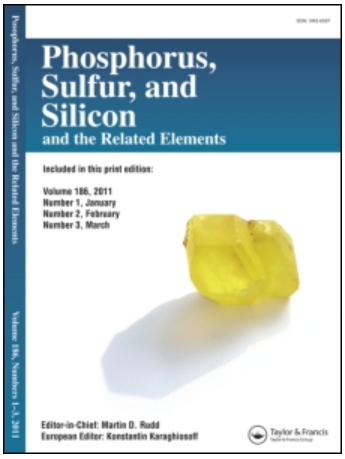

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MASS SPECTROMETRIC STUDIES OF 3-SUBSTITUTED-5-AMINO-1,3,4-THIADIAZOLIN-2-ONES

Un Chul Lee[a]; Won Lee[a]; Yun Je Kim[b]; Song Ja Park[b]; Do Young Ra[c]; Nam Sook Cho[c]
[a] Research Institute for Basic Science and Department of Chemistry, Kyung Hee University, Seoul, Korea [b] Dopping Control Center, Korea Institute of Science and Technology, Seoul, Korea [c] Department of Chemistry, Chung Nam National University, Taejeon, Korea

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MASS SPECTROMETRIC STUDIES OF 3-SUBSTITUTED-5-AMINO-1,3,4-THIADIAZOLIN-2-ONES

UN CHUL LEE[a], WON LEE[a], YUN JE KIM[b], SONG JA PARK[b], DO YOUNG RA[c] and NAM SOOK CHO[c]

[a]*Research Institute for Basic Science and Department of Chemistry, KyungHee University, Seoul 130–701, Korea,* [b]*Dopping Control Center, Korea Institute of Science and Technology, Seoul 130650, Korea and* [c]*Department of Chemistry, ChungNam National University, Taejeon 320–800, Korea*

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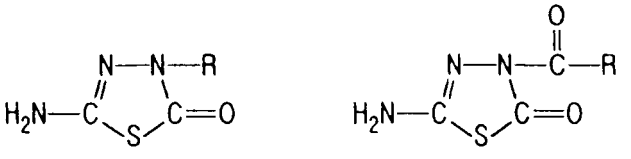
Fragment pathways of 3-alkyl and acyl-5-amino-1,3,4-thiadiazolin-2-ones were completely assigned by mass analyzed kinetic energy spectra (MIKE), collisional activated dissociation (CAD) spectra and high resolution mass spectra. $[NH_2CS]^+$ and $[S{=}C{=}O]^+$ ions were directly formed from molecular ion of the 3-alkyl compounds and from 5-amino-*3H*-1,3,4 -thiadiazolin-2-one ion ***(1)*** which was produced by McLafferty rearrangement from molecular ion of 3-acyl compounds. A loss of neutral SCO was only detected from 3-alkyl substituted molecular ions.

Keywords: 3-substituted-5-amino-1; 3; 4 -thiadiazolin-2-ones; MIKE and CAD; spectra.

INTRODUCTION

1,3,4-thiadiazolin-2-one derivatives have been intensively studied as potential insecticidal, acaricial and fungicidal agents.[1] In continuation of our studies on the synthesis of thiadiazoline derivatives,[2–6] we have synthesized two class of compounds 3-alkyl and 3-acyl-5-amino-1,3,4 -thiadiazolin-2-ones. Within the framework of our interest in these compounds, we have studied the electron impact mass spectral fragmentation patterns of them which will be useful for the determination of the structure of these types of compounds.

In this paper, we report the characteristic of the electron impact mass spectrometric behaviour of 3-alkyl- or acyl-5-amino-thiadiazolin-2-one compounds (Scheme 1) by the use of accurate mass measurements, mass analyzed kinetic energy spectra (MIKE)[7] and collisional activated dissociation (CAD) spectra using linked scan at constant Ua/B.[8]



Compound	R
1.	H
2.	CH_3
3.	C_2H_5

Compound	R
4.	CH_3
5.	C_2H_5
6.	C_3H_7

SCHEME 1

RESULTS AND DISCUSSION

Compounds *1–3*

The 70 eV EI mass spectra of *1*,[9,10] *2*[9] and *3* are shown in Figure 1. The molecular ions of the compounds in electron impact were detected as the base peaks. The fragmentation patterns from the molecular ion in the field free region were clearly observed using MIKE spectra and a typical MIKE spectrum of *1* is illustrated in Figure 2A. Based on the metastable ion transition and exact mass measurement, the two fragmentation pathways from molecular ion of *1–3* were determined and were described in Scheme 2.

The first fragmentation pathways of *1–3* in the field free region was the formation of ion at m/z 60 which was found in the low resolution EI spectra as an intensive single peak. This single peak was separated to doublet at m/z 59.9904 and 59.9677 in high resolution mass spectra. The two peaks were identified as $[H_2NCS]^+$ (calcd. 59.9908; found, 59.9904) and $[S{=}C{=}O]^+$ (calcd 59.9670; found, 59.9677), and the relative intensities were 84 % and 16 %, respectively. The formation of $[H_2NCS]^+$ ion has been observed in the mass spectra of the related heterocyclic compounds

like 5alkylthio-1,3,4 -thiadiazolyl-2-amines.[11] The observation of the formation of $[S{=}C{=}O]^+$ ion from the molecular ion was very interesting because no one observed the pathways in the electron impact mass spectra of those kinds of compound until now.

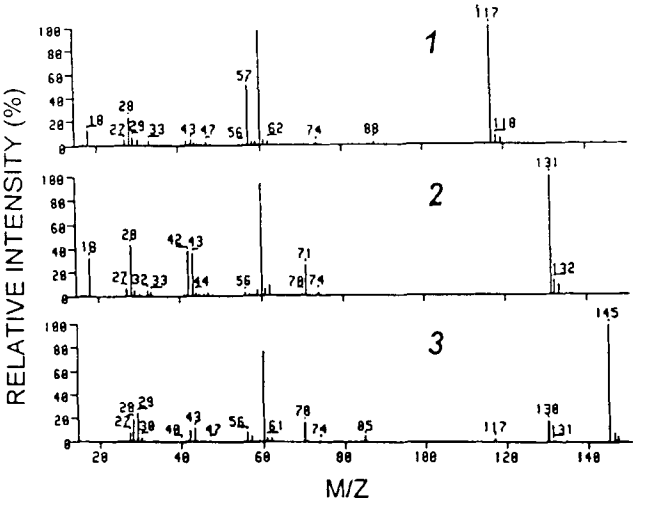
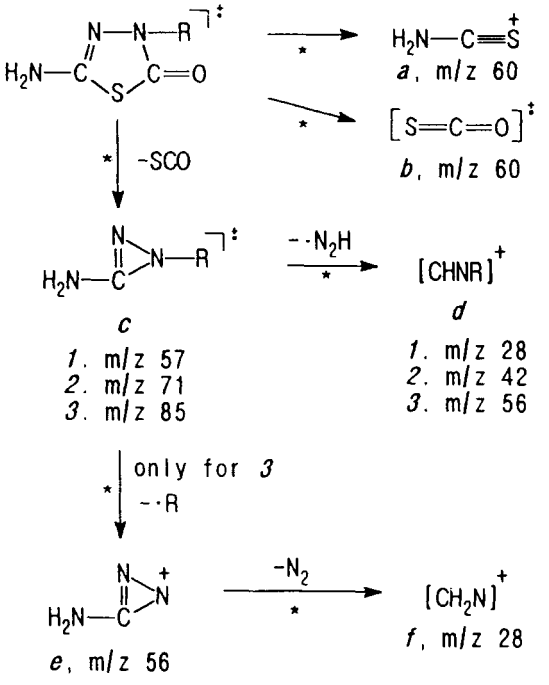


FIGURE I 70 eV EI mass spectra of *1–3*

The second fragmentation pathways was the formation of the ion at m/z 57, 71 and 85 for ***1***, ***2*** and ***3***, respectively, which was named as an ion ***c*** in Scheme 2. The ion ***c*** was observed as a single peak in low and high resolution mass spectra which was corresponding to the loss of neutral SCO from molecular ion. The second fragmentation pathways is the same as that of the closely related compound, 2-phenyl-1,3,4-oxadiazole-5-one derivatives.[12] Ion c was further decomposed by the loss of N_2H radical to give ion ***d*** at m/z 28, 42 and 56 for ***1***, ***2*** and ***3***, respectively.

Fragment ion ***e*** at m/z 56 for ***3*** was also observed as doublet in high resolution mass spectra. The elemental composition of doublet were found as $[C_3H_6N]^+$(calcd. 56.0500; found, 56.0502) from the loss of N_2H radical and $[CH_2N_3]^+$(calcd. 56.0249; found 56.0246) from the cleavage of $N(3)\text{-}CH_2CH_3$. The relative intensities of $[C_3H_6N]^+$ and $[CH_2N_3]^+$ are 21 % and 79 %, respectively. The formation of the ion ***e*** at m/z 56 was formed from ion ***c*** by loss of C_2H_5radical and further decomposed to give ion ***f***at m/z 28.

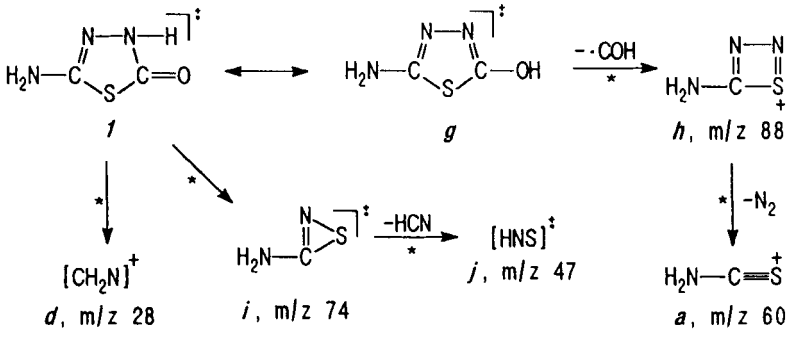


SCHEME 2

The another fragment pathways from molecular ion of ***1***, illustrated in Scheme 3, was give rise to the formation of cyclic ion ***h*** which will be originated from ion ***g***. The lactam-lactim tautomerism in the field free region was confirmed by detection of the elimination of COH radical instead of N_2H radical from ion ***g*** to give ion ***h***, which was identified as $[CH_2N_3S]^+$ (calcd. 87.9969; found, 87.9963) in the high resolution spectra. Even though the relative intensity of ion ***h*** is very lower than the ions ***b***, ***c*** from lactam form which was described in Scheme 2, the formation of ion ***h*** shows that the lactam-lactim tautomerism can occured in gas phase. However, lactam form was exclusively presented in solution by ^{15}NNMR study.[9]

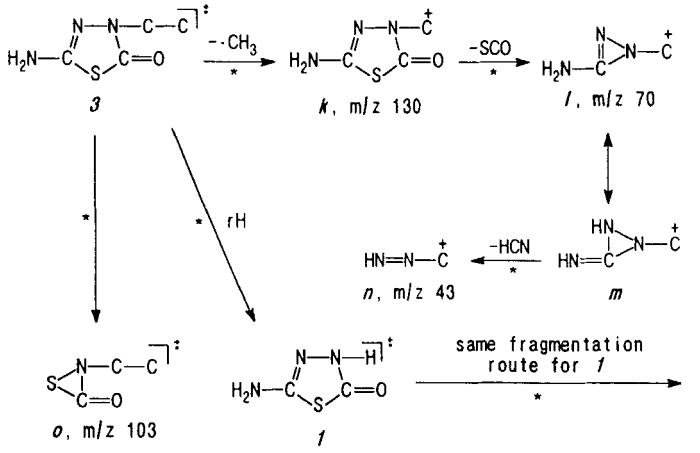
The cyclic ion ***i*** will be formed by cleavage the S(1)-C(2) and N(3)-N(4) bond to give very low intensity (1–3 %). The intensities of fragment ions ***h***(m/z 88) and ***i*** (m/z 74) were very weak in 70 eV El spectrum. However, they gave clearly a MIKE spectrum with reasonable intensity (Figure 2) and ion ***j*** also was detected from MIKE spectrum of ion ***i***. The formation

of the ion ***d*** at m/z 28 was also detected from molecular ion and ion ***c*** using MIKE spectra



SCHEME 3

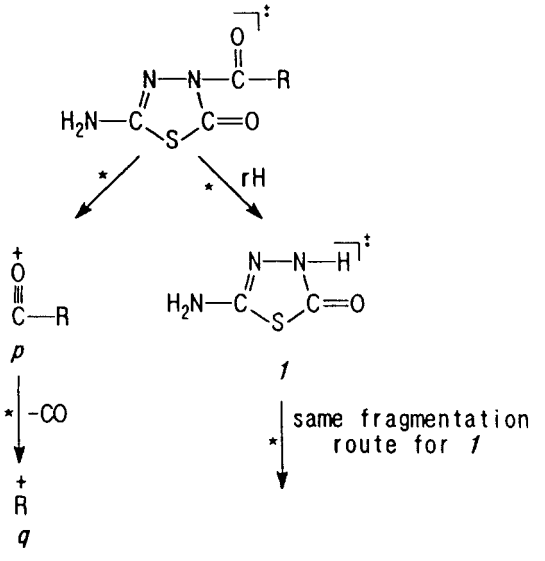
Additional three fragmentation pathways from molecular ion of ***3*** were observed and shown in Scheme 4. The two pathways were originated from the cleavage of 3-substituted C-C bond and McLafferty rearrangement to give ions ***k*** and ***l,*** respectively. The two ions were decomposed via a similar pathways as shown in Scheme 2, 3. The another pathways was the formation of ion ***o*** by intramolecular cyclization via the cleavage of S(1)-C(5) and N(3)-N(4) bond. Actually, this ion was not detected in 70 eV EI spectra but it clearly shown up in metastable spectra.



SCHEME 4

Compounds *4–6*

The 70 eV El mass spectra of ***4–6*** are shown in Table I. The intensities of the molecular ions for 3–acyl substituted compounds ***4–6*** (8–13 %) were relativelyweak in comparision with ***1–3***. Two patterns were observed in the field free region from the molecular ions for ***4–6*** and their fragmentation pathways were shown in Scheme 5. The dominant fragment pathway was the formation of the ion ***p*** at m/z 43, 57 and 71 for ***4***, ***5*** and ***6***, respectively. These fragmentations were commonly observed pathway in the compounds with acyl group by acleavage of the carbonyl group in the El mass spectra.



SCHEME 5

An interesting fragmentation pathway of the ***4–6*** was the formation of ion ***1*** at m/z 117. In the high resolution mass spectra of ***6***, the composition of fragment ion at m/z 117 was found as $[C_2H_3N_3OS]^{+\cdot}$ (calcd. 116.9997; found, 116.9996). Two possible pathways for the hydrogen rearrangement of the ***4–6*** in the gas phase were shown in Scheme 6. One of the pathways was the formation of ion **A** via the α-hydrogen rearrangement from acyl group to carbonyl oxygen in the thiadiazolin-one moiety. The other path-

way is the formation of ion **B** which was the α-hydrogen rearrangement from an acyl group to a N(4) atom, like a related 3-acyl thiazole compound.[13]

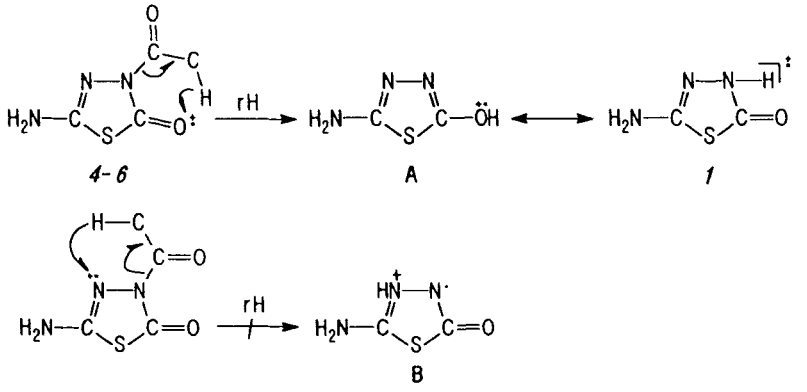
TABLE I The 70 eV EI mass spectra of *4–6:* m/z (relative intensities)

Ionic Species	*4*	*5*	*6*
M^+	159 (12)	173 (13)	187 (9)
1	117 (100)	117 (100)	117 (93)
a,b	60 (21)*	60 (19) *	60 (18) *
c	57 (12)	57 (69) *	57 (10)
d	28 (5)	28 (25)	28 (5)
h	88 (1)	88 (1)	88 (1)
i	74 (1)	74 (2)	74 (1)
j	47 (1)	47 (1)	47 (1)
p	43 (58)	57 (69) *	71 (47)
q	-	29 (55)	43 (100)

* Single peak in low resolution EI mass spectra.

The daughter ion spectra of ion at m/z 117 for ***6*** are shown in Figure 2B.From comparison with the daughter ion spectra of the molecular ion of ***1*** (Figure 2A), we got the information that the structure of the ion at m/z 117 of ***4–6*** was the same as the molecular ion of ***1***. The mechanism which generates the $[C_2H_3N_3OS]^{+\cdot}$ ion has been shown to six-membered McLafferty rearrangement to yield the ion **A** rather than a five-membered rearrangement which would generate the ion **B.** We have observed the formation of ion 1 from 3, which was also formed through McLafferty rearrangement via six-membered intermediates same as that of 3-acyl compounds ***4–6.***

On the basis of high resolution measurement and metastable spectra, it can be concluded that the ***4–6*** is fragmented through the intermediate $[C_2H_3N_3OS]^{+\cdot}$ at m/z 117. It was very interest that there was no loss of SCO directly from the molecular ion. It can be inferred that the presence of a R-C=O side chain provides an altemative low-energy pathway which completely prevents the fission of the thiadiazolin-one moiety in the molecular ion of these compounds.



SCHEME 6

From the results, we have obtained the following key informations for structure identification of 3-substituted-5-amino-1,3,4 -thiadiazolin-2-ones using El mass spectra; (1) 3-alkyl derivatives gave neutral SCO loss from molecular ions. (2) 3-acyl derivatives gave 5-amino-3H-1,3,4 -thiadiazolin-2-one *(1)*through McLafferty rearrangement from molecular ions instead of loss of SCO. And it is the first time to report the formation of $[S{=}C{=}O]^+$ in these related compounds. (3) In compound **1,** We found that lactam-lactim tautomerism occured in gas phase.

EXPERIMENTAL

All melting points were determined on a Fisher-Johns 2572A apparatus but uncorrected. The ^1H and ^{13}C nmr spectra were obtained on a Bruker ARX-400 spectrometer using tetramethylsilan as the internal standard.

Electron impact mass spectra were recorded on a Varian MAT 212 mass spectrometer coupled with SS MAT 300 data system at a nominal voltage of 70 eV. Samples were introduced directly into the ion source at a direct insertion probe temperature varying from 40 °C to 150 °C. The temperature of ion source was controlled to 150 °C. Exact mass measurement were carried out at a resolution of 5000–8000 (10 % valley definition) using release 6 software and peak matching method. Perfluorokerosene (PFK)

was used as an internal reference. The data from 10–20 scans were averaged using 10 mmu mass window.

Metastable ion analysis were performed by MIKE spectroscopy,[7] and CAD using linked scan at constant Ua/B.[8] In CAD experiments, helium was added to the first field free region so that the transmission of the main beam was reduced to 30 % of the value in the absence of collision gas.

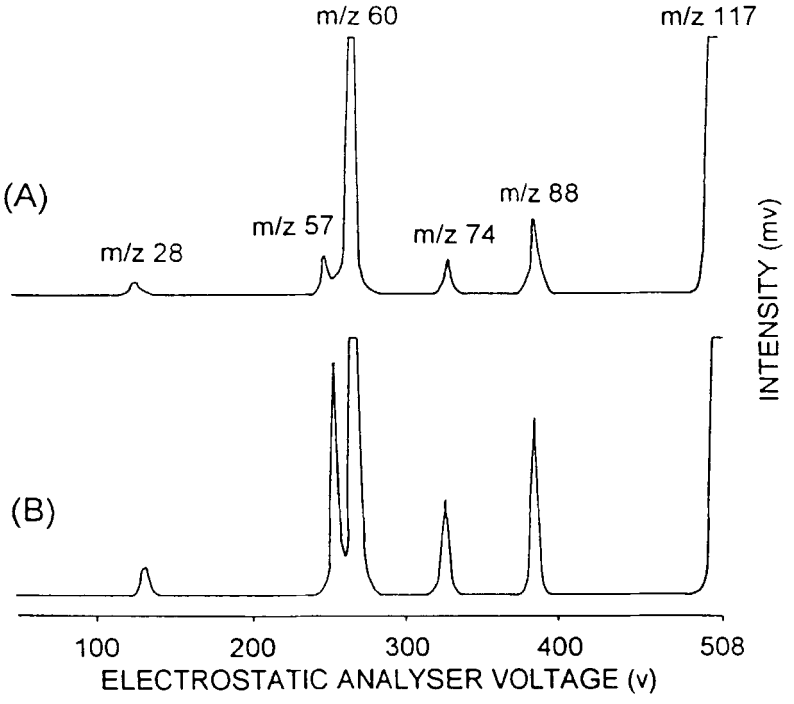


FIGURE II MIKE spectra of (A) molecular ion for *1* (B) fragment ion at m/z 117 for *6*.

5-Amino-3H-1,3,4-thiadiazolin-2-one (1)

It followed a pattern that we had described in the literature.[9,10]

3-Methyl-5-amino-1,3,4-thiadiazolin-2-one (2)

Potassium hydroxide (0.5 g, 9.4 mmol) was dissolved in 20 ml of ethanol. Compound 1 (1g, 8.54 mmol) was added to above solution. Dimethylsul-

fate (0.81 ml, 8.54 mmol) was added dropwise to the stirred mixture in course of half hour at room temperature. The mixture was stirred for one and half hour. After the reaction, the resulting precipitate was filtered off and filtrate was distilled off under the reduced pressure. The residue was washed with water to obtain compound 2 (1.1 g, 84 %). To afford an analytical sample, the product was recrystallized from toluene. m.p. 133 °C, ^{1}H NMR (DMSO-d_6, δ, ppm); 6.55 (2H, b, NH_2), 3.22 (3H, s, CH_3); ^{13}C NMR (DMSO-d_6,δ, ppm); 166.0 (ring C=N), 151.0 (ring C=O), 33.0 (CH_3).

3-Ethyl-5-amino- 1,3, 4-thiadiazolin-2-one (3)

Compound *3* was obtained with ethylbromide instead of dimethylsulfate by the above same procedure. To afford an analytical sample, the product was recrystallized from ethanol. m.p. 126–128 °C, ^{1}H NMR (DMSO-d_6, δ, ppm); 6.67 (2H, b, NH_2), 3.60 (2H, q, CH_2) 1.16 (3H, t, CH_3) ^{13}C NMR (DMSO-d_6, δ, ppm); 165.6 (ring C=N), 151.1 (ring C=O), 40.6 (CH_2), 13.5 (CH_3).

3-Acetyl-5-amino-1,3,4 -thiadiazolin-2-one (4)

Compound *(1)* (2 g, 17 mmol) was suspened in 40 *ml* of dioxane. Triethylamine (5.9 *ml,* 40 mmol) and acetic anhydride (3.85 *ml,* 40 *m*mol) was added respectively to the above solution. The reaction solution was stirred at 50 °C for 3 hour. The thin layer chromatography was used to determine the completion of the reaction. The reaction mixture was the cooled to room temperature. The solid separated was collected (2.0 g, 74 %) and recrystallized from ethanol to obtain the analytical sample. m.p. 224 °C, ^{1}H NMR (DMSO-d_6, δ, ppm); 7.03 (2H, b, NH_2), 2.36 (3H, s, CH_3); ^{13}C NMR (DMSO-d_6, δ, ppm); 167.9 (ring C=N), 166.1 (amide C=O), 150.1 (ring C=O), 25.2 (CH_3).

3-Propanoyl-5-amino-1,3,4 -thiadiazolin-2-one (5)

The reaction of the compound *1* and propanoic anhydride in the presence of triethylamine gave, after the usual work-up, the product *(5)* which was recrystallized from ethanol. m.p. 154–155 °C, ^{1}H NMR (DMSO-d_6, δ,

ppm); 7.09 (2H, b, NH_2), 2.75 (2H, q, CH_2), 1.04 (3H, t, CH_3); ^{13}C NMR (DMSO-d_6, δ, ppm); 169.9 (ring C=N), 167.6 (amide C=O), 150.0 (ring C=O), 30. 1 (CH_2), 8.2 (CH_3).

3-Butanoyl-5-amino-1,3,4-thiadiazolin -2-one (6)

The same procedure as described above yielded, from butyric anhydride, the product ***(6)*** which was recrystallized from ethanol. m.p. 137–140 °C. ^1H NMR (DMSO-d_6, δ, ppm); 7.04 (2H, b, NH_2), 2.61 (2H, t, CH_2), 1.54 (2H, m, CH_2), 0.97 (3H, t, CH_3); ^{13}C NMR (DMSO-d_6, δ, ppm); 169.0 (ring C=N), 167.7 (amide C=O), 150.0 (ring C=O), 38.54 (CH_2), 17.05 (CH_2), 13.45 (CH_3).

Acknowledgements

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