

Heterocyclic synthesis using nitrilimines. Part 17. Synthesis of some new thiadiazinone and thiadiazepinone derivatives

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A series of new 5-arylhydrazono-5-aryl-3-carboxy-4-thiapentanoic acids were synthesized by reaction of the corresponding hydrazonoyl halides with mercaptosuccinic acid. These compounds underwent intramolecular cyclization to 1,3,4-thiadiazine-5-one and 1,3,4-thiadiazepine-5-one derivatives in presence of dicyclohexylcarbodiimide (DCC). The structure of the synthesized compounds has been established by their elemental analysis and spectral data.

Key words: nitrilimines, mercaptosuccinic acid, 1,3,4-thiadiazine-5-one, 1,3,4-thiadiazepine-5-one

INTRODUCTION

In recent years, cyclocondensations using nitrilimines have received considerable attention because they have been shown to be an efficient synthetic tool for the preparation of various thia-aza heterocycles [1–3]. Hydrazonoyl halides (nitrilimine precursors) have been employed in the synthesis of thiadiazinone derivatives, where the reactive nitrilimines are found to react with 2-sulfanyl alcanoic acids [2] or ethyl sulfanylacetate [3], yielding acyclic adducts (4-arylhydrazono-5-oxo-3-thiahexanoic acid or ethyl 6-aryl-4-aryl-3-,5,6-thiadiazinone-4-hexenoate) which underwent cyclization to 1,3,4-thiadiazinone rings in the presence of dicyclohexylcarbodiimide (DCC) or lithium hydride, or methanolic sodium methoxide. 1,3,4-Thiadiazine derivatives exhibit marked biological and pharmacological effects. Some 1,3,4-thiadiazinones have been used for the prevention and / or treatment of anemia [4] as phosphodiesterase III/IV inhibitors [5,6], for the treatment of tumours and of acquired immune deficiency syndrome (AIDS) [6, 7]. The other compounds, described in the literature, exhibit spasmolytic effects and biological activity [8–12]. Recently, we have reported the syn-

thesis of 1,2,4,5-tetrazepe-6-ones by the reaction of acetylhydrazide pyridinium chloride with different nitrilimines [13]. Thiadiazepines are reported for their potent antimicrobial [14], anti-fungal activity [15] and metalloproteinase inhibition [16]. The literature survey has shown that some fused thiadiazepines exhibit antidepressant [17], central nervous depressant [18], bactericidal [19, 20], fungicidal [19, 20], and anticancer activity [21]. Recently, 1,4,5-dibenzo[b,f]thiadiazepine has been reported to show good neuroprotective properties against neurodegenerative diseases without anticholinergic effects [22]. In extension of our research interests dealing with the construction of heterocyclic systems by means of the nitrilimine cyclocondensation methodology [23, 24], we investigated the reaction of C-substituted N-aryl-nitrilimines 2 with mercaptosuccinic acid 3 in an attempt to synthesize new derivatives of 1,3,4-thiadiazine-5-ones 4 and 1,3,4-thiadiazepine-5-ones 5 in anticipation of expected interesting biological activities.

RESULTS AND DISCUSSION

Recently, we have found that ethyl mercaptoacetate reacts readily with nitrilimines generated *in situ* from the action of triethylamine on hydrazonoyl halides, yielding 3,5,6-

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thiadiaza-4-hexenoates which underwent cyclization to the corresponding 1,3,4-thiadiazine-5-ones in the presence of methanolic sodium methoxide or lithium hydride [3]. Similarly, the reaction of the nitrilimines **2** with mercaptosuccinic acid **3** for 4–6 days at room temperature gave acyclic electrophilic addition products **4 a–k** (Scheme). The acyclic adducts **4 b, d, h, j** were cyclized intramolecularly to the corresponding 1,3,4-thiadiazin-5-ones **5 b, d, h, j** and 1,3,4-thiazepine-5-ones **6 b, d, h, j** by heating them with DCC in tetrahydrofuran (THF) (Scheme).

Spectral data analysis

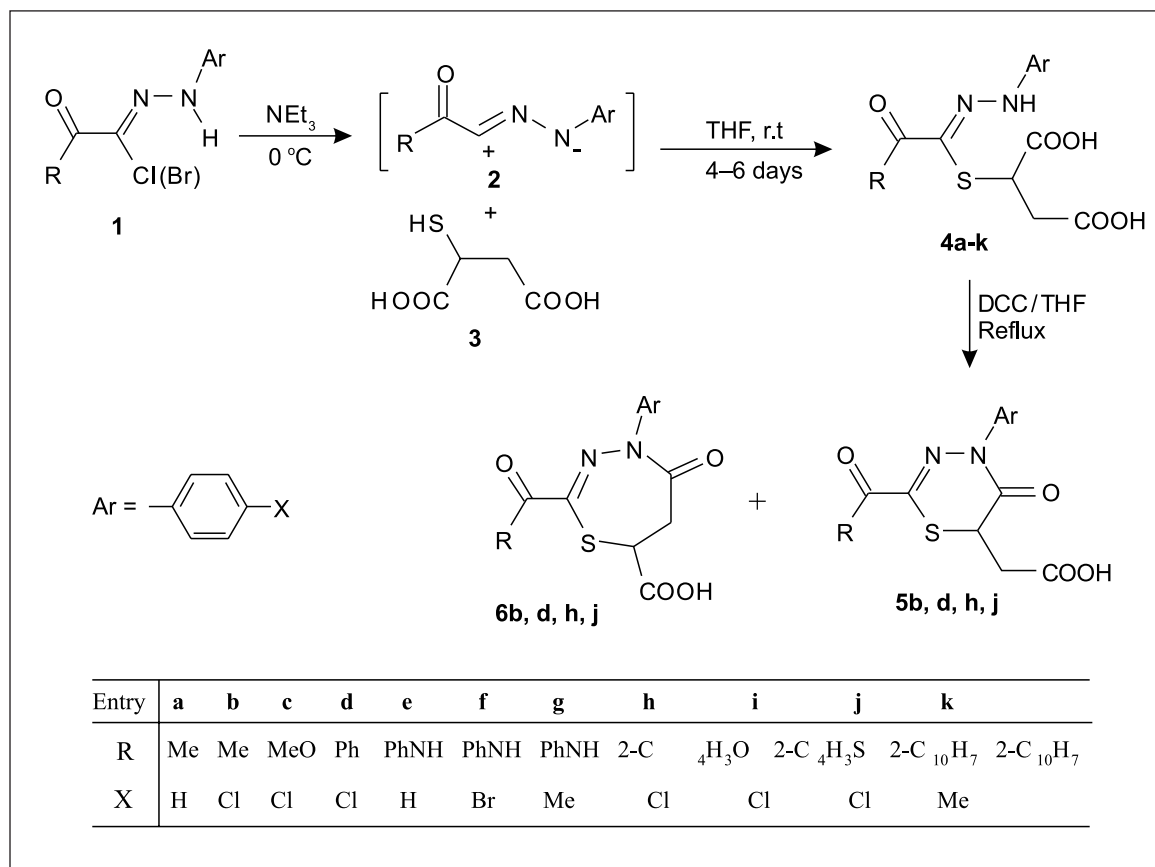
The characteristic data of compounds **4 a–k** are given in the Experimental section. These compounds gave a satisfactory combustion analysis of the proposed structures which are confirmed on the basis of their spectroscopic data. The electron impact (EI) mass spectra displayed correct molecular ions (M^+) in accordance with the suggested structures. The IR spectra of compounds **4 a–k** are characterized by the NH band in the region 3230–3340 cm^{-1} , a broad hydroxyl band in the region 2520–3200 cm^{-1} indicating a carboxyl group, a strong and broad carbonyl of the carboxyl group band in the region 1720–1730 cm^{-1} , a C = N band at 1600–1630 cm^{-1} , and a C–S stretching band appeared in the region 1220–1240 cm^{-1} . The ^1H NMR spectra of compounds **4 a–k** showed characteristic signals of the aliphatic and aro-

matic protons, especially the triplet at 4.2–4.4 ppm for the proton at C-3, and a doublet at 3.7–3.9 ppm for the protons at C-2. In addition, the NHAr proton appeared as a singlet at 10.4–10.6 ppm.

The structure of the resultant 1,3,4-thiadiazin-5-ones **5 b, d, h, j** and 1,3,4-thiazepine-5-ones **6 b, d, h, j** elucidated by their analytical and spectral data summarized in the Experimental section. Their mass spectra displayed correct molecular ion peaks [M^+] in accordance with the suggested structures. The IR spectra of compounds **5** and **6** supported the formation of cyclic structures by the absence of the NH band and the appearance of a new absorption band for lactam (C = O of the ring) in the region 1670–1680 cm^{-1} . Their ^1H NMR spectra showed all the signals of the proposed structures and the disappearance of the signal of the NHAr proton. Finally, the ^{13}C NMR data have illustrated compounds **5 b, d, h, j** and **6 b, d, h, j** to have the assigned cyclic structure supported by the presence of the signal at 159–160 ppm, which is typical of the lactam group, whereas the signal of the C = N carbon is found at 143–144 ppm.

CONCLUSION

The results demonstrate that nitrilimines react in a two-step reaction with mercaptosuccinic acid to give the 1,3,4-thiadiazine-5-one and 1,3,4-thiazepine-5-one derivatives.



Scheme. Synthetic pathway for the preparation of compounds **4**, **5** and **6**

EXPERIMENTAL

Reagents and instrumentation

Mercaptosuccinic acid, triethylamine (TEA), tetrahydrofuran (THF), dicyclohexyl-carbodiimide (DCC) and 1,4-dioxane were purchased from the Avocado Chemical Company (England) and used as purchased. Melting points were determined on a thermal melting point apparatus and are uncorrected. The IR spectra were measured as KBr pellets using a Shimadzu FT-IR 8101 PC infrared spectrophotometer. The ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AM 300 MHz spectrometer at room temperature in DMSO-d_6 solution using tetramethylsilane (TMS) as the internal reference. Chemical shifts were recorded as δ values in parts per millions (ppm) downfield from internal TMS. Electron impact (EI) mass spectra were run on a GCMS-QP1000 EX spectrometer at 70 eV. Elemental analyses were performed at the Microanalytical Center of the Cairo University, Egypt. Hydrazonoyl halides **1** were prepared according to the methods reported in the literature [14].

SYNTHESIS OF COMPOUNDS 4 (GENERAL PROCEDURE)

Reaction of nitrilimines with mercaptosuccinic acid. To a mixture of the appropriate hydrazonoyl halide **1** (0.01 mol) and mercaptosuccinic acid **3** (7.50 g, 0.05 mol) in dry tetrahydrofuran or 1,4-dioxane (100 mL), triethylamine (5 mL, 0.05 mol) was added at room temperature, and the reaction mixture was followed by TLC. The stirring continued until the starting substrates were completely consumed (4–6 days). The triethylammonium chloride salt was filtered off, the solvent was removed under reduced pressure, and the residue was partitioned between ethyl acetate and water. The aqueous layer was extracted further with ethyl acetate, and the combined organic layers were extracted with a saturated NaHCO_3 solution, washed twice with brine and dried over MgSO_4 . The solvent was evaporated *in vacuo* and the residue was treated with ethanol, whereby **4** could be isolated by slow evaporation or immediately cyclized to **5** and **6**.

The following compounds were prepared using this method:

2-(2-Oxo-N-phenylpropanehydrazonoyl)thiosuccinic acid **4a**

White solid, yield 71%, mp 230–232 °C, ^1H NMR (DMSO-d_6) δ : 2.54 (s, 3H, CH_3), 3.67 (d, 2H, $J = 6.7$ Hz, CH_2), 3.71 (t, 1H, $J = 6.7$ Hz, CH), 7.14–7.38 (m, 4H, Ar-CH), 10.60 (s, 1H, ArNH). ^{13}C NMR (DMSO-d_6) δ : 24.3 (CH_3), 39.7 (CH_2), 42.3 (CH), 125.2–141.6 (Ar-C), 145.9 (C = N), 171.8, 172.5 (COOH), 192.6 (RC = O). IR (KBr) ν/cm^{-1} : 1228 (C-S), 1628 (C = N), 1692 (RC = O), 1723, 1734 (C = O), 2525–3230 (OH), 3337 (NH), MS, (m/z): 310 $[\text{M}]^+$. Analysis (% calculated / found) for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_5\text{S}$ (Mw 310.33) C: 50.32 / 50.10, H: 4.55 / 4.45, N: 9.03 / 8.90.

2-[N-(4-Chlorophenyl)-2-oxopropanehydrazonoyl]thiosuccinic acid **4b**

White solid, yield 73%, mp 212–214 °C, ^1H NMR (DMSO-d_6) δ : 2.52 (s, 3H, CH_3), 3.70 (t, 1H, $J = 6.7$ Hz, CH), 3.66 (d, 2H, $J = 6.7$ Hz, CH_2), 7.33–7.46 (m, 4H, Ar-CH), 10.57 (s, 1H, ArNH). ^{13}C NMR (DMSO-d_6) δ : 24.6 (CH_3), 39.7 (CH_2), 42.3 (CH), 125.2–141.6 (Ar-C), 145.9 (C = N), 171.8, 172.5 (COOH), 192.4 (RC = O). IR (KBr) ν/cm^{-1} : 1224 (C-S), 1626 (C = N), 1691 (RC = O), 1721, 1732 (C = O), 2546–3235 (OH), 3342 (NH). MS, (m/z): 344 $[\text{M}]^+$, 346 $[\text{M} + 2]^+$. Analysis (% calculated / found) for $\text{C}_{13}\text{H}_{13}\text{ClN}_2\text{O}_5\text{S}$ (Mw 344.78) C: 45.29 / 45.65, H: 3.80 / 3.97, N: 8.13 / 8.03.

2-[N-(4-Chlorophenyl)-2-methoxy-2-oxoethanehydrazonoyl]thiosuccinic acid **4c**

White solid, yield 76%, mp 187–189 °C, ^1H NMR (DMSO-d_6) δ : 3.61 (s, 3H, OCH_3), 3.68 (d, 2H, $J = 6.7$ Hz, CH_2), 3.72 (t, 1H, $J = 6.7$ Hz, CH), 7.34–7.45 (m, 4H, Ar-CH), 10.58 (s, 1H, ArNH). ^{13}C NMR (DMSO-d_6) δ : 39.7 (CH_2), 42.3 (CH), 53.3 (OCH_3), 125.2–141.6 (Ar-C), 145.9 (C = N), 161.3 (RC = O), 171.8, 172.5 (COOH). IR (KBr) ν/cm^{-1} : 1226 (C-S), 1621 (C = N), 1715 (RC = O), 1720, 1731 (C = O), 2544–3235 (OH), 3345 (NH). MS, (m/z): 360 $[\text{M}]^+$, 362 $[\text{M} + 2]^+$. Analysis (% calculated / found) for $\text{C}_{13}\text{H}_{13}\text{ClN}_2\text{O}_6\text{S}$ (Mw 360.78) C: 43.28 / 43.05, H: 3.63 / 3.50, N: 7.76 / 7.65.

2-[N-(4-Chlorophenyl)-2-oxo-2-phenylethanehydrazonoyl]thiosuccinic acid **4d**

White solid, yield 81%, mp 193–195 °C, ^1H NMR (DMSO-d_6) δ : 3.69 (d, 2H, $J = 6.7$ Hz, CH_2), 3.77 (t, 1H, $J = 6.7$ Hz, CH), 7.12–8.20 (m, 9H, Ar-CH), 10.54 (s, 1H, ArNH). ^{13}C NMR (DMSO-d_6) δ : 39.7 (CH_2), 42.3 (CH), 125.2–141.6 (Ar-C), 145.9 (C = N), 171.8, 172.5 (COOH), 185.6 (RC = O). IR (KBr) ν/cm^{-1} : 1232 (C-S), 1618 (C = N), 1660 (RC = O), 1723, 1734 (C = O), 2530–3236 (OH), 3260, 3331 (NH). MS, (m/z): 406 $[\text{M}]^+$, 408 $[\text{M} + 2]^+$. Analysis (% calculated / found) for $\text{C}_{18}\text{H}_{15}\text{ClN}_2\text{O}_5\text{S}$ (Mw 406.85) C: 53.14 / 53.35, H: 3.72 / 3.60, N: 6.89 / 7.02.

2-[2-Anilino-2-oxo-N-phenylethanehydrazonoyl]thiosuccinic acid **4e**

White solid, yield 78%, mp 211–213 °C, ^1H NMR (DMSO-d_6) δ : 3.66 (d, 2H, $J = 6.7$ Hz, CH_2), 3.76 (t, 1H, $J = 6.7$ Hz, CH), 7.24–8.22 (m, 10H, Ar-CH), 9.86 (NH anilino), 10.52 (s, 1H, ArNH), ^{13}C NMR (DMSO-d_6) δ : 39.7 (CH_2), 42.3 (CH), 125.2–141.6 (Ar-C), 145.9 (C = N), 159.6 (RC = O), 171.8, 172.5 (COOH). IR (KBr) ν/cm^{-1} : 1237 (C-S), 1621 (C = N), 1654 (RC = O), 1723, 1734 (C = O), 2539, 3240 (OH), 3265, 3347 (NH). MS, (m/z): 387 $[\text{M}]^+$. Analysis (% calculated / found) for $\text{C}_{18}\text{H}_{18}\text{N}_3\text{O}_5\text{S}$ (Mw 387.42) C: 55.81 / 56.05, H: 4.42 / 4.55, N: 10.85 / 10.70.

2-[2-Anilino-N-(4-bromophenyl)-2-oxoethanehydrazonoyl]thiosuccinic acid **4f**

White solid, yield 74%, mp 200–202 °C, ^1H NMR (DMSO-d_6) δ : 3.67 (d, 2H, $J = 6.7$ Hz, CH_2), 3.74 (t, 1H, $J = 6.7$ Hz, CH),

7.26–7.28 (m, 9H, Ar-CH), 9.88 (NH anilino), 10.51 (s, 1H, ArNH). ¹³C NMR (DMSO-d₆) δ: 39.7 (CH₂), 42.3 (CH), 125.2–141.6 (Ar-C), 145.9 (C = N), 159.5 (RC = O), 171.8–172.5 (COOH). IR (KBr) ν/cm^{-1} : 1236 (C-S), 1 623 (C = N), 1656 (RC = O), 1723, 1734 (C = O), 2533–3240 (OH), 3248–3341 (NH). MS, (*m/z*): 466 [M]⁺. Analysis (% calculated / found) for C₁₈H₁₆BrN₃O₅S (Mw 466.31) C: 46.36 / 46.55, H: 3.46 / 3.55, N: 9.01 / 8.95.

2-[2-Anilino-N-(4-methylphenyl)-2-oxoethanehydrazonoyl]thiosuccinic acid 4g

White solid, yield 74%, mp 230–232 °C, ¹H NMR (DMSO-d₆) δ: 2.26 (s, 3H, CH₃), 3.68 (d, 2H, *J* = 6.7 Hz, CH₂), 3.76 (t, 1H, *J* = 6.7 Hz, CH), 6.98–7.31 (m, 9H, Ar-CH), 9.86 (NH anilino), 10.54 (s, 1H, ArNH). ¹³C NMR (DMSO-d₆) δ: 21.6 (CH₃), 39.7 (CH₂), 42.3 (CH), 125.2–141.6 (Ar-C), 145.9 (C = N), 159.7 (RC = O), 171.8, 172.5 (COOH). IR (KBr) ν/cm^{-1} : 1238 (C-S), 1 625 (C = N), 1665 (RC = O), 1723, 1734 (C = O), 2534–3227 (OH), 3241, 3334 (NH). MS, (*m/z*): 401 [M]⁺. Analysis (% calculated / found) for C₁₉H₁₉N₃O₅S (Mw 401.44) C: 56.85 / 57.05, H: 4.77 / 4.65, N: 10.47 / 10.60.

2-[N-(4-Chlorophenyl)-2-(2-furyl)-2-oxoethanehydrazonoyl]thiosuccinic acid 4h

White solid, yield 68%, mp 160–162 °C, ¹H NMR (DMSO-d₆) δ: 3.70 (d, 2H, *J* = 6.7 Hz, CH₂), 3.81 (t, 1H, *J* = 6.7 Hz, CH), 7.18–8.23 (m, 7H, Ar-CH), 10.60 (s, 1H, ArNH). ¹³C NMR (DMSO-d₆) δ: 39.7 (CH₂), 42.3 (CH), 125.2–141.6 (Ar-C), 145.9 (C = N), 171.8, 172.5 (COOH), 174.8 (RC = O). IR (KBr) ν/cm^{-1} : 1228 (C-S), 1619 (C = N), 1662 (RC = O), 1723, 1734 (C = O), 2546–3234 (OH), 3346 (NH). MS, (*m/z*): 396 [M]⁺, 398 [M + 2]⁺. Analysis (% calculated / found) for C₁₆H₁₃ClN₂O₆S (Mw 396.81) C: 48.43 / 48.55, H: 3.30 / 3.43, N: 7.06 / 6.90.

2-[N-(4-Chlorophenyl)-2-oxo-2-(2-thienyl)ethanehydrazonoyl]thiosuccinic acid 4i

White solid, yield 66%, mp 167–169 °C, ¹H NMR (DMSO-d₆) δ: 3.69 (d, 2H, *J* = 6.7 Hz, CH₂), 3.80 (t, 1H, *J* = 6.7 Hz, CH), 7.11–8.31 (m, 7H, Ar-CH), 10.62 (s, 1H, ArNH). ¹³C NMR (DMSO-d₆) δ: 39.7 (CH₂), 42.3 (CH), 125.2–141.6 (Ar-C), 145.9 (C = N), 171.8, 172.5 (COOH), 176.6 (RC = O). IR (KBr) ν/cm^{-1} : 1226 (C-S), 1618 (C = N), 1 665 (RC = O), 1723, 1734 (C = O), 2539–3241 (OH), 3 345 (NH). MS, (*m/z*): 412 [M]⁺, 414 [M + 2]⁺. Analysis (% calculated / found) for C₁₆H₁₃ClN₂O₅S₂ (Mw 412.87) C: 46.55 / 46.35, H: 3.17 / 3.30, N: 6.78 / 6.65.

2-[N-(4-Chlorophenyl)-2-(2-naphthyl)-2-oxoethanehydrazonoyl]thiosuccinic acid 4j

White solid, yield 61%, mp 231–233 °C, ¹H NMR (DMSO-d₆) δ: 3.68 (d, 2H, *J* = 6.7 Hz, CH₂), 3.79 (t, 1H, *J* = 6.7 Hz, CH), 7.26–8.78 (m, 11H, Ar-CH), 10.59 (s, 1H, ArNH). ¹³C NMR (DMSO-d₆) δ: 39.7 (CH₂), 42.3 (CH), 125.2–141.6 (Ar-C), 145.9 (C = N), 171.8, 172.5 (COOH), 187.4 (RC = O).

IR (KBr) ν/cm^{-1} : 1219 (C-S), 1612 (C = N), 1647 (RC = O), 1723, 1734 (C = O), 2530–3230 (OH), 3341 (NH). MS, (*m/z*): 456 [M]⁺, 458 [M + 2]⁺. Analysis (% calculated / found) for C₂₂H₁₇ClN₂O₅S (Mw 456.91) C: 57.83 / 58.15, H: 3.75 / 3.60, N: 6.13 / 6.00.

2-[N-(4-Methylphenyl)-2-(2-naphthyl)-2-oxoethanehydrazonoyl]thiosuccinic acid 4k

White solid, yield 63%, mp 224–226 °C, ¹H NMR (DMSO-d₆) δ: 2.27 (s, 3H, CH₃), 3.68 (d, 2H, *J* = 6.7 Hz, CH₂), 3.77 (t, 1H, *J* = 6.7 Hz, CH), 7.24–8.75 (m, 11H, Ar-CH), 10.57 (s, 1H, ArNH). ¹³C NMR (DMSO-d₆) δ: 21.7 (CH₃), 39.7 (CH₂), 42.3 (CH), 125.2–141.6 (Ar-C), 145.9 (C = N), 171.8, 172.5 (COOH), 187.2 (RC = O). IR (KBr) ν/cm^{-1} : 1221 (C-S), 1610 (C = N), 1645 (RC = O), 1723, 1734 (C = O), 2546, 3230 (OH), 3341 (NH). MS, (*m/z*): 436 [M]⁺. Analysis (% calculated / found) for C₂₃H₂₀N₂O₅S (Mw 436.49) C: 63.29 / 63.55, H: 4.62 / 4.50, N: 6.42 / 6.60.

SYNTHESIS OF COMPOUNDS 5 AND 6 (GENERAL PROCEDURE)

Cyclization of compounds 4 b, d, h, j. To a stirred solution of compounds **4 b, d, h, j** in THF (30 mL) 1 equivalent DCC in THF (10 mL) was added at room temperature. The stirring continued until the starting substrates were completely consumed (2–3 h). The precipitate (dicyclohexyl urea) was filtered off, and the filtrate was evaporated under reduced pressure. The residue (viscous or crude solid) was dissolved in hot ethanol, and by slow cooling and evaporation of the solvent the desired cyclic compounds were obtained as a mixture which was chromatographed on preparative TLC plates, using Merck silica gel 60 HF₂₅₄ as the adsorbent, and CHCl₃ / EtOAc (5 : 1). The characteristic data of the title compounds **5 b, d, h, j** and **6 b, d, h, j** are listed below.

[2-Acetyl-4-(4-chlorophenyl)-5-oxo-5,6-dihydro-4H-1,3,4-thiadiazine-6-yl]acetic acid 5b

Yellow solid, yield 54%, mp 196–198 °C, ¹H NMR (DMSO-d₆) δ: 2.51 (s, 3H, CH₃), 3.61 (d, 2H, *J* = 7.1 Hz, CH₂), 4.59 (t, 1H, *J* = 7.1 Hz, CH), 7.26–7.48 (m, 4H, Ar-CH). ¹³C NMR (DMSO-d₆) δ: 24.7 (CH₃), 32.5 (CH₂), 34.3 (CH), 126.3–139.2 (Ar-C), 144.6 (C = N), 159.8 (C = O lactam), 171.4 (COOH), 193.7 (CH₃C = O). IR (KBr) ν/cm^{-1} : 1248 (C-S), 1 626 (C = N), 1690 (RC = O), 1 723 (C = O), 2550–3200 (OH). MS, (*m/z*): 326 [M]⁺, 328 [M + 2]⁺. Analysis (% calculated / found) for C₁₃H₁₁ClN₂O₄S (Mw 326.76) C: 47.79 / 47.50, H: 3.39 / 3.45, N: 8.57 / 8.60.

[2-Benzoyl-4-(4-chlorophenyl)-5-oxo-5,6-dihydro-4H-1,3,4-thiadiazine-6-yl]acetic acid 5d

Pale yellow solid, yield 51%, mp 183–185 °C, ¹H NMR (DMSO-d₆) δ: 3.68 (d, 2H, *J* = 7.1 Hz, CH₂), 4.55 (t, 1H, *J* = 7.1 Hz, CH), 7.13–8.20 (m, 9H, Ar-CH). ¹³C NMR (DMSO-d₆) δ: 32.7 (CH₂), 34.5 (CH), 126.6–139.7 (Ar-C), 143.7 (C = N), 159.5

(C = O lactam), 171.6 (COOH), 185.4 (PhC = O). IR (KBr) ν/cm^{-1} : 1247 (C–S), 1624 (C = N), 1655 (RC = O), 1723 (C = O), 2535–3230 (OH). MS, (m/z): 388 [M]⁺, 390 [M + 2]⁺. Analysis (% calculated / found) for C₁₈H₁₃ClN₂O₄S (Mw 388.83) C: 55.60 / 55.35, H: 3.37 / 3.25, N: 7.20 / 7.05.

[4-(4-Chlorophenyl)-2-(2-furoyl)-5-oxo-5,6-dihydro-4H-1,3,4-thiadiazine-6-yl]acetic acid 5h

White off solid, yield 53%, mp 146–148 °C, ¹H NMR (DMSO-d₆) δ : 3.61 (d, 2H, J = 7.1 Hz, CH₂), 4.59 (t, 1H, J = 7.1 Hz, CH), 7.21–8.24 (m, 7H, Ar–CH). ¹³C NMR (DMSO-d₆) δ : 32.2 (CH₂), 33.7 (CH), 126.6–139.7 (Ar–C), 143.8 (C = N), 159.8 (C = O lactam), 171.9 (COOH), 176.4 (RC = O). IR (KBr) ν/cm^{-1} : 1224 (C–S), 1626 (C = N), 1660 (RC = O), 1721 (C = O), 2540–3235 (OH). MS, (m/z): 378 [M]⁺, 380 [M + 2]⁺. Analysis (% calculated / found) for C₁₆H₁₁ClN₂O₅S (Mw 378.79) C: 50.73 / 50.95, H: 2.93 / 3.10, N: 7.40 / 7.28.

[4-(4-Chlorophenyl)-2-(2-naphthoyl)-5-oxo-5,6-dihydro-4H-1,3,4-thiadiazine-6-yl]acetic acid 5j

White solid, yield 47%, mp 213–215 °C, ¹H NMR (DMSO-d₆) δ : 3.60 (d, 2H, J = 6.9 Hz, CH₂), 4.52 (t, 1H, J = 6.9 Hz, CH), 7.05–8.56 (m, 11H, Ar–CH). ¹³C NMR (DMSO-d₆) δ : 32.0 (CH₂), 33.6 (CH), 126.6–139.7 (Ar–C), 143.7 (C = N), 159.3 (C = O lactam), 171.6 (COOH), 184.6 (RC = O). IR (KBr) ν/cm^{-1} : 1218 (C–S), 1624 (C = N), 1690 (RC = O), 1723 (C = O), 2530–3200 (OH). MS, (m/z): 438 [M]⁺, 440 [M + 2]⁺. Analysis (% calculated / found) for C₂₂H₁₅ClN₂O₄S (Mw 438.89) C: 60.21 / 60.40, H: 3.44 / 3.55, N: 6.38 / 6.25.

2-Acetyl-4-(4-chlorophenyl)-5-oxo-4,5,6,7-tetrahydro-1,3,4-thiadiazepine-7-carboxylic acid 6b

Yellow solid, yield 27%, mp 202–204 °C, ¹H NMR (DMSO-d₆) δ : 3.64 (d, 2H, J = 6.9 Hz, CH₂), 4.89 (t, 1H, J = 6.9 Hz, CH), 7.26–7.51 (m, 9H, Ar–CH). ¹³C NMR (DMSO-d₆) δ : 24.7 (CH₃), 31.9 (CH₂), 36.8 (CH), 126.6–139.7 (Ar–C), 144.3 (C = N), 160.5 (C = O ring), 171.4 (COOH), 193.6 (CH₃C = O), IR (KBr) ν/cm^{-1} : 1208 (C–S), 1624 (C = N), 1692 (RC = O), 1723 (C = O), 2560–3210 (OH). MS, (m/z): 326 [M]⁺, 328 [M + 2]⁺. Analysis (% calculated / found) for C₁₅H₁₁ClN₂O₄S (Mw 326.76) C: 47.79 / 47.95, H: 3.39 / 3.25, N: 8.57 / 8.70.

2-Benzoyl-4-(4-chlorophenyl)-5-oxo-4,5,6,7-tetrahydro-1,3,4-thiadiazepine-7-carboxylic acid 6d

Yellow solid, yield 26%, mp 179–181 °C, ¹H NMR (DMSO-d₆) δ : 3.46 (d, 2H, J = 6.9 Hz, CH₂), 4.66 (t, 1H, J = 6.9 Hz, CH), 7.10–8.12 (m, 9H, Ar–CH). ¹³C NMR (DMSO-d₆) δ : 31.7 (CH₂), 36.6 (CH), 126.6–139.7 (Ar–C), 144.7 (C = N), 160.8 (C = O ring), 171.4 (COOH), 187.6 (CH₃C = O). IR (KBr) ν/cm^{-1} : 1208 (C–S), 1624 (C = N), 1665 (RC = O), 1723 (C = O), 2520–3230 (OH). MS, (m/z): 388 [M]⁺, 390 [M + 2]⁺. Analysis (% calculated / found) for C₁₈H₁₃ClN₂O₄S (Mw 388.83) C: 55.60 / 55.34, H: 3.37 / 3.55, N: 7.20 / 7.30.

4-(4-Chlorophenyl)-2-(2-furoyl)-5-oxo-4,5,6,7-tetrahydro-1,3,4-thiadiazepine-7-carboxylic acid 6h

White solid, yield 23%, mp 154–156 °C, ¹H NMR (DMSO-d₆) δ : 3.48 (d, 2H, J = 6.9 Hz, CH₂), 4.61 (t, 1H, J = 6.9 Hz, CH), 7.20–8.32 (m, 9H, Ar–CH). ¹³C NMR (DMSO-d₆) δ : 31.4 (CH₂), 36.7 (CH), 126.6–139.7 (Ar–C), 144.4 (C = N), 160.8 (C = O ring), 171.3 (COOH), 176.2 (RC = O). IR (KBr) ν/cm^{-1} : 1208 (C–S), 1624 (C = N), 1660 (RC = O), 1723 (C = O), 2530–3235 (OH). MS, (m/z): 378 [M]⁺, 380 [M + 2]⁺. Analysis (% calculated / found) for C₁₆H₁₁ClN₂O₅S (Mw 378.79) C: 50.73 / 50.55, H: 2.93 / 2.85, N: 7.40 / 7.50.

4-(4-Chlorophenyl)-2-(2-naphthoyl)-5-oxo-4,5,6,7-tetrahydro-1,3,4-thiadiazepine-7-carboxylic acid 6j

White solid, yield 24%, mp 198–201 °C, ¹H NMR (DMSO-d₆) δ : 3.44 (d, 2H, J = 6.9 Hz, CH₂), 4.59 (t, 1H, J = 6.9 Hz, CH), 7.12–8.52 (m, 9H, Ar–CH). ¹³C NMR (DMSO-d₆) δ : 31.3 (CH₂), 36.5 (CH), 126.6–139.7 (Ar–C), 144.7 (C = N), 160.4 (C = O ring), 171.4 (COOH), 183.6 (RC = O). IR (KBr) ν/cm^{-1} : 1208 (C–S), 1624 (C = N), 1650 (RC = O), 1723 (C = O), 2545–3240 (OH). MS, (m/z): 438 [M]⁺, 440 [M + 2]⁺. Analysis (% calculated / found) for C₂₂H₁₅ClN₂O₄S (Mw 438.89) C: 60.21 / 50.45, H: 3.44 / 3.30, N: 6.38 / 6.50.

Received 18 May 2011

Accepted 27 June 2011

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HETEROCIKLŲ SINTEZĖ NAUDOJANT NITRILIMINUS. 17 DALIS. KAI KURIŲ NAUJŲ TIADIAZINONO IR TIADIAZEPINONO DARINIŲ SINTEZĖ

S a n t r a u k a

Naujos 5-arilhidrazono-5-aroil-3-karboksi-4-tiapentano rūgštys buvo susintetintos paveikus atitinkamus hidrazono halidus merkaptogintaro rūgštimi. Veikiant dicikloheksilkarbodiimidu, šie junginiai ciklizuojasi intramolekuliniu būdu, susidarant 1,3,4-tiadiazin-5-onui ir 1,3,4-tiadiazepin-5-onui.