.8, 114.4, 113.2 (2Ph), 55.7 (OMe), 55.5 (OMe)
2d	*p*-Cl	3200 (NH), 3080 (CH), 1720, 1700, 1660 (C=O), 1540 (C=N) 8.22, 8.11, 7.70, 7.60 (4H, dd, Ph), 7.81, 7.71, 7.58, 7.74 (5H, dd, Ph + NH) 171.6 (C=N), 167.6 (C=O), 138.8, 136.8, 131.9, 130.9, 130.7, 130.4, 129.0, 127.8 (2Ph)
2e	*p*-NO_2	3110 (NH), 3070 (CH), 1760, 1660, 16.20 (C=O), 1520 (C=N) 8.39 (4H, s, Ph), 8.37, 8.26, 8.00, 7.89. (5H, dd, Ph + NH) 175.6 (C=N), 17.3.1 (C=O), 167.0, 150.1 (amide), 148.8, 130.6, 130.5, 130.0, 129.7. 123.9, 123.8, 122.9 (Ph)
2f	*m*-OMe	3110 (NH), 3080, 2900 (CH), 1710, 1660 (C=O), 1550 (C=N) 7.94~7.21 (9H, m, Ph 8H + NH), 3.84 (3H, s, OMe), 3.79 (3H, s, OMe) 171.5 (C=N), 168.5 (C=O), 159.5, 158.6 (amide), 158.5, 134.5, 130.2, 129.1, 121.5, 120.9, 120.3, 117.9, 114.0, 113.5 (2Ph), 55.5 (0Me), 55.4 (0Me)
2g	*m*-NO_2	3300 (NH), 3080 (CH), 1740, 1680 (C=O), 1520 (C=N) 8.91~7.76 (m, Ph 8H + NH) 1752 (C=N), 172.4 (C=O), 166.4, 151.6 (amide), 147.9, 146.8, 135.1, 134.9 134.7, 133.4, 130.8, 129.5, 128.0, 126.2, 123.6 (2Ph)
2h	*o*-Me	3110 (CH), 3050, 2950 (CH), 1700, 1660 (C=O), 1540 (C=N) 7.96, 7.87, 7.4 ~ 7.24 (9H, m, Ph 8H + NH), 2.59 (3H, s, Me), 2.36 (3H, s, Me) 175.6 (C=N), 170.5 (C=O), 169.0, 153.6 (amide), 138.8, 134.6, 134.5, 132.5, 131.5, 130.7, 130.1, 130.0, 129.7, 126.9, 125.8, 125.3 (2Ph), 20.4 (Me), 18.9 (Me)
2i	*o*-Cl	3350 (NH), 3080, 3010 (CH), 1710, 1660 (C=0), 1540 (C=N) 7.95~7.89 (4H, m, Ph), 7.67~7.46 (5H, m, Ph 4H + NH) 173.1 (C=N), 170.7 (C=O), 165.9, 153.9 (amide), 134.1, 133.5, 131.5, 131.4, 131.0, 130.8, 130.5, 129.3, 129.0, 128.4, 127.3, 127.1 (2Ph)
2j	*o*-NO_2	3130 (NH), 3080 (CH), 1740, 1680, 1620 (C=O), 1550 (C=N) 10.5~9.5 (1H, b, NH), 8.34~8.13 (4H, m, Ph),7 .99~7.71 (4H, m, Ph) 172.4 (C=N), 170.9 (C=O), 165.5, 155.0 (amide), 146.9, 144.8, 135.2, 134.1, 133.2, 131.3, 130.5, 130.1, 128.8, 127.5, 124.5, 124.0 (2Ph)

the diaroylation of **1** through **3** is quite similar to the alkylation of cytosine at N (**1**) [17]. To understand the experimental results theoretically, the *ab initio* calculations were carried out on the tautomers of 5-amino-2*H*-1,3,4-thiadiazolin-3-one, **1**, with the GAUSSIAN 92 package [18]. Standard 3-21G and 3-21G* basis sets [19] were used to optimize geometries at the Hartree-Fock level. The optimized geometries of two important tautomers of compound **1** (**1-1** and **1-2**) are presented in Scheme 3.

The most significant changes in molecular geometry with lactam-lactim tautomerism (**1-1**⇌**1-2**) are in the C-O and C-N bond lengths. The C=O bond length of 1.202 Å in **1-1** is increased by 0.135 Å to form the C-O single bond length of 1.337 Å in **1-2**. The C-N bond length of 1.400 Å in lactam **1-1** tautomer is reversibly decreased to be 1.289 Å in lactim **1-2** tautomer. These changes, C-O: 0.135 Å and C-N: 0.111 Å, are in good agreement with other *ab initio* studies on the tautomerism of the pyrimidine bases [20]. The relative energies and Mulliken charges for **1-1** and **1-2** tautomers are summarized in Table IV.

The energies of **1-1** were computed to be 9.82 and 6.84 kcal/mol more stable than those of **1-2** at 3-21G and 3-21G* basis sets, respectively [4]. The computed negative charges on N(2) atom (-1.0357 and -0.9559) are largest ones in the lactam **1-1** form at both basis sets (atomic numbering systems are given in Scheme 3). However, in the lactim **1-2** form, the charges on the N(7) atom are larger than those on the O(6) atom. These results

Table IV

Relative Energies and Milliken Charges for Tautomers [a] of 5-Amino-2*H*-1,2,4-thiadiazolin-3-one in 3-21G and 3-21G* basis set. The relative energies [b] are listed in kcal/mol.

Tautomers	Basis Sets	Rel. E [4]	N(2)	N(4)	N(7)	O(6)
1-1	3-21G	0.00	-0.9559	-0.7459	-0.9440	-0.6242
	3-21G*	0.00	-1.0357	-0.7304	-0.9260	-0.6187
1-2	3-21G	6.84	-0.7349	-0.7070	-0.9538	-0.7103
	3-21G*	9.82	-0.7791	-0.6922	-0.9344	0.7041

[a] The structures of tautomers and numbering system are shown in Scheme 3. [b] The total energies of **1-1** tautomer at 3-21G and 3-21G* are -709.47018 and -709.5842 hartrees, respectively.

support the fact that the first reaction site of 5-amino-2*H*-1,2,4-thiadiazolin-3-one during aroylation is at N(2). Thus the intermediates of the aroylation of **1** should be 5-amino-2-aroyl-1,2,4-thiadiazolin-3-ones **3**. Compound **3** is eventually aroylated to provide compound **2**. If compound **1** exists as a lactim form, the aroylation of **1** can take place at the N(7) position to lead to the N-(5) aroylated compounds 5-aroylamino-2*H*-1,2,4-thiadiazolin-3-ones **4**, which are not detected during the reactions. Consequently, our experimental results reconfirm that compound **1** exists in the lactam form and the aroylated products are 5-aroylamino-2-aroyl-1,2,4-thiadiazoilin-3-ones. Further studies on the selective aroylation of compound **1** at N(2) and N(7) are in progress.

EXPERIMENTAL

All melting points were determined on an electrically heated Thomas-Hoover capillary melting point apparatus, but uncorrected. The ir spectra were measured on a Jasco Report-100 spectrophotometer. The ^1H and ^{13}C nmr spectra were recorded on either a 80 MHz Bruker AC-80 or a 300 MHz Bruker AM-300 using tetramethylsilane as the internal standard. The mass spectrum was obtained on a Varian MAT 212 spectrophotometer and an exact mass measurement was determined from a Spectra system SSMAT computer. Elemental analyses were carried out on a Perkin-Elmer apparatus, model 240, at the Korea Research Institute of Chemical Technology, Taejon, Korea. The progress of the reaction and the purity of all compounds were checked by thin layer chromatography on precoated glass plates with silica gel 60 F-254 as the absorbent (purchased from Whatman cat. No. 4861110). The eluent for tlc was used a mixture of *n*-hexane, ethyl acetate and acetic acid (4:8:1, v/v). The hplc analyses were performed with a system that consists of a Waters Model 510 pump and a variable wavelength detector, Waters 486. The wavelength of the detector was set at 310 nm. The 30 cm column (3.9 mm I.D.) was utilized, which is prepacked with 10 μm 125 Å μ-parasil (purchased from Waters Catalog No. Wat 027477). All chromatographic data were obtained using the same solvent mixture as the eluent of tlc, *n*-hexane, ethyl acetate and acetic acid (4:8:1, v/v), as the mobile phase with a flow rate of 1.5 ml/minute. Most of the commercially available starting materials and solvents were purchased from Aldrich Chemical Company, Milwaukee, WI.

5-Amino-2*H*-1,2,4-thiadiazolin-3-one was prepared by the published procedure [1].

Synthesis of 2-Aroyl-5-aroylamino-1,2,4-thiadiazolin-3-one (**2**) from 5-Amino-2*H*-1,2,4-thiadiazolin-3-one (**1**).

5-Amino-2*H*-1,2,4-thiadiazolin-3-one (**1**) (0.6 g, 5.1 mmoles) was suspended in anhydrous pyridine (20 ml) at 56~58°. A substituted benzoyl chloride (11.8 mmoles) was added once to the stirred mixture and heated at 56~58° for seven hours. The thin layer chromatography was used to determine the completion of the reaction. The reaction mixture was then cooled to room temperature and the resulting precipitate product was collected by filtration and washed with water and *n*-hexane. To obtain an analytical sample of the corresponding aroyl derivative **2**, the precipitate was recrystallized from mixture of DMF and ethanol (5:1 v/v). The yields, melting points, elemental analysis and spectral data of the products are shown in Tables I and II.

Synthesis of 2-Benzoyl-5-benzoylamino-1,2,4-thiadiazolin-3-one (**2a**) from 5-Benzoylamino-2*H*-1,2,4-thiadiazolin-3-one (**4a**).

5-Benzoylamino-2*H*-1,2,4-thiadiazolin-3-one (0.3 g, 1.4 mmoles), synthesized using a procedure described in the literature [3], was suspended in anhydrous pyridine (20 ml) at 56~58°. Benzoyl chloride (1.6 ml, 1.4 mmoles) was added once to the stirred mixture and heated at 56~58° for three hours. The tlc was performed for the determination of the end point of the reaction. The reaction mixture was concentrated to 10 ml, then cooled to room temperature. The white resulting precipitate was filtered off and washed with water and *n*-hexane to give 2-benzoyl-5-benzoylamino-1,2,4-thiadiazolin-3-one (0.4 g, 91%). The R_F values of the starting compound **4a** and the product **2a** are 0.31 and 0.44 respectively on silica gel tlc using a mixture of *n*-hexane, ethyl acetate and acetic acid (4:8:1, v/v) as the eluent. The melting point and spectral data of this compound are identical with those of the product obtained from diaroylation of 5-amino-2*H*-1,2,4-thiadiazolin-3-one (**1**) with benzoyl chloride.

2-Benzoyl-5-amino-1,2,4-thiadiazolin-3-one (**3a**).

5-Amino-2*H*-1,2,4-thiadiazolin-3-one (**1**) (0.5 g, 4.3 mmoles) was suspended in anhydrous pyridine (40 ml) at -15 ~ -10°. Benzoic acid anhydride (1.0 g, 4.3 mmoles) in pyridine (40 ml) was added dropwise to the stirred mixture during the course of three hours maintaining the temperature of -15 ~ -10°. The mixture was stirred for 21 hours at the same temperature. The unreacted starting compound (0.1 g, 20%) was filtered off and ice water (20 ml) was added to the filtrate and stirred for 10 minutes. The mixture was concentrated under reduced pressure. The residue was dispersed in ether and filtered off to give compound

3a as a slight yellowish solid (0.41 g, 55%). The R_F values of starting compound **1** and product **3a** are 0.06 and 0.16 respectively on silica gel tlc using the mixture of *n*-hexane, ethyl acetate and acetic acid (4:8:1, v/v) as the eluent. The precipitate was recrystallized from pyridine to obtain 2-benzoyl-5-amino-1,2,4-thiadiazolin-3-one (0.25g, 33%), mp 265~268°; ^{1}H nmr (DMSO-d_6): δ 9.35 (b, 1H, NH), 8.68 (b, 1H, NH), 7.47-7.70 ppm (m, 5H, Ph); ^{13}C nmr (DMSO-d_6): δ 171.8 (C=N), 167.7 (C=O), 158.5 (amide C=O), 133.5, 131.5, 128.7, 127.6 ppm (phenyl carbons); ir (potassium bromide): ν 3280 (NH_2), 3060 (CH), 1700 (C=O), 1670 (C=O), 1530 cm^{-1} (C=N); hrms: m/z, $C_9H_7N_3O_2S$: Calcd. for 221.0259. Found: 221.0251 (M^+).

Acknowledgments.

This work was supported by the Korea Science and Engineering Foundation (921-0300-00902). SKK is grateful to Center for Inorganic Materials Chemistry for partial financial support. We thank Miss Kye Young Lee for her help with the preparation starting material.

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