Synthesis of novel 3-(2-bromophenyl)-4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thiones derivatives

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

A wide range of biological activity of 1,2,4-triazole derivatives (anti-inflammatory, antiviral, antitumor, immunostimulating, etc.) and the availability of sources for their preparation determine the prospects of using compounds of this class to create modified derivatives based on them and, as a result, medicines. Derivatives of 1,2,4-triazole have already established themselves both in the agricultural sector and in veterinary medicine and pharmacy.

The aim of work was to synthesize 3-(2-bromophenyl)-4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thiones, 2-((5-(2-bromophenyl)-4-methyl-4*H*-1,2,4-triazole-3-yl)thio)acetic acids and their salts.

Materials and methods. 3-(2-Bromophenyl)-4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thiones (4a-4c) were synthesized by refluxing 1 mol 2-(2-bromobenzoyl)-N-substitutedhydrazinecarbothioamides (3a-3c) with 2 mol KOH in water medium and after cooling neutralized with acetic acid. 2-((5-(2-Bromophenyl)-4-substituted-4*H*-1,2,4-triazole-3-yl)thio)acetic acids (5a-5c) were obtained by refluxing the solution of 0,1 mol NaOH and substances 4a-4c respectively. It was dissolved in 2-propanol medium with 0,1 mol 2-chloroacetic acid. 2-((5-(2-Bromophenyl)-4-substituted-4*H*-1,2,4-triazole-3-yl)thio)acetic acid salts (6a-6o) were synthesized by adding organic amines or inorganic salts to substances 5a-5c respectively in 2-propanol or water medium. The elemental analysis of synthesized compounds was established by the universal analyzer Elementar Vario L cube (CHNS). The 1H spectra (at 400 MHz and 100 MHz) were recorded in DMSO-d6 on a Varian MR-400 spectrometer and analyzed with the ADVASP™ Analyzer program. The completeness of the reactions and the individuality of the resulting compounds were controlled by the gas chromatograph Agilent 7890B with a 5977B mass spectrometry detector.

Results. It was synthesized new 3-(2-bromophenyl)-4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thionesand there derivatives, the structure of compounds was confirmed using Elemental analysis (CHNS), ^{1}HNMR and Chromatographic mass spectral analysis.

Conclusions. As a result, 21 novel compounds of 3-(2-bromophenyl)-4-substituted-1H-1,2,4-triazole-5(4H)-thiones were synthesized and characterized.

Синтез нових похідних 3-(2-бромфеніл)-4-заміщених-1*H*-1,2,4-тріазол-5(4*H*)-тіонів

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Широкий спектр біологічної активності похідних 1,2,4-тріазолу (протизапальна, противірусна, протипухлинна, імуностимулювальна тощо) і доступність джерел їх отримання визначають перспективність використання сполук цього класу для створення на їхній основі модифікованих похідних, а отже і лікарських препаратів. Похідні 1,2,4-тріазолу зарекомендували себе в аграрному секторі, ветеринарії та фармації.

Мета роботи – синтез 3-(2-бромфеніл)-4-заміщених-1*H*-1,2,4-тріазол-5(4*H*)-тіонів, 2-((5-(2-бромфеніл)-4-метил-4*H*-1,2,4-тріазол-3-іл)тіо)оцтових кислот і їхніх солей.

Матеріали та методи. 3-(2-Бромофеніл)-4-заміщені-1*H*-1,2,4-тріазол-5(4*H*)-тіони (4а–4с) синтезували під час кип'ятіння зі зворотним холодильником 1 моль 2-(2-бромбензоїл)-N-заміщених гідразинкарботіоамідів (3а–3с) з 2 моль КОН у водному середовищі та після охолодження нейтралізували оцтовою кислотою. 2-((5-(2-Бромофеніл)-4-заміщені-4*H*-1,2,4-тріазол-3-іл)тіо)оцтові кислоти (5а–5с) отримали під час кипіння розчину 0,1 моль NaOH та речовин 4а–4с і 0,1 моль 2-хлороцтової кислоти в середовищі 2-пропанолу. Солі 2-((5-(2-бромофеніл)-4-заміщені-4*H*-1,2,4-тріазол-3-іл)тіо)оцтової кислоти (6а–6о) синтезували шляхом додавання органічних амінів або неорганічних солей до речовини 5а–5с відповідно у 2-пропанолі або водному середовищі. Елементний аналіз синтезованих сполук встановили за допомогою універсального аналізатора Elementar Vario L cube (CHNS). ^{1}HNMR спектри записували в DMSO-d6 на спектрометрі Varian MR-400 (на 400 МГц та 100 МГц) та аналізували за допомогою програми ADVASP ™ Analyzer. Повноту реакцій та індивідуальність сполук контролювали газовим хроматографом Agilent 7890B із детектором мас-спектрометрії 5977B.

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Результати. Синтезували нові похідні 3-(2-бромфеніл)-4-заміщених-1*H*-1,2,4-тріазол-5(4*H*)-тіонів, структура яких підтверджена за допомогою елементного аналізу (CHNS), ^{1}HNMR та хроматографічного мас-спектрального аналізу.

Висновки. В результаті синтезували й схарактеризували 21 сполуку похідних 3-(2-бромофеніл)-4-заміщених-1*H*-1,2,4-триазол-5(4*H*)-тіонів.

Ключові слова: 1,2,4-тріазол, тіони, кислоти, солі, гетероциклічні сполуки.

Актуальні питання фармацевтичної і медичної науки та практики. 2020. Т. 13, № 1(32). С. 11–16

Синтез новых производных 3-(2-бромфенил)-4-замещенных-1*H*-1,2,4-триазол-5(4*H*)-тионов

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Широкий спектр биологической активности производных 1,2,4-триазола (противовоспалительная, противовирусная, противоопухолевая, иммуностимулирующая и т. д.) и доступность источников их получения определяют перспективность использования соединений этого класса для создания на их основе модифицированных производных и, как следствие, лекарственных препаратов. Производные 1,2,4-триазола зарекомендовали себя в аграрном секторе, ветеринарии и фармации.

Цель работы – синтез 3-(2-бромфенил)-4-замещенных-1*H*-1,2,4-триазол-5(4*H*)-тионов, 2-((5-(2-бромфенил)-4-метил-4*H*-1,2,4-триазол-3-ил)тио)ацетатных кислот и их солей.

Материалы и методы. 3-(2-Бромофенил)-4-замещенные-1*H*-1,2,4-триазол-5(4*H*)-тионы (4а–4с) синтезировали при кипячении с обратным холодильником 1 моль 2-(2-бромбензоил)-N-замещенных гидразинкарботиоамидов (3а–3с) с 2 моль КОН в водной среде и после охлаждения нейтрализовали уксусной кислотой. 2-((5-(2-Бромофенил)-4-замещенные-4*H*-1,2,4-триазол-3-ил)тио) уксусные кислоты (5а–5с) получены при кипении раствора 0,1 моль NaOH и веществ 4а–4с и 0,1 моль 2-хлоруксусной кислоты в среде 2-пропанола. Соли 2-((5-(2-бромофенил)-4-замещенных-4*H*-1,2,4-триазол-3-ил)тио)уксусной кислоты (6а–6о) синтезировали путем добавления органических аминов или неорганических солей к веществу 5а–5с соответственно в 2-пропаноле или водной среде. Элементный анализ синтезированных соединений установили с помощью универсального анализатора Elementar Vario L cube (CHNS). 1HNMR спектры записывали в DMSO-d6 на спектрометре Varian MR-400 (на 400 МГц и 100 МГц) и анализировали с помощью программы ADVASP ™ Analyzer. Полноту реакций и индивидуальность получаемых соединений контролировали с помощью газового хроматографа Agilent 7890B с детектором масс-спектрометрии 5977B.

Результаты. Синтезированы новые производные 3-(2-бромфенил)-4-замещенных-1*H*-1,2,4-триазол-5(4*H*)-тионов, структура которых подтверждена с помощью элементного анализа (CHNS), 1HNMR и хроматографического масс-спектрального анализа.

Выводы. В результате синтезировано и охарактеризовано 21 соединение производных 3-(2-бромофенил)-4-замещенных-1*H*-1,2,4-триазол-5(4*H*)-тионов.

Ключевые слова: 1,2,4-триазол, тионы, кислоты, соли, гетероциклические соединения.

Актуальные вопросы фармацевтической и медицинской науки и практики. 2020. Т. 13, № 1(32). С. 11–16

A wide range of biological activity of 1,2,4-triazole derivatives (anti-inflammatory, antiviral, antitumor, immunostimulating, etc.) [1–4] and the availability of sources for their preparation determine to use this class of compounds. New derivatives based on 1,2,4-triazole are creating. Derivatives of 1,2,4-triazole have already established themselves both in the agricultural sector and in veterinary medicine and pharmacy [5–7].

Derivatives of 3,4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thiones show diuretic, antimicrobial, analgesic, actoprotective and other types of activities [8–10].

A literature data [11,12] showed that the range of 1,2,4-triazole derivatives is huge. But despite this, there is no data on 3-(2-bromophenyl)-4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thiones, 2-((5-(2-bromophenyl)-4-methyl-4*H*-1,2,4-triazol-3-yl) thio)acetic acids and their salts.

The aim

The aim of work was to synthesize 3-(2-bromophenyl)-4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thiones, 2-((5-(2-bromophenyl)-4-methyl-4H-1,2,4-triazol-3-yl)thio)acetic acids and their salts.

Material and methods

The melting point was defined by the open capillary method on the OptiMelt MPA100 device with platinum RTD sensor and temperature measurements to 400 °C with 0.1 °C resolution (US production).

The elemental analysis of synthesized compounds was established by the universal analyzer Elementar Vario L cube (CHNS) (standard – sulfanilamide) (Analysensysteme GmbH, Germany). The H spectra (at 400 MHz and 100 MHz) were recorded in DMSO-d_6 on a Varian MR-400 spectrometer and analyzed with ADVASP™ Analyzer program (Umatek International Inc.); chemical shifts were reported in ppm (δ scale) downfield with residual protons of the solvent (DMSO-d_6, δ = 2.49 ppm) as internal standard (*Fig. 2*).

The completeness of the reactions and the individuality of these compounds were controlled by the gas chromatograph Agilent 7890B with a 5977B mass spectrometry detector (US production) (*Fig. 2*).

Results

2-(2-Bromobenzoyl)-N-substitutedhydrazinecarbothioamides (3a–3c) were synthesized by refluxing 1 mol of 2-bromobenzo-

hydrazide (1) with 1 mol of isothiocyanate (methylisothiocyanate (2a), ethylisothiocyanate (2b), phenylisothiocyanate (2c)) in 2-propanol medium. After that 1 mol of 2-(2-bromobenzoyl)-N-substitutedhydrazinecarbothioamides (3a–3c) reflux for 2 hours with 2 mol of KOH in water medium and after cooling neutralized with acetic acid. 3-(2-Bromophenyl)-4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thiones (4a–4c) were filtered as precipitates (*Fig. 1*).

On the mass spectrum, there is a cluster of peaks due to two isomers of Bromine, which was divided into m/z 270.9 and m/z 268.9 in a 1 : 1 ratio (*Fig. 2*). Peaks that have less mass-to-charge ratio on the mass spectrum were fragmentary and fragment ions.

0,1 Mol of 3-(2-bromophenyl)-4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thiones (4a-4c) and 0,1 mol of NaOH were dissolved in 2-propanol medium with heating. Then solution was reflux with 0,1 mol of 2-chloroacetic acid for 5 hours. 2-((5-(2-Bromophenyl)-4-substituted-4*H*-1,2,4-triazole-3-yl)thio)acetic acids (5a-5c) were filtered as precipitates (*Fig. 1*).

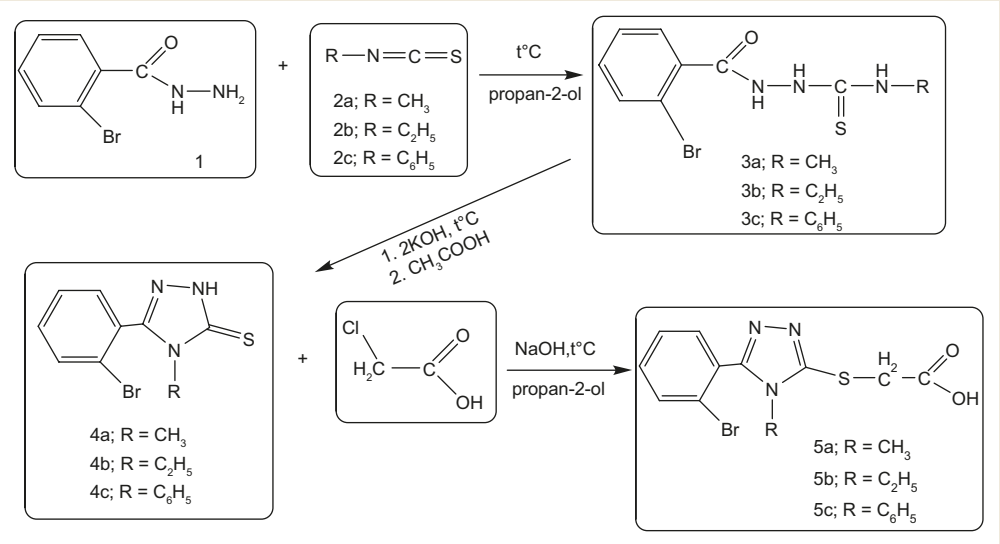
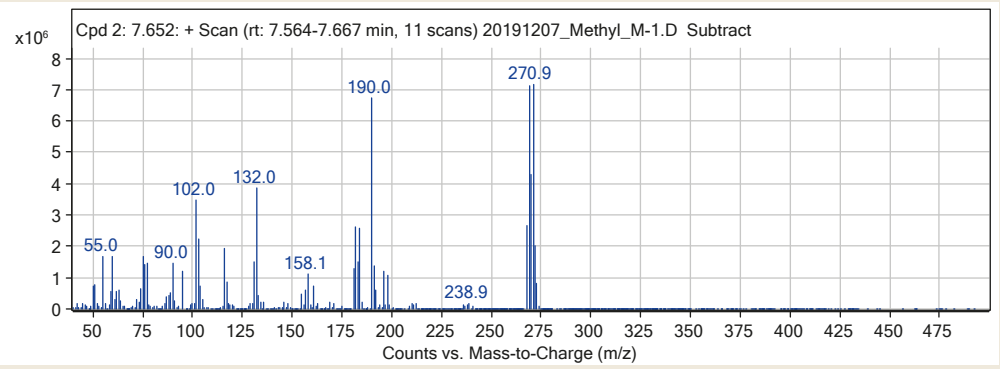


Fig. 1. Synthesis of 3-(2-bromophenyl)-4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thiones (4a–4c) and 2-((5-(2-bromophenyl)-4-substituted-4*H*-1,2,4-triazole-3-yl)thio)acetic acids (5a–5c).



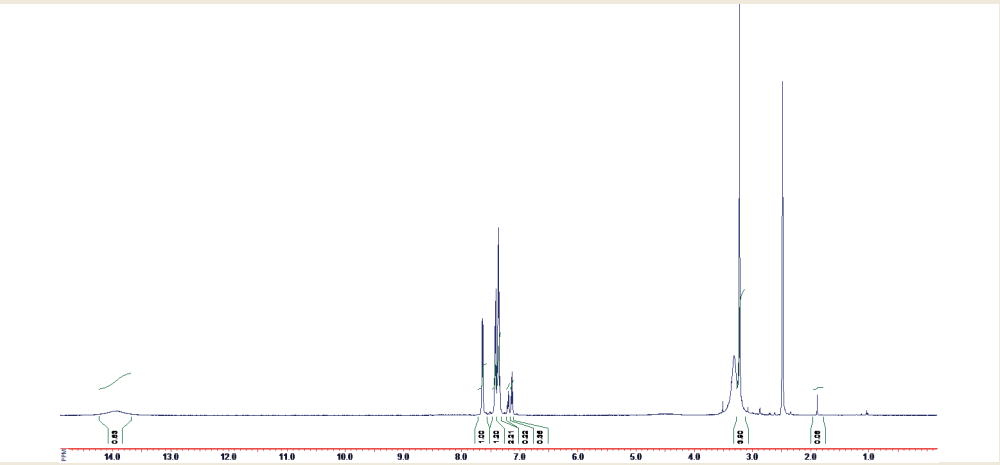


Fig. 2. Mass spectrum (left) and 1HNMR spectrum (right) of 3-(2-bromophenyl)-4-methyl-1*H*-1,2,4-triazole-5(4*H*)-thione (3a).

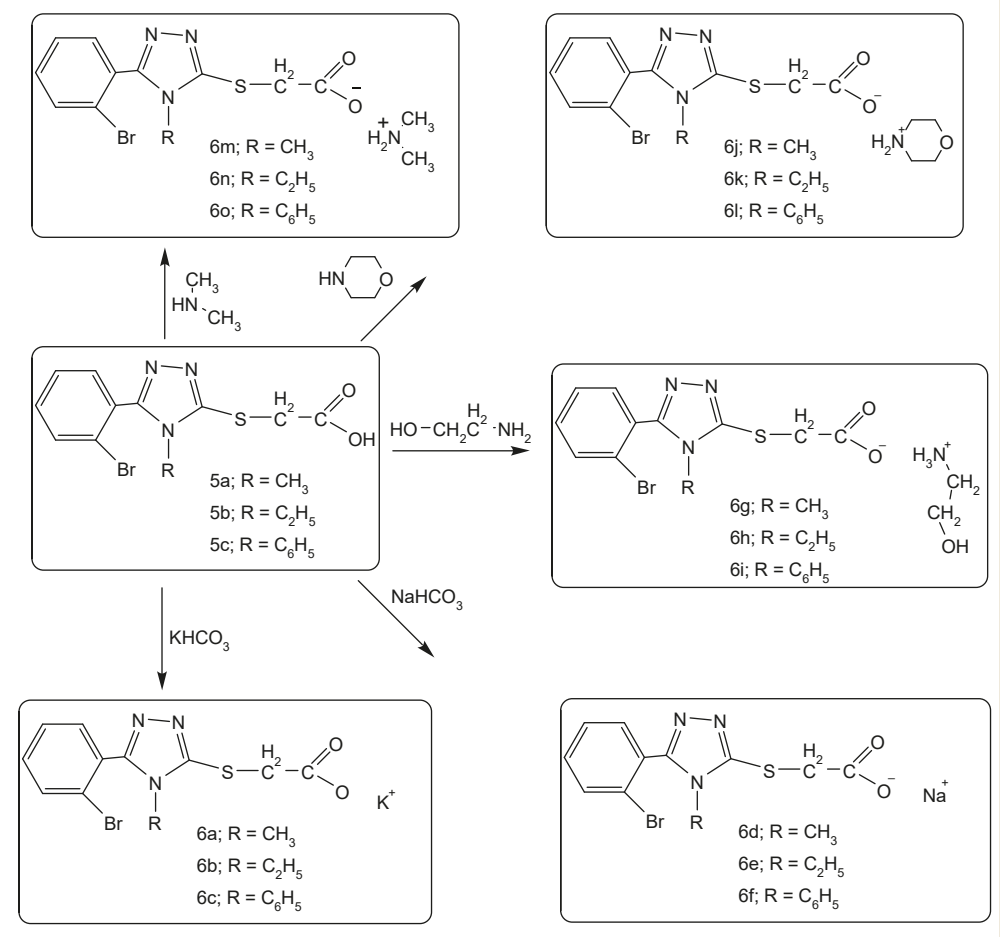


Fig. 3. Synthesis of 2-((5-(2-bromophenyl)-4-substituted-4*H*-1,2,4-triazole-3-yl)thio)acetic acid salts (6a-6o).

2-((5-(2-Bromophenyl)-4-substituted-4*H*-1,2,4-triazole-3-yl)thio)acetic acid salts (6a-6o) were synthesized by adding organic (2-aminoethanol, morpholine, dimethylamine) amines or inorganic ($KHCO_3$, $NaHCO_3$) salts to 2-((5-(2-bromophenyl)-4-substituted-4*H*-1,2,4-triazole-3-yl)thio)acetic acids (5a-5c) in 2-propanol or water medium respectively (*Fig. 3*).

Discussion

Chemical synthesis

General method for synthesis of 3-(2-bromophenyl)-4-substituted-1H-1,2,4-triazole-5(4H)-thiones (4a–4c)

1 mol of 2-(2-bromobenzoyl)-N-R-hydrazinecarbothioamides (R = methyl (3a), ethyl (3b), phenyl (3c)) were reflux for 2 hours with 2 mol of KOH in water medium. Then it was filtered and after cooling was neutralized with acetic acid. Substances 4a–4c were filtered as precipitates and were dried.

3-(2-bromophenyl)-4-methyl-1H-1,2,4-triazole-5(4H)-thione (3a)

White powder; yield 73 %; m.p. 124–126C ; HNMR (400 MHz, DMSO-d6, δ = ppm): 3.31 (CH_3, 3H, s,), 7.17–7.29 (Ar-H, 2H, 7.22 (ddd, *J* = 7.8, 7.4, 1.4 Hz), 7.24 (ddd, *J* = 8.1, 7.4, 1.3 Hz)), 7.54–7.61 (Ar-H, 2H, 7.57 (ddd, *J* = 8.1, 1.4, 0.6 Hz), 7.58 (ddd, *J* = 7.8, 1.3, 0.6 Hz)), 13.92 (NH, 1H, s); CHNS elemental analysis Calcd. for ($C_9H_8BrN_3S$) : found C% 39.90, H% 2.98, N% 15.56, S% 11.85; calculated C% 40.01, H% 2.98, N% 15.55, S% 11.87. GS/MS: 270 (m/z).

3-(2-bromophenyl)-4-ethyl-1H-1,2,4-triazole-5(4H)-thione (3b)

White powder; yield 76 %; m.p. 198–200C ; HNMR (400 MHz, DMSO-d6, δ = ppm): 1.26 (CH_3, 3H, t, *J* = 7.1 Hz), 3.90 (CH_2, 2H, q, *J* = 7.1 Hz), 7.17-7.31 (Ar-H, 2H, 7.22 (ddd, J = 7.8, 7.4, 1.4 Hz), 7.27 (ddd, J = 8.1, 7.4, 1.3 Hz)), 7.54-7.61 (Ar-H, 2H, 7.57 (ddd, J = 8.1, 1.4, 0.6 Hz), 7.58 (ddd, J = 7.8, 1.3, 0.6 Hz)), 13.86 (NH, 1H, s); CHNS elemental analysis Calcd. for ($C_{10}H_{10}BrN_3S$) : found C% 42.30, H% 3.55, N% 14.81, S% 11.29; calculated C% 42.27, H% 3.55, N% 14.79, S% 11.28. GS/MS: 285 (m/z).

3-(2-bromophenyl)-4-phenyl-1H-1,2,4-triazole-5(4H)-thione (3c)

White powder; yield 81 %; m.p. 192-194C ; HNMR (400 MHz, DMSO-d6, δ=ppm): δ 7.19–7.33 (Ar-H, 2H, 7.23 (ddd, *J* = 7.8, 7.5, 1.4 Hz), 7.28 (ddd, *J* = 8.1, 7.5, 1.4 Hz)), 7.34 (Ar-H, 1H, tt, *J* = 7.5, 1.3 Hz), 7.43 (Ar-H, 2H, dddd, *J* = 8.4, 1.6, 1.3, 0.5 Hz), 7.55–7.66 (Ar-H, 4H, 7.61 (dddd, *J* = 8.4, 7.5, 1.5, 0.5 Hz), 7.60 (ddd, *J* = 7.8, 1.4, 0.6 Hz), 7.58 (ddd, *J* = 8.1, 1.4, 0.6 Hz)), 13.64 (NH, 1H, s); CHNS elemental analysis Calcd. for ($C_{14}H_{10}BrN_3S$) : found C% 50.49, H% 3.02, N% 12.65, S% 9.62; calculated C% 50.61, H% 3.03, N% 12.65, S% 9.65. GS/MS: 332 (m/z).

Synthesis of 2-((5-(2-bromophenyl)-4-substituted-4H-1,2,4-triazole-3-yl)thio)acetic acids (5a-5c)

0,1 Mol of 3-(2-bromophenyl)-4-R-1*H*-1,2,4-triazole-5(4*H*)-thiones (R = methyl (4a), ethyl (4b), phenyl (4c)) and 0,1 mol

of NaOH were dissolved with heating in propan-2-ol medium. Then solution was reflux with 0,1 mol of 2-chloroacetic acid for 5 hours. Substances 5a-5c were filtered as precipitates and were dried.

2-((5-(2-bromophenyl)-4-methyl-4H-1,2,4-triazole-3-yl)thio) acetic acid (5a)

White powder; yield 69 %; m.p. 151–153C ; HNMR (400 MHz, DMSO-d6, δ = ppm): 3.74 (3H, s), 3.94 (2H, s), 7.31 (1H, ddd, J = 8.1, 7.8, 1.1 Hz), 7.48 (1H, ddd, J = 8.1, 7.8, 1.5 Hz), 7.64 (1H, ddd, J = 8.1, 1.5, 0.5 Hz), 7.80 (1H, ddd, J = 8.1, 1.1, 0.5 Hz); CHNS elemental analysis Calcd. for ($C_{11}H_{10}BrN_3O_2S$): found C% 40.29, H% 3.06, N% 12.77, S% 9.75; calculated C% 40.26, H% 3.07, N% 12.80, S% 9.77. GS/MS: 327 (m/z).

2-((5-(2-bromophenyl)-4-ethyl-4H-1,2,4-triazole-3-yl)thio) acetic acid (5b)

White powder; yield 67 %; m.p. 172–174C; HNMR (400 MHz, DMSO-d6, δ=ppm): 1.45 (CH_3, 3H, t, *J* = 7.1 Hz), 3.95 (CH_2, 2H, s), 4.13 (CH_2, 2H, q, *J* = 7.1 Hz), 7.32 (Ar-H, 1H, ddd, *J* = 8.1, 7.9, 1.1 Hz), 7.48 (Ar-H, 1H, ddd, *J* = 8.1, 7.9, 1.5 Hz), 7.65 (Ar-H, 1H, ddd, *J* = 8.1, 1.5, 0.5 Hz), 7.80 (Ar-H, 1H, ddd, *J* = 8.1, 1.1, 0.5 Hz); CHNS elemental analysis Calcd. for ($C_{12}H_{12}BrN_3O_2S$): found C% 42.24, H% 3.53, N% 12.29, S% 9.40; calculated C% 42.12, H% 3.53, N% 12.28, S% 9.37. GS/MS: 341 (m/z).

2-((5-(2-bromophenyl)-4-phenyl-4H-1,2,4-triazole-3-yl)thio) acetic acid (5c)

White powder; yield 71%; m.p. 160–162C ; HNMR (400 MHz, DMSO-d6, δ=ppm): 4.08 (CH_2, 2H, s), 7.34-7.46 (Ar-H, 3H, 7.42 (ddd, *J* = 7.8, 7.7, 1.1 Hz), 7.39 (ddt, *J* = 7.8, 7.6, 1.2 Hz), 7.40 (ddd, *J* = 8.1, 7.8, 1.5 Hz)), 7.54 (Ar-H, 2H, dddd, *J* = 7.9, 7.8, 1.5, 0.4 Hz), 7.78-7.88 (Ar-H, 3H, 7.81 (dddd, *J* = 7.9, 1.2, 1.2, 0.4 Hz), 7.85 (ddd, *J* = 8.1, 1.1, 0.4 Hz)), 7.95 (Ar-H, 1H, ddd, *J* = 7.7, 1.5, 0.4 Hz); CHNS elemental analysis Calcd. for ($C_{16}H_{12}BrN_3O_2S$): found C% 49.29, H% 3.10, N% 10.75, S% 8.20; calculated C% 49.24, H% 3.10, N% 10.77, S% 8.22. GS/MS: 390 (m/z).

Synthesis of potassium 2-((5-(2-bromophenyl)-4-R-4H-1,2,4-triazole-3-yl)thio)acetates (6a-6c)

0,01 mol of 2-((5-(2-bromophenyl)-4-R-4*H*-1,2,4-triazole-3-yl)thio)acetic acid (R = methyl (5a), ethyl (5b), phenyl (5c)) and 0,01 mol of $KHCO_3$ were dissolved in 50 ml water. The reaction mixture was filtered, the filtrate was evaporated. The obtained substances were recrystallized from 2-propanol for analysis.

potassium 2-((5-(2-bromophenyl)-4-methyl-4H-1,2,4-triazole-3-yl)thio)acetate (6a)

Yellow powder; yield 86 %; m.p. 219–221C;

potassium 2-((5-(2-bromophenyl)-4-ethyl-4H-1,2,4-triazole-3-yl)thio)acetate (6b)

Bright yellow powder; yield 78%; m.p. 178–180C;

potassium 2-((5-(2-bromophenyl)-4-phenyl-4H-1,2,4-triazole-3-yl)thio)acetate (6c)

Bright yellow powder; yield 82 %; m.p. 222-224C;

Synthesis of sodium 2-((5-(2-bromophenyl)-4-R-4H-1,2,4-triazole-3-yl)thio)acetates (6d-6f)

0,01 mol of 2-((5-(2-bromophenyl)-4-R-4*H*-1,2,4-triazole-3-yl)thio)acetic acid (R = methyl (5a), ethyl (5b), phenyl (5c)) and 0,01 mol of $NaHCO_3$ dissolved in 50 ml water. The reaction mixture was filtered, the filtrate was evaporated. For analysis the obtained substances were recrystallized from 2-propanol.

sodium 2-((5-(2-bromophenyl)-4-methyl-4H-1,2,4-triazole-3-yl)thio)acetate (6d)

Bright yellow powder; yield 83 %; m.p. 192-194C;

sodium 2-((5-(2-bromophenyl)-4-ethyl-4H-1,2,4-triazole-3-yl)thio)acetate (6e)

White powder; yield 84 %; m.p. 231-233C;

sodium 2-((5-(2-bromophenyl)-4-phenyl-4H-1,2,4-triazole-3-yl)thio)acetate (6f)

Bright yellow powder; yield 78 %; m.p. <240C;

Synthesis of 2-hydroxyethanaminium 2-((5-(2-bromophenyl)-4-R-4H-1,2,4-triazole-3-yl)thio)acetate (6g-6i)

0,01 mol of 2-((5-(2-bromophenyl)-4-R-4*H*-1,2,4-triazole-3-yl)thio)acetic acid (R = methyl (5a), ethyl (5b), phenyl (5c)) and 0,01 mol of 2-hydroxyethanamine were dissolved in 50 ml of 2-propanol with heating. The reaction mixture was filtered, the filtrate was evaporated. For analysis the obtained substances were recrystallized from 2-propanol.

2-hydroxyethanaminium 2-((5-(2-bromophenyl)-4-methyl-4H-1,2,4-triazole-3-yl)thio)acetate (6g)

Yellow powder; yield 3%; m.p. 141–143C; CHNS elemental analysis Calcd. for ($C_{13}H_{17}BrN_4O_3S$): found C% 40.19, H% 4.41, N% 14.41, S% 8.23; calculated C% 40.11, H% 4.40, N% 14.39, S% 8.24.

2-hydroxyethanaminium 2-((5-(2-bromophenyl)-4-ethyl-4H-1,2,4-triazole-3-yl)thio)acetate (6h)

Yellow powder; yield 67 %; m.p. 105–107C; CHNS elemental analysis Calcd. for ($C_{14}H_{19}BrN_4O_3S$): found C% 41.64, H% 4.76, N% 13.87, S% 7.93; calculated C% 41.69, H% 4.75, N% 13.89, S% 7.95.

2-hydroxyethanaminium 2-((5-(2-bromophenyl)-4-phenyl-4H-1,2,4-triazole-3-yl)thio)acetate (6i)

White powder; yield 69 %; m.p. 210–212C; CHNS elemental analysis Calcd. for ($C_{18}H_{19}BrN_4O_3S$): found C% 47.83, H% 4.25, N% 12.44, S% 7.08; calculated C% 47.90, H% 4.24, N% 12.41, S% 7.10.

Synthesis of morpholinium 2-((5-(2-bromophenyl)-4-R-4H-1,2,4-triazole-3-yl)thio)acetate (6j-6l)

0,01 mol of 2-((5-(2-bromophenyl)-4-R-4*H*-1,2,4-triazol-3-yl)thio)acetic acid (R = methyl (5a), ethyl (5b), phenyl (5c)) and 0,01 mol of morpholine were dissolved in 50 ml of 2-propanol with heating. The reaction mixture was filtered, the filtrate was evaporated. For analysis the obtained substances were recrystallized from 2-propanol.

morpholinium 2-((5-(2-bromophenyl)-4-methyl-4H-1,2,4-triazole-3-yl)thio)acetate (6j)

Yellow powder; yield 80%; m.p. 79–81C; CHNS elemental analysis Calcd. for ($C_{15}H_{19}BrN_4O_3S$): found C% 43.26, H% 4.63, N% 13.49, S% 7.74; calculated C% 43.38, H% 4.61, N% 13.49, S% 7.72.

morpholinium 2-((5-(2-bromophenyl)-4-ethyl-4H-1,2,4-triazole-3-yl)thio)acetate (6k)

White powder; yield 81%; m.p. 218–220C; CHNS elemental analysis Calcd. for ($C_{16}H_{21}BrN_4O_3S$): found C% 44.80, H% 4.94, N% 13.04, S% 7.48; calculated C% 44.76, H% 4.93, N% 13.05, S% 7.47.

morpholinium 2-((5-(2-bromophenyl)-4-phenyl-4H-1,2,4-triazole-3-yl)thio)acetate (6l)

White powder; yield 76 %; m.p. 238–240C; CHNS elemental analysis Calcd. for ($C_{20}H_{21}BrN_4O_3S$): found C% 50.24, H% 4.42, N% 11.73, S% 6.70; calculated C% 50.32, H% 4.43, N% 11.74, S% 6.72.

Synthesis of dimethylammonium 2-((5-(2-bromophenyl)-4-R-4H-1,2,4-triazole-3-yl)thio)acetate (6m-6o)

0,01 mol of 2-((5-(2-bromophenyl)-4-R-4*H*-1,2,4-triazole-3-yl)thio)acetic acid (R = methyl (5a), ethyl (5b), phenyl (5c)) and 0,01 of mol dimethylamine were dissolved in 50 ml of 2-propanol with heating. The reaction mixture was filtered, the filtrate was evaporated. For analysis the obtained substances were recrystallized from 2-propanol.

dimethylammonium 2-((5-(2-bromophenyl)-4-methyl-4H-1,2,4-triazole-3-yl)thio)acetate (6m)

Yellow powder; yield 82 %; m.p. 124–126C; CHNS elemental analysis Calcd. for ($C_{13}H_{17}BrN_4O_2S$): found C% 41.85, H% 4.58, N% 14.98, S% 8.60; calculated C% 41.83, H% 4.59, N% 15.01, S% 8.59.

dimethylammonium 2-((5-(2-bromophenyl)-4-ethyl-4H-1,2,4-triazole-3-yl)thio)acetate (6n)

White powder; yield 83%; m.p. 149–151C; CHNS elemental analysis Calcd. for ($C_{14}H_{19}BrN_4O_2S$): found C% 43.55, H% 4.95, N% 14.44, S% 8.26; calculated C% 43.42, H% 4.94, N% 14.47, S% 8.28.

dimethylammonium 2-((5-(2-bromophenyl)-4-phenyl-4H-1,2,4-triazole-3-yl)thio)acetate (6o)

White powder; yield 83 %; m.p. 200–202C; CHNS elemental analysis Calcd. for ($C_{18}H_{19}BrN_4O_2S$): found C% 49.76, H% 4.42, N% 12.89, S% 7.38; calculated C% 49.66, H% 4.40, N% 12.87, S% 7.37.

Conclusions

As a result, 21 novel compounds of 3-(2-bromophenyl)-4-substituted-1*H*-1,2,4-triazole-5(4*H*)-thiones and their derivatives were synthesized and characterized.

The structure of synthesized compounds was confirmed using Elemental analysis (CHNS), HNMR and Chromatographic mass spectral analysis.

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