Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS

J. Serb. Chem. Soc. *77* (7) 867–871 (2012)
JSCS–4315

UDC 547.7+547–304.9+66.095.25:542.913:
535.33.004.12
Short communication

SHORT COMMUNICATION

Synthesis and spectral properties of novel thiadiazolotriazinone derivatives

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(Received 30 September, revised 7 December 2011)

Abstract: A series of new 7-substitued-4*H*-1,3,4-thiadiazolo[2,3-*c*][1,2,4]-triazin-4-ones were synthesized in good yields by the reaction of 4-amino-3-mercapto-1,2,4-triazin-5(4*H*)-one with various aromatic carboxylic acids in the presence of phosphorus oxychloride. All the synthesized compounds were confirmed by FT-IR, NMR (^{1}H and ^{13}C) and ESI-MS spectroscopic techniques and analytical methods.

Keywords: heterocyclic; 1,2,4-triazine; cyclization; thiadiazolotriazinones.

INTRODUCTION

Triazines and their derivatives are important groups of heterocyclic compounds. They have attracted considerable interest because of their great biological importance, such as their antitumor,[1,2] anti-HIV,[3] antiviral,[4] antimalarial,[5] antibacterial,[6] antifungal[7] and antioxidant activities.[8]

Triazines have also found wide applications as herbicides[9,10] and pesticides[11] in the field of agriculture. In addition, a number of thiadiazole derivatives exhibit a broad range of biological activities due to the presence of the NCS moiety.[12]

Herein, the synthesis of 7-substitued-4*H*-1,3,4-thiadiazolo[2,3-*c*][1,2,4]triazin-4-ones **3** (Scheme 1) by condensation of 4-amino-3-mercapto-1,2,4-triazin-5(4*H*)-one **1** with various aromatic carboxylic acids **2** and their characterization using analytical and spectroscopic techniques are described.

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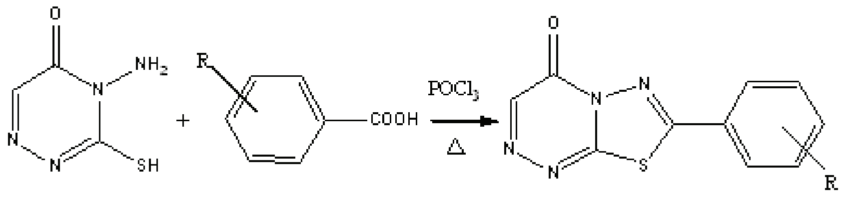
doi: 10.2298/JSC110930217G

RESULTS AND DISCUSSION

For the present work, 4-amino-3-mercapto-1,2,4-triazin-5(4*H*)-one **1** was prepared by the reaction of thiocarbohydrazide with glyoxalic acid monohydrate following a literature method.[13] Thirteen novel thiadiazolotriazine derivatives were synthesized for the first time in this study. The physical and chemical data of the synthesized compounds are given in Table I.



1 **2** **3**

Scheme 1. Synthesis of 7-substitued-4*H*-[1,3,4]thiadiazolo[2,3-*c*][1,2,4]triazin-4-ones.

TABLE I. Physical and chemical data of the synthesized compounds

Compound	R^1	Formula	M.p., °C	Yield, %	Solvent for crystallization
3a	2-Cl	$C_{10}H_5ClN_4OS$	200–201.5	52	Dioxane
3b	4-F	$C_{10}H_5FN_4OS$	190–192	62	Dioxane
3c	4-CH_3	$C_{11}H_8N_4OS$	217–219	75	Dioxane
3d	3-OCH_3	$C_{11}H_9N_4O_2S$	208–209	92	Dioxane
3e	4-OCH_3	$C_{11}H_9N_4O_2S$	240–241.5	55	Dioxane
3f	4-SCH_3	$C_{11}H_9N_4OS_2$	183–184	87	Dioxane–ethanol (1:1)
3g	4-CF_3	$C_{11}H_6F_3N_4OS$	219.5–221	55	Dioxane–ethanol (1:1)
3h	3-CH_3-4-NO_2	$C_{11}H_7N_5O_3S$	249–250	79	Dioxane
3i	2,4-Cl	$C_{10}H_4Cl_2N_4OS_2$	205–207	65	Dioxane
3j	3,4-Cl	$C_{10}H_4Cl_2N_4OS_2$	246–248	87	Dioxane
3k	3,4-OH	$C_{10}H_6N_4O_3S$	307–308.5	40	Dioxane
3l	3,4-CH_3	$C_{12}H_{10}N_4OS$	212–214	80	Dioxane
3m	3,4-OCH_3	$C_{12}H_{12}N_4O_3S$	245–247	83	Dioxane

The IR spectra of all cyclized compounds (**3a**–**m**) showed no absorption band due to the NH_2 and SH groups. These observations gave clear evidence for the formation of a fused ring system. The IR spectrum of **3c** showed absorption bands at 1715 cm^{-1} due to carbonyl group and 1615 cm^{-1} assigned to the C=N stretching mode. The characteristic C–H modes of the ring residues were observed at 3061 cm^{-1}. The C–H stretching vibration bands of the CH_3 group were at 2984–2938 cm^{-1}. The presence of aromatic rings was identified by their characteristic ring vibrations at 1461 cm^{-1} and in the 821–715 cm^{-1} range. Similarly, the IR spectrum of **3i** exhibited absorption bands at 3092 cm^{-1} due to aromatic protons and at 1707 cm^{-1} due to the C=O of the triazine carbonyl group.

Other absorption bands were observed at 1584 (C=N), 1469 (C=C) and at 869 and 715cm^{-1} (C–Cl).

In the ^{1}H-NMR spectra of the cyclized compounds, peaks due to NH$_2$ and SH groups were absent, which confirmed the involvement of these functional groups in the cyclization of triazine to thiadiazolotriazines. The ^{1}H-NMR (DMSO-d_6) spectrum of compound **3c** showed a singlet at δ 2.40 ppm, integrating for three protons arising from CH$_3$ groups. The protons of the *p*-methylphenyl ring resonated as two doublets at δ 7.45 ppm (J = 8.3 Hz) and 7.91 ppm (J = 8.29 Hz), each integrating for two protons. The signal due to the triazine ring proton appeared as a singlet at 8.58 ppm. The ^{13}C-NMR (DMSO-d_6) spectrum of compound **3c** showed signals at 21.88, 125.42, 128.46, 131.03, 144.89, 146.06, 148.57, 160.53 and 162.03 ppm. According to this APT spectral data, C$^{2\prime}$ and C$^{6\prime}$ as well as C$^{3\prime}$ and C$^{5\prime}$ are magnetically equivalent to each other. They exhibited a single signal at 128.46 and 131.03 ppm, respectively. The ^{1}H-NMR (DMSO-d_6) spectrum of compound **3i** showed a doublet of doublets at 6.73 ppm (J = 1.96, 8.79) and two doublets at 8.01 ppm (J =1.96 Hz) and 8.10 ppm (J = 8.79 Hz), confirming the presence of the aromatic group. The signal due to the triazine ring appeared as a singlet at 8.63 ppm. The ^{13}C-NMR (DMSO-d_6) spectrum of **3i** showed the following signals 126.06, 129.41, 131.38, 133.17, 134.05, 138.97, 146.01, 148.45, 156.62 and 161.92 ppm, which account for the ten different carbon atoms present in the molecule.

The molecular ion peaks were determined for all the synthesized compounds. The mass spectrum of **3c** showed a protonated molecular ion peak at m/z = = 245.15 (100, [M+1]$^+$), which is consistent with molecular formula $C_{11}H_8N_4OS$. The mass spectrum of **3i** showed the presence of a molecular ion peak at m/z = = 299.27 (100, [M]$^+$), which is in agreement with the molecular formula $C_{10}H_4Cl_2N_4OS$. The spectral data of all the newly synthesized compounds are presented in the Supplementary Material to this paper.

EXPERIMENTAL

All chemicals and solvents were of reagent grade and used without further purification. The reactions were monitored by thin layer chromatography (TLC) using Merck silica gel 60 F$_{254}$ coated alumina plates with ultraviolet light detection. The elemental data were obtained with a Thermo Finnigan Flash EA 1112 analyzer. The melting points were determined using a Büchi melting point apparatus. The FT-IR spectra were recorded in KBr disks on a Mattson 1000 FT-IR spectrometer. The ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Unity Inova instrument operating at 500 MHz. The residual DMSO-d_6 signal was also used as an internal reference. The Electron Spray Ionization-Mass Spectroscopy (ESI–MS) analyses were realized in positive ion modes using a Thermo Finnigan LCQ Advantage MAX LC/MS/MS spectrometer.

*General procedure for the synthesis of compounds **3a–m***

A mixture of 4-amino-3-mercapto-1,2,4-triazin-5(4*H*)-one **1** (0.001 mol) and mono- or di-substituted carboxylic acids **2** (0.001 mol) in 10 mL phosphorus oxychloride was refluxed on a water bath for about 8–10 h. The extent of the reaction was monitored by TLC. After cooling, the excess of phosphorus oxychloride was removed under vacuum. The reaction mixture was poured onto crushed ice. The precipitate was filtered, washed with sodium bicarbonate and water. The crude product was recrystallized from appropriate solvents, given in Table I.

CONCLUSIONS

In conclusion, thirteen novel 7-substitued-4*H*-1,3,4-thiadiazolo[2,3-*c*]1,2,4-triazin-4-ones (**3a**–**m**) were synthesized for the first time in this study. The structures of products were determined by FT-IR, NMR (^{1}H and ^{13}C) and ESI-MS spectroscopic techniques and analytical methods.

SUPPLEMENTARY MATERIAL

Analytic and spectral data of the synthesized compounds are available electronically from http://www.shd.org.rs/JSCS/, or from the corresponding author on request.

Acknowledgement. This work was supported by the Research Fund of Istanbul University, Project No.: 2085.

ИЗВОД

СИНТЕЗА И СПЕКТРАЛНЕ КАРАКТЕРИСТИКЕ НОВИХ ДЕРИВАТА ТИЈАДИАЗОЛОТРИАЗИНОНА

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Синтетисана је серија 7-супституисаних деривата 4*H*-1,3,4-тијадиазоло[2,3-*c*][1,2,4]-триазин-4-она, у добром приносу, реакцијом 4-амино-3-меркапто-1,2,4-триазин-5(4*H*)-она са различитим ароматичним карбоксилним киселинама у присуству фосфор-оксихлорида. Структура свих добијених деривата потврђена је помоћу FT-IR, NMR (^{1}H и ^{13}C) и ESI-MS спектроскопских и аналитичких метода.

(Примљено 30. септембра, ревидирано 7. децембра 2011)

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