Heterocyclic Synthesis Using Nitrilimines: Part 9. Synthesis of New 1,3,4-Thiadiazin-5-one Derivatives

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A series of new 3,5,6-thiadiaza-4-hexenoates (**4a** – **k**) were synthesized from the reaction of the corresponding hydrazonoyl halides **1** with ethyl mercaptoacetate (**3**). These compounds underwent intramolecular cyclization to 1,3,4-thiadiazin-5-one derivatives (**5a** – **k**) in the presence of MeONa or LiH. The structures of the synthesized compounds were confirmed by their elemental analyses and spectral data.

Key words: Nitrilimines, Intramolecular Cyclization, Ethyl Mercapto-acetate, 1,3,4-Thiadiazin-5-ones

Introduction

1,3,4-Thiadiazines and their derivatives represent a class of heterocyclic compounds that have been associated with several pharmacological [1, 2] and medicinal applications [3]. Some thiadiazinones described in the literature exhibit spasmolytic effects and biological activities [4 – 8]. Different methods were used to synthesize 1,3,4-thiadiazin-5-one derivatives, some of which employed thiosemicarbazide [9], mercaptoacetyl hydrazine [10], and 4-arylhydrazono-5-oxo-3-thiahexanoic acid [11]. The other methods afforded the fused 1,3,4-thiadiazin-5-ones through basic or thermal cyclization of 4-amino-3-ethoxycarbonylmethylthio-1,2,4-triazoles [12 – 15] or 4-amino-3-carboxymethylthio-1,2,4-triazinon-5-ones [16]. In continuation of our research line dealing with the construction of heterocyclic systems by means of the nitrilimine cyclocondensation methodology [17, 18], we investigated the reaction of C-substituted N-arylnitrilimines **2** with ethyl mercaptoacetate (**3**) in an attempt to synthesize new derivatives of 1,3,4-thiadiazin-5-ones **5a** – **k** in anticipation of expected interesting biological activities.

Results and Discussion

Recently we found that α-amino esters react readily with nitrilimines, generated *in situ* from triethylamine and hydrazonoyl halides, yielding the corresponding 4,5-dihydro-1,2,4-triazin-5-ones [19, 20]. On the other hand, the reaction of the nitrilimines **2** with ethyl mercaptoacetate (**3**) for 2 – 3 d at r. t. gave acyclic electrophilic addition products (**4a** – **k**) (Scheme 1). Cyclization to the corresponding 1,3,4-thiadiazin-5-ones **5a** – **k** did not occur. This behavior is similar to that reported by Abuthaher *et al*. [11], where α-mercaptoalkanoic acids and N-aryl acetohydrazonoyl chlorides reacted to afford 4-arylhydrazono-5-oxo-3-thiahexanoic acids, which underwent cyclization to thiadiazinone rings in the presence of dicyclohexylcarbodimide (DCC).

The acyclic adducts **4a** – **k** were cyclized intramolecularly to the corresponding 2,4-disubstituted 1,3,4-thiadiazin-5-ones **5a** – **k** by heating them with methanolic sodium methoxide or lithium hydride (Scheme 1). The antimicrobial and antitumor activities of compounds **5a** – **k** are now under investigation at the Free University of Berlin, Germany.

Spectral data analysis

The characteristic data of compounds **4a** – **k** are given in detail in the Experimental Section. All compounds gave satisfactory combustion analysis for the proposed structures which were confirmed on the basis of their spectroscopic data.

The electron impact (EI) mass spectra displayed the correct molecular ions ($M^{+\cdot}$) in accordance with the suggested structures.

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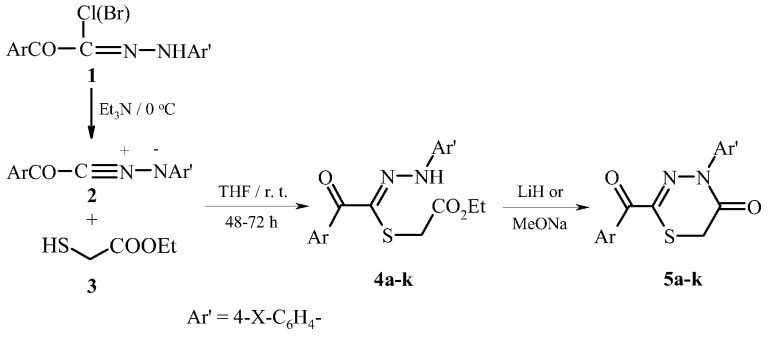

Entry	a	b	c	d	e	f	g	h	i	j	k
Ar	PhNH-	PhNH-	PhNH-	PhNH-	PhNH-	Ph	2-Furyl	2-Thienyl	2-Naphthyl	2-Naphthyl	2-Naphthyl
X	H	Cl	Br	F	Me	Cl	Cl	Cl	H	Cl	Me

Scheme 1. Synthetic pathway for the preparation of compounds **4a – k** and **5a – k**.

The IR spectra showed the strong absorption band of NH of the ring in the region 3300 – 3200 cm^{-1}. The carbonyl absorption of the ester group appeared in the region 1730 – 1710 cm^{-1}, and the C–S stretching band appeared in the region 1230 – 1220 cm^{-1}. The ^1H NMR spectra of compounds **4a – k** showed signals of the ethyl protons at δ = 1.3 – 1.1 ppm (t, 3H, CH_3) and 4.2 – 4.1 ppm (q, 2H, OCH_2), indicating clearly that the ethyl group of the ester was not lost, and that the compounds have the acyclic structure. Also the N–NH proton appeared as a singlet at δ = 10.4 – 10.3 ppm.

The ^{13}C NMR spectra illustrate that compounds **4a – k** have the assigned acyclic structures. The carbonyl carbon of the ester group appeared at about δ = 170 ppm, and the signals of the CH_2 and CH_3 carbon atoms of the ethoxy group appeared at about δ = 61 and 14 ppm, respectively. The methylene carbon of S–CH_2 appeared at about δ = 34 – 33 ppm, and the signal at $\delta \approx$ 141 ppm is attributed to the C=N carbon atom.

Structure elucidation of the obtained thiadiazinones **5a – k** was achieved by analytical and spectral data summarized in the Experimental Section. Their mass spectra displayed the correct molecular ion peaks $[M]^+$ in accordance with the suggested structures and showed the loss of an ethoxy group from the acyclic adducts **4a – k** *via* ethanol elimination. The IR spectra of compounds **5a – k** support the formation of the cyclic structure by the absence of NH and C=O vibrations of the ester, and the appearance of a new absorption band for a lactam (C=O of the ring) in the region 1680 – 1670 cm^{-1}. The ^1H NMR spectra of compounds **5a – k** showed all the signals of the proposed structures, indicating the disappearance of ethyl ($CO_2CH_2CH_3$) and N–NH protons. Finally, also the ^{13}C NMR data illustrated that compounds **5a – k** have the assigned cyclic structure by the absence of signals for ethoxy carbons and the presence of the signal at $\delta \approx$ 159 ppm which is typical for a lactam group. Furthermore, the signal of the methylene carbon of the thioester moiety in the acyclic adducts **4a – k** ($\delta \approx$ 34 ppm) is shifted upfield to $\delta \approx$ 26 ppm in compounds **5a – k**, whereas the signal of the C=N carbon is recorded at $\delta \approx$ 143 ppm.

In conclusion, the results demonstrate that nitrilimines **2** react in a two-step reaction with ethyl mercaptoacetate to give the cyclic derivatives **5a – k**.

Experimental Section

Melting points were determined using an electrothermal melting temperature apparatus and are uncorrected. The IR spectra were measured as KBr pellets using a Satellite 3000 Mid infrared spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 300 MHz spectrometer at r. t. in [D_6]DMSO solution using tetramethylsilane (TMS) as internal reference. Electron impact (EI) mass spectra were run on a Shimadzu GCMS-QP1000 EX spectrometer at 70 eV. Elemental analyses were performed at Cairo University, Egypt. The hydrazonoyl halides **1** were prepared according to literature procedures [21 – 24], and ethyl mercaptoacetate (**3**) was purchased from Avocado Research Chemicals, England, and used without further purification.

*Synthesis of compounds **4a – k***

General method: To a stirred solution of the appropriate hydrazonoyl halide **1** (5 mmol) and ethyl mercaptoacetate

(**3**) (10 mmol) in tetrahydrofuran (THF) (50 mL), triethylamine (4 mL, 3 mmol) in THF (10 mL) was dropwise added at r. t. Stirring was continued for 2 – 3 d, then the solvent was removed under vacuum, and the residual solid was washed with water (100 mL). The solid products were collected and recrystallized from an appropriate solvent to afford the desired compounds. The following compounds were prepared by this method.

*Ethyl 6-phenyl-4-phenylaminocarbonyl-3,5,6-thiadiaza-4-hexenoate (**4a**)*

M. p. 113 – 115 °C (ethanol). – Yield 82 %. – IR: ν = 3320, 3270 (N–H), 1715 (ester C=O), 1650 (amide C=O), 1600 (C=N), 1225 (C–S) cm^{-1}. – ^1H NMR: δ = 10.33 (s, 1H, N–H), 9.93 (s, 1H, PhN–H), 7.76 – 7.02 (m, 10H, Ar-H), 4.21 – 4.02 (q, 2H, OCH_2, J = 7 Hz), 3.90 (s, 2H, SCH_2), 1.25 – 1.13 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 169.9 (ester C=O), 159.9 (amide C=O), 140.0 (C=N), 139.9 – 119.3 (Ar-C), 61.3 (OCH_2), 33.2 (SCH_2), 13.8 (CH_3) ppm. – MS: *m/z* = 357 $[M]^+$. – $C_{18}H_{19}N_3O_3S$ (357.43): calcd. C 60.49, H 5.36, N 11.76; found C 60.27, H 5.57, N 11.55.

*Ethyl 6-(4-chlorophenyl)-4-phenylaminocarbonyl-3,5,6-thiadiaza-4-hexenoate (**4b**)*

M. p. 136 – 138 °C (ethanol). – Yield 75 %. – IR: ν = 3320, 3270 (N–H), 1718 (ester C=O), 1655 (amide C=O), 1615 (C=N), 1226 (C–S) cm^{-1}. – ^1H NMR: δ = 10.30 (s, 1H, N–H), 9.93 (s, 1H, PhN–H), 7.80 – 7.10 (m, 9H, Ar-H), 4.20 – 4.03 (q, 2H, OCH_2, J = 7 Hz), 3.96 (s, 2H, SCH_2), 1.27 – 1.11 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 169.9 (ester C=O), 160.2 (amide C=O), 140.0 (C=N), 139.9 – 119.8 (Ar-C), 61.3 (OCH_2), 33.2 (SCH_2), 13.8 (CH_3) ppm. – MS: *m/z* = 391/393 $[M]^+$. – $C_{18}H_{18}ClN_3O_3S$ (391.88): calcd. C 55.17, H 4.63, N 10.72; found C 55.44, H 4.59, N 10.63.

*Ethyl 6-(4-bromophenyl)-4-phenylaminocarbonyl-3,5,6-thiadiaza-4-hexenoate (**4c**)*

M. p. 150 – 152 °C (ethanol). – Yield 75 %. – IR: ν = 3320, 3270 (N–H), 1715 (ester C=O), 1650 (amide C=O), 1612 (C=N), 1225 (C–S) cm^{-1}. – ^1H NMR: δ = 10.36 (s, 1H, N–H), 9.95 (s, 1H, PhN–H), 7.78 – 7.06 (m, 9H, Ar-H), 4.13 – 4.01 (q, 2H, OCH_2, J = 7 Hz), 3.89 (s, 2H, SCH_2), 1.25 – 1.13 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 169.8 (ester C=O), 160.9 (amide C=O), 140.5 (C=N), 139.8 – 118.4 (Ar-C), 61.1 (OCH_2), 33.4 (SCH_2), 13.8 (CH_3) ppm. – MS: *m/z* = 436/438 $[M]^+$. – $C_{18}H_{18}BrN_3O_3S$ (436.33): calcd. C 49.55, H 4.16, N 9.63; found C 49.71, H 3.95, N 9.56.

*Ethyl 6-(4-fluorophenyl)-4-phenylaminocarbonyl-3,5,6-thiadiaza-4-hexenoate (**4d**)*

M. p. 118 – 120 °C (ethanol). – Yield 81 %. – IR: ν = 3320, 3270 (N–H), 1720 (ester C=O), 1650 (amide C=O), 1616 (C=N), 1226 (C–S) cm^{-1}. – ^1H NMR: δ = 10.25 (s, 1H, N–H), 9.90 (s, 1H, PhN–H), 7.77 – 7.05 (m, 9H, Ar-H), 4.10 – 3.98 (q, 2H, OCH_2, J = 7 Hz), 3.86 (s, 2H, SCH_2), 1.21 – 1.10 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 169.5 (ester C=O), 160.9 (amide C=O), 140.5 (C=N), 139.2 – 115.7 (Ar-C), 61.6 (OCH_2), 33.9 (SCH_2), 14.3 (CH_3) ppm. – MS: *m/z* = 375 $[M]^+$. – $C_{18}H_{18}FN_3O_3S$ (375.42): calcd. C 57.59, H 4.83, N 11.19; found C 57.37, H 4.69, N 11.19.

*Ethyl 6-(4-methylphenyl)-4-phenylaminocarbonyl-3,5,6-thiadiaza-4-hexenoate (**4e**)*

M. p. 129 – 130 °C (ethanol). – Yield 77 %. – IR: ν = 3320, 3270 (N–H), 1710 (ester C=O), 1650 (amide C=O), 1620 (C=N), 1229 (C–S) cm^{-1}. – ^1H NMR: δ = 10.36 (s, 1H, N–H), 9.90 (s, 1H, PhN–H), 7.78 – 7.00 (m, 9H, Ar-H), 4.18 – 4.06 (q, 2H, OCH_2, J = 7 Hz), 3.91 (s, 2H, SCH_2), 2.25 (s, 3H, CH_3), 1.23 – 1.11 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 169.9 (ester C=O), 160.3 (amide C=O), 141.6 (C=N), 139.1 – 114.5 (Ar-C), 61.2 (OCH_2), 33.7 (SCH_2), 20.5 (CH_3), 14.0 (CH_3) ppm. – MS: *m/z* = 371 $[M]^+$. – $C_{19}H_{21}N_3O_3S$ (371.46): calcd. C 61.44, H 5.70, N 11.31; found C 65.18, H 5.67, N 11.18.

*Ethyl 4-benzoyl-6-(4-chlorophenyl)-3,5,6-thiadiaza-4-hexenoate (**4f**)*

M. p. 136 – 138 °C (methanol). – Yield 72 %. – IR: ν = 3316 (N–H), 1705 (ester C=O), 1645 (C=O), 1605 (C=N), 1232 (C–S) cm^{-1}. – ^1H NMR: δ = 10.35 (s, 1H, N–H), 8.05 – 7.07 (m, 9H, Ar-H), 4.25 – 4.14 (q, 2H, OCH_2, J = 7 Hz), 3.89 (s, 2H, SCH_2), 1.33 – 1.23 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 187.50 (C=O), 169.2 (ester C=O), 141.7 (C=N), 136.9 – 115.5 (Ar-C), 61.9 (OCH_2), 33.4 (SCH_2), 14.1 (CH_3) ppm. – MS: *m/z* = 376/378 $[M]^+$. – $C_{18}H_{17}ClN_2O_3S$ (376.86): calcd. C 57.37, H 4.55, N 7.43; found C 57.25, H 4.65, N 7.32.

*Ethyl 6-(4-chlorophenyl)-4-(2-furoyl)-3,5,6-thiadiaza-4-hexenoate (**4g**)*

M. p. 144 – 146 °C (methanol). – Yield 78 %. – IR: ν = 3333 (N–H), 1725 (ester C=O), 1665 (C=O), 1620 (C=N), 1230 (C–S) cm^{-1}. – ^1H NMR: δ = 10.41 (s, 1H, N–H), 8.20 – 7.16 (m, 7H, Ar-H), 4.28 – 4.19 (q, 2H, OCH_2, J = 7 Hz), 3.90 (s, 2H, SCH_2), 1.29 – 1.18 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 173.6 (C=O), 169.5 (ester C=O), 141.4 (C=N), 139.9 – 119.8 (Ar-C), 62.1 (OCH_2), 33.4 (SCH_2), 14.1 (CH_3) ppm. – MS: *m/z* = 366/368 $[M]^+$. –

$C_{16}H_{15}ClN_2O_4S$ (366.83): calcd. C 52.39, H 4.12, N 7.64; found C 52.50, H 4.00, N 7.73.

*Ethyl 6-(4-chlorophenyl)-4-(2-thenoyl)-3,5,6-thiadiaza-4-hexenoate (**4h**)*

M. p. 155 – 157 °C (methanol). – Yield 75 %. – IR: ν = 3330 (N–H), 1725 (ester C=O), 1660 (C=O), 1622 (C=N), 1232 (C–S) cm^{-1}. – ^1H NMR: δ = 10.44 (s, 1H, N–H), 8.25 – 7.20 (m, 7H, Ar-H), 4.30 – 4.20 (q, 2H, OCH_2, J = 7 Hz), 3.91 (s, 2H, SCH_2), 1.30 – 1.19 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 174.5 (C=O), 169.6 (ester C=O), 141.3 (C=N), 139.9 – 119.8 (Ar-C), 62.3 (OCH_2), 33.6 (SCH_2), 14.3 (CH_3) ppm. – MS: *m/z* = 382/384 $[M^+]$. – $C_{16}H_{15}ClN_2O_3S$ (382.89): calcd. C 50.19, H 3.95, N 7.32; found C 50.98, H 4.11, N 7.41.

*Ethyl 4-(2-naphthoyl)-6-phenyl-3,5,6-thiadiaza-4-hexenoate (**4i**)*

M. p. 173 – 175 °C (methanol). – Yield 78 %. – IR: ν = 3314 (N–H), 1711 (ester C=O), 1647 (C=O), 1605 (C=N), 1222 (C–S) cm^{-1}. – ^1H NMR: δ = 10.38 (s, 1H, N–H), 8.75 – 7.13 (m, 11H, Ar-H), 4.31 – 4.20 (q, 2H, OCH_2, J = 7 Hz), 3.89 (s, 2H, SCH_2), 1.32 – 1.21 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 187.2 (C=O), 169.2 (ester C=O), 141.9 (C=N), 140.6 – 115.4 (Ar-C), 62.0 (OCH_2), 33.2 (SCH_2), 14.6 (CH_3) ppm. – MS: *m/z* = 392 $[M]^+$. – $C_{22}H_{20}N_2O_3S$ (392.48): calcd. C 67.33, H 5.14, N 7.14; found C 67.20, H 5.26, N 7.23.

*Ethyl 6-(4-chlorophenyl)-4-(2-naphthoyl)-3,5,6-thiadiaza-4-hexenoate (**4j**)*

M. p. 168 – 170 °C (methanol). – Yield 72 %. – IR: ν = 3305 (N–H), 1707 (ester C=O), 1640 (C=O), 1600 (C=N), 1220 (C–S) cm^{-1}. – ^1H NMR: δ = 10.40 (s, 1H, N–H), 8.72 – 7.10 (m, 11H, Ar-H), 4.32 – 4.22 (q, 2H, OCH_2, J = 7 Hz), 3.92 (s, 2H, SCH_2), 1.31 – 1.19 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 187.0 (C=O), 169.4 (ester C=O), 141.9 (C=N), 140.2 – 116.5 (Ar-C), 61.3 (OCH_2), 33.5 (SCH_2), 14.6 (CH_3) ppm. – MS: *m/z* = 426/428 $[M]^+$. – $C_{22}H_{19}ClN_2O_3S$ (426.93): calcd. C 61.89, H 4.49, N 6.56; found C 62.05, H 4.37, N 6.50.

*Ethyl 6-(4-methylphenyl)-4-(2-naphthoyl)-3,5,6-thiadiaza-4-hexenoate (**4k**)*

M. p. 143 – 145 °C (methanol). – Yield 74 %. – IR: ν = 3310 (N–H), 1718 (ester C=O), 1645 (C=O), 1610 (C=N), 1227 (C–S) cm^{-1}. – ^1H NMR: δ = 10.39 (s, 1H, N–H), 8.75 – 7.11 (m, 11H, Ar-H), 4.30 – 4.21 (q, 2H, OCH_2, J = 7 Hz), 3.88 (s, 2H, SCH_2), 2.27 (s, 3 H, CH_3), 1.28 – 1.14 (t, 3H, CH_3, J = 7 Hz) ppm. – ^{13}C NMR: δ = 187.2 (C=O), 169.0 (ester C=O), 141.8 (C=N), 139.8 – 116.1 (Ar-C), 62.3 (OCH_2), 33.5 (SCH_2), 20.7 (CH_3), 14.5 (CH_3) ppm. – MS: *m/z* = 406 $[M]^+$. – $C_{23}H_{22}N_2O_3S$ (406.51): calcd. C 97.96, H 5.46, N 6.89; found C 68.05, H 5.35, N 6.95.

*Cyclization of compounds **4a – k***

Method A: Compounds **4a – k** (5 mmol) were added to a methanolic solution of sodium methoxide – prepared from sodium metal (0.12 g, 5 mmol) and methanol (20 mL) – under stirring at r. t. The resulting solution was refluxed for 2 – 3 h. After cooling the solvent was removed under reduced pressure, and the residue was washed with water. The solid was collected and recrystallized from ethanol to give the desired cyclic compounds **5a – k**.

Method B: To a stirred solution of compounds **4a – k** (5 mmol) in dry THF (30 mL) was carefully added lithium hydride (0.08 g, 10 mmol) at r. t. The resulting reaction mixture was refluxed for 30 min. After cooling excess lithium hydride was destroyed with some drops of glacial acetic acid. The solvent was evaporated under reduced pressure and the product extracted three times with chloroform. The combined organic extracts were dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The resulting solid product was collected and recrystallized from ethanol to give compounds **5a – k** that were identical with the ones prepared by method A.

*4-Phenyl-2-phenylaminocarbonyl-6H-1,3,4-thiadiazin-5-one (**5a**)*

M. p. 151 – 153 °C (ethanol). – Yield 70 %. – IR: ν = 3273 (N–H), 1678 (lactam C=O), 1652 (amide C=O), 1590 (C=N) cm^{-1}. – ^1H NMR: δ = 10.32 (s, 1H, PhN–H), 7.77 – 7.13 (m, 10H, Ar-H), 3.90 (s, 2H, CH_2) ppm. – ^{13}C NMR: δ = 159.4 (lactam C=O), 158.2 (amide C=O), 143.4 (C=N), 138.7 – 115.6 (Ar-C), 26.0 (CH_2) ppm. – MS: *m/z* = 311 $[M]^+$. – $C_{16}H_{13}N_3O_2S$ (311.36): calcd. C 61.72, H 4.21, N 13.50; found C 61.55, H 4.10, N 13.65.

*4-(4-Chlorophenyl)-2-phenylaminocarbonyl-6H-1,3,4-thiadiazin-5-one (**5b**)*

M. p. 170 – 172 °C (ethanol). – Yield 68 %. – IR: ν = 3273 (N–H), 1678 (lactam C=O), 1652 (amide C=O), 1596 (C=N) cm^{-1}. – ^1H NMR: δ = 10.34 (s, 1H, PhN–H), 7.77 – 7.18 (m, 9H, Ar-H), 3.91 (s, 2H, CH_2) ppm. – ^{13}C NMR: δ = 159.9 (lactam C=O), 158.5 (amide C=O), 143.1 (C=N), 138.9 – 115.9 (Ar-C), 26.0 (CH_2) ppm. – MS: *m/z* = 345/347 $[M]^+$. – $C_{16}H_{12}ClN_3O_2S$ (345.81): calcd. C 55.57, H 3.50, N 12.15; found C 55.42, H 3.61, N 12.08.

*4-(4-Bromophenyl)-2-phenylaminocarbonyl-6H-1,3,4-thiadiazin-5-one (**5c**)*

M. p. 180 – 182 °C (ethanol). – Yield 75 %. – IR: ν = 3272 (N–H), 1675 (lactam C=O), 1652 (amide C=O), 1598

(C=N) cm^{-1}. – ^1H NMR: δ = 10.33 (s, 1H, PhN–H), 7.78 – 7.14 (m, 9H, Ar-H), 3.92 (s, 2H, CH_2) ppm. – ^{13}C NMR: δ = 159.5 (lactam C=O), 158.4 (amide C=O), 143.3 (C=N), 139.9 – 120.0 (Ar-C), 26.1 (CH_2) ppm. – MS: *m/z* = 390/392 $[M]^+$. – $C_{16}H_{12}BrN_3O_2S$ (390.26): calcd. C 49.24, H 3.10, N 10.77; found C 49.35, H 2.98, N 10.86.

*4-(4-Fluorophenyl)-2-phenylaminocarbonyl-6H-1,3,4-thiadiazin-5-one (**5d**)*

M. p. 190 – 192 °C (ethanol). – Yield 70 %. – IR: ν = 3273 (N–H), 1678 (lactam C=O), 1652 (amide C=O), 1594 (C=N) cm^{-1}. – ^1H NMR: δ = 10.36 (s, 1H, PhN–H), 7.60 – 7.13 (m, 9H, Ar-H), 3.91 (s, 2H, CH_2) ppm. – ^{13}C NMR: δ = 159.8 (lactam C=O), 158.5 (amide C=O), 141.6 (C=N), 139.0 – 115.2 (Ar-C), 26.0 (CH_2) ppm. – MS: *m/z* = 329 $[M]^+$. – $C_{16}H_{12}FN_3O_2S$ (329.36): calcd. C 58.35, H 3.67, N 12.76; found C 58.15, H 3.80, N 12.83.

*4-(4-Methylphenyl)-2-phenylaminocarbonyl-6H-1,3,4-thiadiazin-5-one (**5e**)*

M. p. 195 – 197 °C (ethanol). – Yield 68 %. – IR: ν = 3272 (N–H), 1675 (lactam C=O), 1652 (amide C=O), 1598 (C=N) cm^{-1}. – ^1H NMR: δ = 10.02 (s, 1H, PhN–H), 7.87 – 7.14 (m, 9H, Ar-H), 3.92 (s, 2H, CH_2), 2.37 (s, 2H, CH_3) ppm. – ^{13}C NMR: δ = 159.2 (lactam C=O), 158.1 (amide C=O), 142.2 (C=N), 139.7 – 114.9 (Ar-C), 26.0 (CH_2), 20.9 (CH_3) ppm. – MS: *m/z* = 325 $[M]^+$. – $C_{17}H_{15}N_3O_2S$ (325.39): calcd. C 62.75, H 4.65, N 12.91; found: C 62.90, H 4.52, N 13.05.

*2-Benzoyl-4-(4-chlorophenyl)-6H-1,3,4-thiadiazin-5-one (**5f**)*

M. p. 153 – 155 °C (ethanol). – Yield 71 %. – IR: ν = 1680 (lactam C=O), 1645 (C=O), 1605 (C=N), 1208 (C–S) cm^{-1}. – ^1H NMR: δ = 8.1 – 7.15 (m, 10H, Ar-H), 3.86 (s, 2H, CH_2) ppm. – ^{13}C NMR: δ = 186.5 (C=O), 158.9 (lactam C=O), 143.5 (C=N), 139.2 – 115.1 (Ar-C), 26.3 (CH_2) ppm. – MS: *m/z* = 330/332 $[M]^+$. – $C_{16}H_{11}ClN_2O_2S$ (330.80): calcd. C 58.10, H 3.35, N 8.47; found C 57.90, H 3.15, N 8.53.

*4-(4-Chlorophenyl)-2-(2-furoyl)-6H-1,3,4-thiadiazin-5-one (**5g**)*

M. p. 173 – 175 °C (ethanol). – Yield 73 %. – IR: ν = 1682 (lactam C=O), 1660 (C=O), 1600 (C=N), 1207 (C–S) cm^{-1}. – ^1H NMR: δ = 8.20 – 7.13 (m, 10H, Ar-H), 3.90 (s, 2H, CH_2) ppm. – ^{13}C NMR: δ = 172.8 (C=O), 159.1 (lactam C=O), 143.9 (C=N), 141.7 – 115.5 (Ar-C), 26.3 (CH_2) ppm. – MS: *m/z* = 320/322 $[M]^+$. – $C_{14}H_9ClN_2O_3S$ (320.76): calcd. C 52.42, H 2.83, N 8.73; found C 52.33, H 3.00, N 8.90.

*4-(4-Chlorophenyl)-2-(2-thenoyl)-6H-1,3,4-thiadiazin-5-one (**5h**)*

M. p. 184 – 186 °C (ethanol). – Yield 72 %. – IR: ν = 1681 (lactam C=O), 1656 (C=O), 1602 (C=N), 1205 (C–S) cm^{-1}. – ^1H NMR: δ = 8.28 – 7.20 (m, 10H, Ar-H), 3.88 (s, 2H, CH_2) ppm. – ^{13}C NMR: δ = 173.6 (C=O), 159.0 (lactam C=O), 143.7 (C=N), 141.3 – 115.4 (Ar-C), 26.2 (CH_2) ppm. – MS: *m/z* = 336/338 $[M]^+$. – $C_{14}H_9ClN_2O_2S_2$ (336.82): calcd. C 49.92, H 2.69, N 8.32; found C 50.15, H 2.58, N 8.26.

*2-(2-Naphthoyl)-4-phenyl-6H-1,3,4-thiadiazin-5-one (**5i**)*

M. p. 203 – 205 °C (ethanol). – Yield 71 %. – IR: ν = 1677 (lactam C=O), 1640 (C=O), 1608 (C=N), 1212 (C–S) cm^{-1}. – ^1H NMR: δ = 8.55 – 7.03 (m, 10H, Ar-H), 3.86 (s, 2H, CH_2) ppm. – ^{13}C NMR: δ = 185.9 (C=O), 158.5 (lactam C=O), 144.3 (C=N), 139.6 – 115.2 (Ar-C), 26.4 (CH_2) ppm. – MS: *m/z* = 346 $[M]^+$. – $C_{20}H_{14}N_{42}O_2S$ (346.41): calcd. C 69.35, H 4.07, N 8.09; found C 69.43, H 3.90, N 7.95.

*4-(4-Chlorophenyl)-2-(2-naphthoyl)-6H-1,3,4-thiadiazin-5-one (**5j**)*

M. p. 193 – 195 °C (ethanol). – Yield 67 %. – IR: ν = 1671 (lactam C=O), 1635 (C=O), 1599 (C=N), 1209 (C–S) cm^{-1}. – ^1H NMR: δ = 8.45 – 7.10 (m, 10H, Ar-H), 3.84 (s, 2H, CH_2) ppm. – ^{13}C NMR: δ = 185.5 (C=O), 158.8 (lactam C=O), 143.8 (C=N), 139.4 – 125.5 (Ar-C), 26.2 (CH_2) ppm. – MS: *m/z* = 380/382 $[M]^+$. – $C_{20}H_{13}ClN_2O_2S$ (380.86): calcd. C 63.07, H 3.44, N 7.36; found C 62.85, H 3.53, N 7.22.

*4-(4-Methylphenyl)-2-(2-naphthoyl)-6H-1,3,4-thiadiazin-5-one (**5k**)*

M. p. 210 – 212 °C (ethanol). – Yield 65 %. – IR: ν = 1675 (lactam C=O), 1637 (C=O), 1607 (C=N), 1210 (C–S) cm^{-1}. – ^1H NMR: δ = 8.50 – 7.15 (m, 10H, Ar-H), 3.87 (s, 2H, CH_2), 2.37 (s, 3H, CH_3) ppm. – ^{13}C NMR: δ = 185.6 (C=O), 158.6 (lactam C=O), 144.0 (C=N), 139.1 – 114.6 (Ar-C), 26.3 (CH_2), 20.7 (CH_3) ppm. – MS: *m/z* = 360 $[M]^+$. – $C_{21}H_{16}N_2O_2S$ (360.44): calcd. C 69.98, H 4.47, N 7.77; found C 67.12, H 4.38, N 7.70.

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