Aroylation of 5-Amino-2*H*-1,2,4-thiadiazolin-3-ones

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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°C. 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.

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We became interested in 5-amino-2*H*-1,2,4-thiadiazolin-3-one (**1**) [1-4] because it is an analog of cytosine. 5-Amino-2*H*-1,2,4-thiadiazolin-3-one is the compound in which the carbon-carbon double bond of cytosine is replaced by a divalent sulfur. The analogy between -HC=CH- of benzenoid heterocycles(cytosine) and the divalent -S- in their sulfur-containing counterparts is well-known both in benzenoid and also in heterocyclic chemistry. The derivatives of compound **1** were reported to be antimicrobal agents [5]. Most studies on 5-amino-2*H*-1,2,4-thiadiazolin-3-one deal with their synthesis [5-9] while very little is known about their reactivity [10,11]. Like cytosine, 5-amino-2*H*-1,2,4-3-thiadiazolin-one can exist in two stable tartomeric forms: lactam (oxo) and lactim (enol). Investigation of the relative stability of tautomers in biologically active compounds is important for understanding the relationship of chemical structure-biological activity.

Thus we have studied on the tautomerism and a 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 been also examined [2,3]. It has been established 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 forms rather than in their lactim forms as a result of their ^{13}C nmr and ^{1}H nmr, ir spectra and *ab initio* molecular orbital calculations.

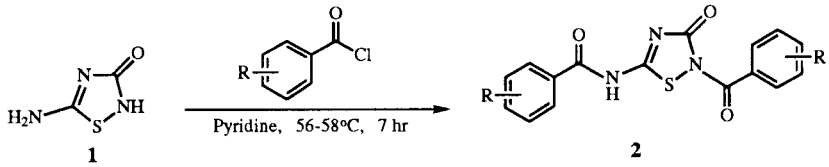
However, the acylation of 5-*N*,*N*-dimethyl-2*H*-1,2,4-thiadiazolin-3-one with *N*,*N*-dimethylcarbamoyl chloride was reported to give a mixture of *O*-acyl and *N*-acyl derivatives [10]. In the same way the methylation of 5-phenyl-2*H*-1,2,4-thiadiazolin-3-one with dimethyl sulfate led to *O*-methyl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

The starting compound, 5-amino-2*H*-1,2,4-thiadiazolin-3-one (**1**) was prepared by the procedure published in the literature [1,4]. When the 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 to 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 products, 5-aroylamino-2*H*-1,2,4-thiadiazolin-3-ones were not detected. During the course of the reactions, tlc was used for the detection of intermediates. In the case of the reaction of **1** with benzoyl chloride, the tlc R_F value of the

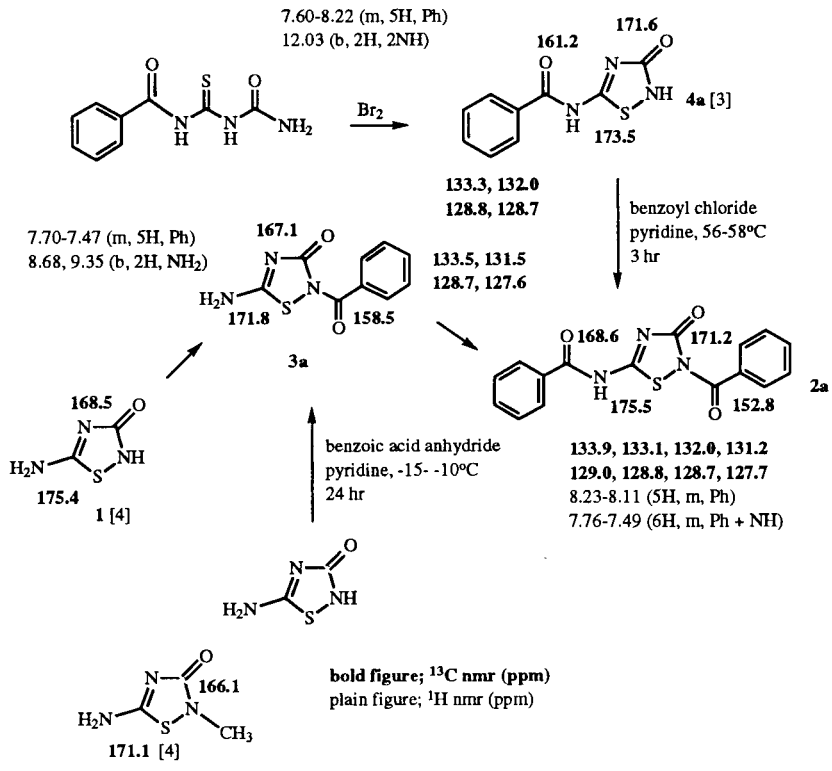
Scheme 1



1 **2**

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

Scheme 2



reaction intermediate **3a** was 0.31 on silica gel with *n*-hexane, ethyl acetate and acetic acid (4:8:1 v/v) as the eluent. One possible intermediate of this reaction is 5-benzoyl-2*H*-1,2,4-thiadiazolin-3-one (**4a**). Authentic **4a** was prepared by oxidative cyclization of 1-benzoyl-2-thiobiuret. To our surprise, the R_F value of **4a** was 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**.

The structure of **3a** was verified as 5-amino-2-benzoyl-1,2,4-thiadiazolin-3-one by ^{1}H nmr, ^{13}C nmr, ir and hrms. In the ir spectrum, the carbonyl groups had 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 ester should appear at 1730~1750 cm^{-1} instead of 1700 and 1670 cm^{-1}. The ^{1}H nmr indicates the presence of an amino group at 9.35 and 8.68 ppm and a phenyl group at 7.47~7.70 ppm for compound **3a**. To confirm the structure of **3a** the ^{13}C nmr spectrum was compared with that of 5-amino-2-methyl-1,2,4-thiadiazolin-3-one (Scheme 2). The chemical shifts of ring carbons in the two spectra are nicely matched with each other. Compound **3a** also gave satisfactory hrms.

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 progress of the reaction, the reaction mixture became a solution for a while and then product was isolated as a precipitate. The effects of reaction temperature and the substituents on the 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 the aroyl chloride in this aroylation are

Table I

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

Run No.	Reaction Temperature (°C)	Reaction Time (hours)	Yield (%)	HPLC Purity (%)
1	110~120	9	13.3	—
2	110	1	25.0	—
3	65~70	2.5	75.1	—
4	65~70	3	83.3	99.0
5	56~58	4	79 7	—
6	56~58	7	97.7	—
7	50~55	24	73.9	98.8
8	45~50	20	76.2	98.7
9	35~40	40	82.2	98.6
10	30~40	50	71.2	97.1
11	0~ -5	6	48.9	14.4

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

Table II

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

Compound No.	R	Rex. time hours	Yield (%)	Mp °C [a]	Molecular Formula (mol wt)	Analysis Calcd./Found % C	H	N
2a	H	6	93.8	234~237	$C_{16}H_{11}N_3SO_3$ (325.34)	59.07 58.99	3.41 3.37	12.92 12.98
2b	*p*-Me	7	97.7	241~244	$C_{18}H_{15}N_3SO_3$ (353.40)	61.18 61.32	4.28 4.15	11.89 11.84
2c	*p*-OMe	7	92.7	232~234	$C_{18}H_{15}N_3SO_5$ (385.40)	56.10 55.20 [b]	3.92 4.03	10.90 10.70
2d	*p*-Cl	0.1	84.6	256~257	$C_{16}H_9N_3SO_3Cl_2$ (394.23)	48.75 48.79	2.30 2.29	10.66 10.60
2e	*p*-NO_2	1	98.0	253~254	$C_{16}H_9N_5SO_7$ (415.34)	46.27 46.44	2.18 2.12	16.86 16.83
2f	*m*-OMe	4	74.5	190~192	$C_{18}H_{15}N_3SO_5$ (385.40)	56.10 55.30 [b]	3.92 3.81	10.90 11.00
2g	*m*-NO_2	0.5	97.3	222~124	$C_{16}H_9N_5SO_7$ (415.34)	46.27 46.58	2.18 2.14	16.86 16.75
2h	*o*-Me	7	58.7	196~199	$C_{18}H_{15}N_3SO_3$ (353.40)	61.18 61.71 [b]	4.28 4.22	11.89 11.85
2i	*o*-Cl	2	61.3	193~195	$C_{16}H_9N_3SO_3Cl_2$ (394.23)	48.75 48.95	2.30 2.34	10.66 10.57
2j	*o*-NO_2	4	90.7	242~244	$C_{16}H_9N_5SO_7$ (415.34)	46.27 46.42	2.18 2.13	16.86 16.82

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

nicely followed as shown in the esterification of benzoyl chloride [12]. At high reaction temperatures compound **1** was decomposed to a tar thus the yield was low. At low temperature compound **1** provided 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-3ones **2** are colorless solids.

The structures of the new compounds **2** were established on the basis of their elemental analysis, ^1H nmr, ^{13}C nmr, and ir spectra. The elemental analyses and melting points of the compounds **2** are shown in Table II. Table III contains the ir, ^1H mnr and ^{13}C nmr spectra.

In the ^1H nmr spectra, the disappearance of the NH_2 (8.0 ppm) present in the original 5-amino-2*H*-1,2,4-thiadiazolin-3-one (**1**) and the appearance of the amide NH at 6.93~10.5 ppm and the two phenyl groups at 6.93~8.91 ppm 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 is observed 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 the 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 the C=O(NH_2) group (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 **2a** prepared by the method of diaroylation of compound **1**. All these spectral and experimental data support the structures of the 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 similar to those of 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 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

Table III

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

Compound No.	R	Ir spectrum (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, 152.8 (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, 1620 (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), 173.1 (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 (OMe), 55.4 (OMe)
2g	*m*-NO_2	3300 (NH), 3080 (CH), 1740, 1680 (C=O), 1520 (C=N) 8.91~7.76 (m, Ph 8H + NH) 175.2 (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=O), 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)

of two important tautomers of compound **1** (**1-1** and **1-2**) are shown in Scheme 3.

The most significant changes in molecular geometry with lactam-lactim tautomerism (**1-1** $\rightleftharpoons$ **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 1.289 Å in the 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 the N(2) atom (-1.0357 and -0.9559) are the 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 provide support that the first reaction site of 5-amino-2*H*-1,2,4-thiadiazolin-3-one in the 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 compound **2**. If compound **1**

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.

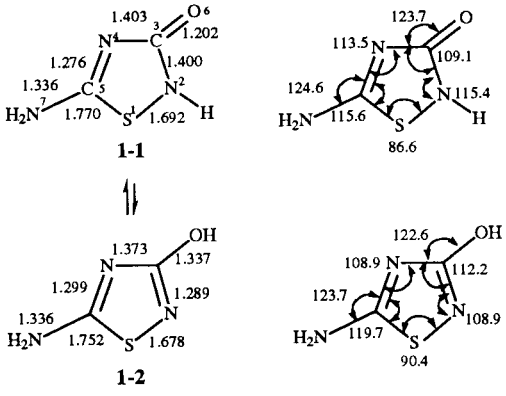
Tautomers	Basis Sets	Rel. E [4]	N(2)	N(4)	N(7)	O(6)
1-1	3-21G	0.00	-0.9559	-0.7459	-0.9440	-0.6242
	3-21G*	0.00	-1.0357	-0.7304	-0.9260	-0.6187
1-2	3-21G	6.84	-0.7349	-0.7070	-0.9538	-0.7103
	3-21G*	9.82	-0.7791	-0.6922	-0.9344	0.7041

[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.

exists as a lactim form, the aroylation of **1** can take place at the N(7) position to lead to the N-(5) aroylated compound 5-aroylamino-2*H*-1,2,4-thiadiazolin-3-ones **4**, which is not detected during the reactions. Consequently our experimental results reconfirm that compound **1** exists as a lactam form and the aroylated products are 5-aroylamino-2-aroyl-1,2,4-thiadiazolin-3-ones. Further studies on the selective aroylation of compound **1** at N(2) and N(7) are in progress.

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



EXPERIMENTAL

All melting points were determines on an electrically heated Thomas-Hoover capillary melting point apparatus and are uncorrected. The ir spectra were measures on a Jasco Report-100 spectrophotometer. The ^1H and ^{13}C nmr spectra were recorded on either a 80 MHz Broker 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 the exact mass measurements were determined with 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 wish silica gel 60 F-254 as the absorbent (purchased from Whatman No. 4861110). The eluent for tlc was used as a mixture of *n*-hexane, ethyl acetate and acetic acid (4:8:1, v/v). Analyses (hplc) were performed with a system that consists of a Waters Model 510 pump and a variable wavelength detector, Waters 486. The wavelenth 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 No. Wat 027477). All chromatographic data were obtained using the same solvent mixture as the eluent for 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 all at once to the stirred mixture and heated at 56-58° for seven hours. Thin layer chromatography was used to determine the completion of the reaction. The reaction mixture was then cooled to room temperature and the resulting precipitated 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 analyses and spectral data ofthe 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 all at 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 resulting white 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 -10 to -15°. 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 a temperature of -10 to -15°. 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 the compound **3a** as a slight yellowish solid (0.41 g, 55%). The R_F values of the starting compound **1** and the product **3a** are 0.06 and 0.16 respectively on the silica gel tlc using a 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-benzyl-5-amino-1,2,4-thiadiazolin-3-one (0.25 g, 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: 221.0259. Found: 221.0251 (M^+).

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