Scientific paper

Synthesis and Biological Evaluation of Novel Pyrane Glycosides

Avula Srinivas,^{1,*} Malladi Sunitha² and Sriramoju Shamili¹¹ Department of Chemistry, Vaagdevi Degree & PG College
Kishanpura, Warangal, Telangana, India 506001² Jayamukhi Institute of Technological Sciences, Narsampet, Warangal, Telangana

* Corresponding author: E-mail: avula.sathwikreddy@gmail.com

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Abstract

A series of novel (5*R*)-5-((2*S*,3*S*)-3-((1-(4-chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2*H*-pyran-2-yl)-3-(4-fluorophenyl)-2,6-diphenyl-3,3a,5,6-tetrahydro-2*H*-pyrazolo[3,4-*d*]thiazoles **11a–g** and (5*R*)-5-((2*S*,3*S*)-3-((1-(4-chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2*H*-pyran-2-yl)-3-(4-fluorophenyl)-6-phenyl-3,3a,5,6-tetrahydroisoxazolo[3,4-*d*]thiazoles **12a–g** were synthesized by the reaction of chalcone derivatives of (*R*,*Z*)-2-((2*S*,3*S*)-3-((1-(4-chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2*H*-pyran-2-yl)-5-(4-fluorobenzylidene)-3-phenylthiazolidin-4-ones **10a–g** with phenylhydrazine and hydroxylamine hydrochloride. The chemical structures of newly synthesized compounds were elucidated by IR, NMR, MS and elemental analysis. The compounds **11a–g** and **12a–g** were evaluated for their antibacterial activity and antifungal activity.

Keywords: Glycosides; click reaction; cyclisation; thiazolopyrazoles; thiazoloisoxazoles; antimicrobial activity

1. Introduction

Carbohydrates, are the most ample class of bio-molecules, a vital source of energy and structural components having an important role in biological processes. Carbohydrates, besides being the most abundant class of bio-molecules, a vital source of energy and structural components, have an important role in biological processes, organic synthesis and chemical industries.¹ They have been mostly used in chemical industries and their large scale applications include their use as feedstocks in different chemical industries, like pharmaceutical, food, cosmetic and detergent industries.² In the formation of glycoconjugates (glycolipids, glycoproteins and polysaccharides) and in many biological processes they play decisive role in cell physiology such as intercellular recognition, bacterial and viral infection, cancer metastasis, apoptosis and neuronal proliferation, etc.³

Their fascinating properties, such as hydrophilicity, lowered toxicity and emphasized bioactivities, in addition of carbohydrates affiliation to many systems make them often very effective.⁴ Organic chemists have linked carbohydrates to various biologically potent compounds to enhance their biological applications, such as steroids, ami-

noacids and other therapeutic agents.⁵ One of the chemical reactions which is involved in making such links is carbohydrate affiliation with a potential compound through a triazole ring.⁶ To obtain cyclised products with biological potential a process according to an efficient method is used, being an alkyne-azide cyclization reaction and the introduction of a triazole ring.⁷ The strategy of linking a carbohydrate moiety with another species *via* a triazole ring is gaining importance in organic synthesis, natural products chemistry and biochemistry.⁸ The combination of biocompatibility and presence of stereogenic centres stemming from the carbohydrate, together with the polar nature and possible hydrogen bonding ability of a triazole ring, makes gluco-based triazoles very fascinating for organic synthetic chemists.

The derivatives of thiazolidinone are known to possess significant pharmacological⁹ and biological activities,¹⁰ like sedative,¹¹ anti inflammatory,¹² anti tubercular,¹³ anticancer,¹⁴ anti tumor,¹⁵ anti-HIV,¹⁶ anti bacterial,¹⁷ anti fungal,¹⁸ analgesic, hypotermic,¹⁹ anesthetic,²⁰ nematocidal,²¹ and CNS stimulant.²² Furthermore, thiazolidinones have been used for the treatment of cardiac diseases,²³ diabetic complications, like contract nephropathy, neuropathy,²⁴ and as a selective anti platelet activating fac-

tor.²⁵ Moreover, isoxazole derivatives are an important class of bio active molecules, which exhibit significant activities, such as anti fungal.²⁶ The cardinal derivatives include such having antidepressant activity, hampering protein kinase,²⁷ possessing antiviral,²⁸ antihelminthic,²⁹ anti inflammatory,³⁰ anticonvulsant,³¹ insecticidal,³² antitubercular,³³ immunomodulatory,³⁴ and hypolipemic activities. Additionally, derivatives of pyrazole are considered as feasible antimicrobial agents.³⁵

We have developed a series of novel triazole-linked pyrene glycosides; additionally we screened them for their antimicrobial activity, connected with the affluent introduction of pyrazoles, thiazolidinones, and triazoles as shown by parts of our previous work on biologically active heterocyclics.^{36–43} We have also developed a series of novel triazole-linked pyrene glycosides and evaluated their antimicrobial activity.

2. Results and Discussion

For the synthesis, the title compound was prepared according to the procedure outlined in the Scheme 1, where the key intermediate **8** is required. From 3,4,6-tri-*O*-acetyl-D-glucal (**1**) by treating with triethylsilane and boron trifluoride diethyl etherate, diacetyl-D-glucal (**2**) was prepared, giving with NaOMe in methanol at 0 °C after 1 h compound **3** (77%), which has on subsequent treatment with TBDMSCl in dichloromethane in the presence of NEt₃ after 12 h afforded TBS ether **4** (80%), which on treatment with propargyl bromide in toluene in the presence of tetrabutylammonium hydrogensulphate produced diether **5**. After deprotection of TBS ether **5**, the propargyl ether **6** was converted into triazole **7** (82%) by using 1,3-di-

polar cycloaddition with *para*-chlorophenyl azide carried out at ambient temperature in the presence of CuSO₄ and sodium ascorbate in a mixture of 1:1 CH₂Cl₂–H₂O. The synthesis of triazole-linked thiazolidinone glycosides was carried out by the condensation reaction of **8**, obtained by the oxidation of **7** with IBX in acetonitrile. Compound **8** was in the next step reacted with *R*-substituted primary aromatic amine and thioglycolic acid in the presence of ZnCl₂ under microwave irradiation (Scheme 1) furnishing set of compound **9a–g**. These compounds were isolated by conventional work-up, when the reaction was completed in only 5–10 minutes, the **9a–g** were obtained in satisfactory yields. Then the compounds **9a–g** were reacted with *para*-fluorobenzaldehyde in the presence of anhydrous NaOAc in glacial AcOH at reflux temperature giving chalcone derivatives of triazole-linked thiazolidinone glycosides **10a–g**. Further, these compounds upon cyclocondensation with arylhydrazines in the presence of anhydrous NaOAc in glacial AcOH at reflux temperature gave **11a–g** in good yields. Compound **10a–g** on cyclocondensation with hydroxylamine hydrochloride in the presence of anhydrous NaOAc in glacial AcOH at reflux temperature gave compounds **12a–g**. By IR, NMR, and MS the structures of the synthesized compounds were confirmed and then evaluated for their antimicrobial activity.

3. Antimicrobial Activity

By the filter paper disc method, the antimicrobial activity of the synthesized compounds **11a–g** and **12a–g** has been evaluated⁴⁴ against *Staphylococcus aureus* ATCC-6538P, *Bacillus subtilis* ATCC6633, *Pseudomonas aeruginosa* ATCC9027, and *Escherichia coli* ATCC8739. Antifun-

Table 1. Antimicrobial and antifungal activity of 11a–g and 12a–g

Compounds	Gram positive		Gram Negative		Fungi	
	<i>Staphylococcus aureus</i>	<i>Bacillus subtilis</i>	<i>Pseudomonas aeruginosa</i>	<i>Escherichia coli</i>	<i>Candida albicans</i>	<i>Aspergillus niger</i>
11a	17	16	18	20	15	13
11b	24	22	20	19	14	12
11c	15	16	15	14	15	14
11d	20	23	10	7	14	15
11e	15	16	11	9	21	15
11f	16	17	19	17	9	7
11g	22	24	15	14	22	16
12a	16	18	19	18	17	14
12b	20	23	19	18	15	13
12c	10	8	15	16	14	13
12d	20	22	6	10	14	12
12e	16	15	12	10	20	17
12f	17	16	19	18	7	8
12g	20	21	16	15	21	16
Ampicilin	22	26	20	19	–	–
Micostatin	–	–	–	–	22	16

gal activity of the synthesized compounds has been tested against *Candida albicans* ATCC2091, and *Aspergillus niger*, at a concentration of 500 µg/mL in DMF.

To culture the bacteria and fungi, nutrient agar and potato dextrose agars were used, respectively. The plates were cultured by the bacteria or fungi and incubated for 24 h at 37 °C for bacteria and for 72 h at 27 °C for fungi and then the inhibition zones of microbial growth surrounding the filter paper disc (5 mm) were measured in millimeters. Ampicillin and mycostatin, at a concentration 500 µg/mL, were used as standard against bacteria and fungi, respectively. All test results are shown in Table 1. From the data it is clear that compounds **11b**, **12b**, **11d**, **12d**, **11g**, and **12g** possess high activity, while compounds **11a**, **12a**, **11c**, **11e**, **12e**, **11f**, and **12f** possess moderate activity against Gram

positive bacteria. The compounds **11a**, **12a**, **11b**, **12b**, **11f**, and **12f** showed high activity as Gram negative microorganisms are concerned, while compounds **11c**, **12c**, **11g** and **12g** display moderate activity. Compounds **11e**, **12e**, **11g**, and **12g** also exerted high activity, while compounds **11a**, **12a**, **11c**, **12c**, **11d**, **12d**, **11b**, and **12b** have moderate activity against fungi.

4. Experimental

All the used reagents were supplied as commercially available. According to the literature, when necessary, the solvents used (except analytical reagent and grade) were dried and purified. By thin-layer chromatography (TLC)

R = H, 4-Cl, 4-NO₂, 2-CH₃, 4-CH₃, 3-OH, 4-OH

Reagents and conditions: (a) BF₃, Et₂O, Et₃SiH, CH₂Cl₂; (b) MeOH, NaOMe; (c) TBDMSCl, Et₃N, CH₂Cl₂; (d) propargyl bromide, NaH, *n*-Bu₄N-HSO₄, 35% NaOH, toluene; (e) TBAF, THF; (f) 4-Cl-C₆H₄-N₃, CuSO₄, sodium ascorbate, CH₂Cl₂, H₂O (1:1); (g) IBX, CH₃CN; (h) R-C₆H₄-NH₂, AcOH, SHCH₂COOH, ZnCl₂, C₆H₆; (i) 4-F-C₆H₄-CHO, NaOAc, AcOH; (j) PhNHNH₂, NaOAc, AcOH; (k) NH₂OH, NaOAc, AcOH.

on pre-coated silica gel F254 plates from Merck the reaction progress and purity of the compounds was checked. They were visualized either by exposure to UV light or dipping in 1% aqueous potassium permanganate solution. Silica gel chromatographic columns (60–120 mesh) were used for separations. Optical rotations were measured on an Perkin–Elmer 141 polarimeter by using a 2 mL cell with a path length of 1 dm with CHCl_3 or CDCl_3 as the solvent. By using Fisher–Johns apparatus all the melting points were measured and are corrected. IR spectra were recorded as KBr disks on a Perkin–Elmer FT IR spectrometer. Microwave reactions were carried out in mini lab microwave catalytic reactor (ZZKD, WBFY-201). On Varian Gemini spectrometer (300 MHz for ^1H and 75 MHz for ^{13}C) the ^1H NMR and ^{13}C NMR spectra were recorded; chemical shifts are reported as δ in ppm against TMS as the internal reference, coupling constants (J) are reported in Hz units. On a VG micro mass 7070H spectrometer mass spectra were recorded. Elemental analysis (C, H, N) were determined by a Perkin–Elmer 240 CHN elemental analyzer and were within $\pm 0.4\%$ of theoretical values.

((2R,3S)-3-Acetoxy-3,6-dihydro-2H-pyran-2-yl)methyl Acetate (2)

Tri-*O*-acetyl-D-glucal (**1**) (6.0 g, 22.04 mmol) was dissolved in anhydrous dichloromethane (10 mL). The solution was cooled to about 0 °C, and triethylsilane (3.06 g, 26.44 mmol) was added and the mixture was stirred for five minutes. Then boron trifluoride diethyl etherate (690 μL of a 40 w% solution in diethyl ether, 11.02 mmol) was added drop wise and the reaction mixture was stirred for 90 min. The mixture was poured into a saturated solution of NaHCO_3 . Then the organic layer was washed with water and dried over Na_2SO_4 and concentrated under reduced pressure.

Column chromatography on silica gel (PE/EtOAc, 3:1) yielded the title compound **2** (4.48 g, 20.84 mmol, 95%) as a colorless syrup. $[\alpha]_{\text{D}}^{20}$: +115.5 ($c = 1.00$, CHCl_3). ^1H NMR (300 MHz, CDCl_3) δ 5.87–5.84 (m, 2H, =CH), 4.95 (t, 1H, OCH), 4.03–3.99 (m, 1H, CH), 4.12–4.09 (m, 4H, OCH_2), 2.20 (s, 6H, CO CH_3); ^{13}C NMR (75 MHz, CDCl_3) d 170.2, 127.2, 125.8, 73.6, 65.1, 64.0, 62.5, 21.1; MS m/z ($\text{M}^+ + \text{H}$) 215. Anal. calcd. for $\text{C}_{10}\text{H}_{14}\text{O}_5$: C, 56.07; H, 6.59. Found: C, 55.82; H, 6.35.

((2R,3S)-2-((tert-Butyldimethylsilyloxy)methyl)-3,6-dihydro-2H-pyran-3-ol (4)

At room temperature diacetate **2** (4.20 g, 19.53 mmol) was treated by a catalytic amount of sodium methoxide in 100 mL of methanol. The free hydroxyl unsaturated glycoside **3** was obtained in quantitative yield and used without further purification after evaporation of the solvent. This diol **3** was treated with 5 equiv of TBDMSCL (6.28 g, 42.28 mmol), 4.6 equiv of NEt_3 (6.4 mL, 44.8 mmol), and 0.10 equiv of imidazole (60 mg, 0.86 mmol) in CH_2Cl_2 (60 mL) at room temperature for 24 h (until TLC

analysis showed no more starting material). Thereafter, 25 mL of water were added and extraction with 3×30 mL of CH_2Cl_2 followed; the organic layer was dried, evaporation of solvent under reduced pressure furnished the residue that was purified by column chromatography using petroleum ether/ethyl acetate as the eluent yielding the title compound **4** (3.84 g, 73.70%) as a colourless syrup. ^1H NMR (300 MHz, CDCl_3) δ 6.0–5.82 (m, 2H, =CH), 5.42 (d, $J = 6.5$ Hz, 1H, CH), 4.50 (brs, 1H, OH), 4.20–4.12 (m, 1H, CH), 3.91–3.80 (m, 4H, CH_2), 0.98 (s, 9H, *t*-Bu), 0.24 (s, 6H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) d 127.5, 125.6, 84.6, 81.5, 73.6, 62.7, 25.6, 18.1; MS m/z ($\text{M}^+ + \text{Na}$) 267. Anal. calcd. for $\text{C}_{12}\text{H}_{24}\text{O}_3\text{Si}$: C, 58.97; H, 9.90. Found: C, 58.62; H, 9.75.

tert-Butyldimethyl(((2R,3S)-3-(prop-2-ynyloxy)-3,6-dihydro-2H-pyran-2-yl)methoxy)silane (5)

To a solution of alcohol **4** (3.50 g, 13.10 mmol) in toluene (3.2 mL) was added 35% aqueous solution of NaOH (6.4 mL), propargyl bromide (80% solution in toluene, 363 μL , 2.4 mmol, 1.5 equiv), and *n*-Bu $_4\text{NHSO}_4$ (360 mg, 1.6 mmol, 1 equiv). After 6 h of vigorous stirring at rt, Et $_2\text{NH}$ (6.4 mL) was added. The reaction mixture was stirred for 1 h, poured into ice water, cautiously neutralized by addition of a 3M solution of hydrochloric acid, and extracted with EtOAc. The combined organic extracts were washed with brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography on silica gel (hexane/EtOAc 85:15) to afford propargyl ether **5** as a colorless oil (3.1 g, 83%). ^1H NMR (300 MHz, CDCl_3) δ 6.03–5.80 (m, 2H, =CH), 4.69 (t, $J = 3.9$ Hz, 1H, CH), 3.68 (dd, $J = 8.9$ Hz, 4.1 Hz, 1H, OCH), 3.99–3.89 (m, 6H, CH_2), 3.20 (s, 1H, CH), 0.96 (s, 9H, *t*-Bu), 0.23 (s, 6H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ 127.2, 124.9, 78.0, 76.2, 74.2, 64.2, 63.2, 58.5, 25.3, 18.5; MS m/z ($\text{M}^+ + \text{H}$) 283. Anal. calcd. for $\text{C}_{15}\text{H}_{26}\text{O}_3\text{Si}$: C, 63.78; H, 9.28. Found: C, 63.62; H, 8.95.

((2R,3S)-3-(Prop-2-ynyloxy)-3,6-dihydro-2H-pyran-2-yl)methanol (6)

To a stirred solution of **5** (3 g, 10.600 mmol) in tetrahydrofuran, catalytic amount of TBAF was added and stirred the reaction mixture at room temperature for 15 min, extracted the product with ethyl acetate (50 mL). The combined organic extracts were washed with brine, dried over MgSO_4 , filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography on silica gel (60–120 mesh, hexane/EtOAc 70:30) to afford alcohol **6** as a yellow oil (1.5 g, 83%). ^1H NMR (300 MHz, CDCl_3) δ 5.95–5.75 (m, 2H, =CH), 4.65 (d, $J = 3.9$ Hz, 1H, CH), 4.52 (brs, 1H, OH), 4.09–4.11 (m, 4H, OCH_2), 3.64 (dd, $J = 4.1$ Hz, 8.9 Hz, 1H, OCH), 3.76 (d, $J = 6.8$ Hz, 2H, OCH_2), 3.28 (s, 1H, CH); ^{13}C NMR (75 MHz, CDCl_3) d 127.2, 125.6, 78.3, 76.1, 74.1, 64.2, 61.4, 58.0; MS m/z ($\text{M}^+ + \text{H}$) 169. Anal. calcd. for $\text{C}_9\text{H}_{12}\text{O}_3$: C, 64.27; H, 7.10. Found: C, 64.02; H, 6.95.

((2R,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)methanol (7)

The a solution containing alkyne **6** (1.4 g, 8.28 mmol), *para*-chlorophenylazide (1.25 g, 8.11 mmol) in dichloromethane (10 mL) and water (10 mL) were added $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (0.110 g) and sodium ascorbate (0.114 g). The resulting suspension was stirred at room temperature for 6 h. Then, the mixture was diluted with 5 mL dichloromethane and 5 mL water. The organic phase was separated, dried with sodium sulphate and concentrated under reduced pressure. The crude product was purified by using column chromatography on silica gel (60–120 mesh, hexane/EtOAc 65:35) to afford **7** (2 g, 75%) as a white powder. M.p. 149–151.0 °C. ^1H NMR (300 MHz, CDCl_3) δ 8.05 (s, 1H, Ar-H), 7.56 (d, J = 9.2 Hz, 2H, Ar-H), 7.45 (d, J = 8.9 Hz, 2H, Ar-H), 5.85–5.79 (m, 2H, =CH), 4.59 (s, 2H, OCH_2), 4.50 (brs, 1H, OH), 3.88–3.99 (m, 4H, OCH_2), 3.8–3.75 (m, 2H, OCH); ^{13}C NMR (75 MHz, CDCl_3) d 140.9, 134.5, 134.1, 128.4, 127.5, 125.4, 122.1, 111.5, 78.6, 68.5, 65.7, 64.2, 62.4; MS m/z ($\text{M}^+ + \text{H}$) 322. Anal. calcd. for $\text{C}_{15}\text{H}_{16}\text{ClN}_3\text{O}_3$: C, 55.90; H, 5.01; N, 13.06. Found: C, 55.65; H, 4.95; N, 12.86.

(R)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-phenylthiazolidin-4-ones 9a–g

At room temperature for about 30 min, to the solution of alcohol **7** (1.9 g, 5.90 mmol) in CH_2Cl_2 (10 mL), a catalytic amount of IBX was added at 0 °C and stirred. The reaction mixture was filtered and washed with CH_2Cl_2 (2 $\times$ 10 mL). It was dried (Na_2SO_4) and evaporated to give the aldehyde **8** (1.6 g) in quantitative yield as a yellow liquid, which was used for the next reaction.

To the corresponding aromatic aniline (0.712 mmol), the stirred mixture of **8** (0.712 mmol), anhydrous thioglycolic acid (0.070 g, 0.760 mmol) in dry toluene (10 mL), ZnCl_2 (0.100 g, 0.751 mmol) was added after 2 min and irradiated in microwave bath reactor at 280 W for 4–7 minutes at 110 °C. The filtrate was concentrated to dryness under reduced pressure and the residue was taken up in ethyl acetate after cooling. The ethyl acetate layer was washed with 5% sodium bicarbonate solution and finally it was dried. At reduced pressure, the organic layer was dried over Na_2SO_4 and evaporated to dryness. The crude product **9** was obtained and it was purified by column chromatography on silica gel (60–120 mesh) with hexane–ethyl acetate mixture as the eluent.

(R)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-phenylthiazolidin-4-one (9a). M.p. 157–159 °C. Yield 75% (0.249 g). ^1H NMR (300 MHz, CDCl_3) δ 8.04 (s, 1H, Ar-H), 7.50 (d, J = 9.2 Hz, 2H, Ar-H), 7.40 (d, J = 8.9 Hz, 2H, Ar-H), 7.10–6.20 (m, 5H, Ar-H), 5.80–5.71 (m, 2H, =CH), 4.90 (d, J = 5.2 Hz, 1H, CH-S), 4.52 (s, 2H, OCH_2), 4.09–3.94 (m, 2 $\times$ CH), 3.79 (d, J = 6.6 Hz, 2H, OCH_2),

3.72 (s, 2H, CH_2); ^{13}C NMR (75 MHz, CDCl_3) d 170.4, 144.1, 141.8, 134.1, 128.2, 125.6, 122.4, 119.4, 85.6, 72.6, 66.4, 64.0, 51.4, 33.9; MS m/z ($\text{M}^+ + \text{H}$) 469. Anal. calcd. for $\text{C}_{23}\text{H}_{21}\text{ClN}_4\text{O}_3\text{S}$: C, 58.91; H, 4.51; N, 11.95. Found: C, 58.68; H, 4.35; N, 11.66.

(R)-3-(4-Chlorophenyl)-2-((2S,3S)-3-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)thiazolidin-4-one (9b). M.p. 226–228 °C. Yield 69% (0.256 g). ^1H NMR (300 MHz, CDCl_3) δ 8.05 (s, 1H, Ar-H), 7.54 (d, J = 9.4 Hz, 4H, Ar-H), 7.42 (d, J = 8.6 Hz, 4H, Ar-H), 5.84–5.75 (m, 2H, =CH), 4.94 (d, J = 5.2 Hz, CH-S), 4.50 (s, 2H, OCH_2), 4.06–3.96 (m, 2H, 2 $\times$ CH), 3.80 (t, 2H, OCH_2), 3.72 (s, 2H, CH_2); ^{13}C NMR (75 MHz, CDCl_3) d 170.5, 144.2, 139.2, 134.2, 129.2, 125.5, 122.2, 119.4, 85.4, 72.8, 65.4, 63.4, 51.2, 34.1; MS m/z ($\text{M}^+ + \text{Na}$) 525. Anal. calcd. for $\text{C}_{23}\text{H}_{20}\text{Cl}_2\text{N}_4\text{O}_3\text{S}$: C, 54.88; H, 4.00; N, 11.13. Found: C, 54.58; H, 3.75; N, 10.86.

(R)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-nitrophenyl)thiazolidin-4-one (9c). M.p. 211–213 °C. Yield 71% (0.259 g). ^1H NMR (300 MHz, CDCl_3) δ 8.26 (d, J = 8.7 Hz, 2H, Ar-H), 8.03 (s, 1H, Ar-H), 7.61 (d, J = 9.4 Hz, 2H, Ar-H), 7.46 (d, J = 8.5 Hz, 2H, Ar-H), 6.84 (d, J = 9.8 Hz, 2H, Ar-H), 5.86–5.79 (m, 2H, =CH), 4.96 (d, J = 5.2 Hz, CH-S), 4.55 (s, 2H, OCH_2), 4.05–3.95 (m, 2H, 2 $\times$ CH), 3.85 (d, J = 6.9 Hz, 2H, OCH_2), 3.82 (s, 2H, CH_2); ^{13}C NMR (75 MHz, CDCl_3) d 171.5, 144.0, 141.8, 134.2, 128.5, 125.4, 119.5, 85.4, 72.4, 65.9, 63.6, 51.5, 34.6; MS m/z ($\text{M}^+ + \text{H}$) 514. Anal. calcd. for $\text{C}_{23}\text{H}_{20}\text{ClN}_5\text{O}_5\text{S}$: C, 53.75; H, 3.92; N, 13.63. Found: C, 53.58; H, 3.75; N, 13.39.

(R)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-*o*-tolylthiazolidin-4-one (9d). M.p. 191–193 °C. Yield 65% (0.222 g). ^1H NMR (300 MHz, CDCl_3) δ 8.08 (s, 1H, Ar-H), 7.56 (d, J = 9.2 Hz, 2H, Ar-H), 7.49 (d, J = 8.7 Hz, 2H, Ar-H), 7.45–7.39 (m, 4H, Ar-H), 5.76 (m, 2H, =CH), 4.93 (d, J = 5.2 Hz, 1H, CHS), 4.60 (s, 2H, OCH_2), 4.05–3.96 (m, 2H, CH), 3.90 (t, 2H, OCH_2), 3.81 (s, 2H, CH_2), 2.1 (s, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) d 170.5, 144.2, 138.2, 134.2, 130.7, 128.6, 125.6, 122.0, 119.5, 116.5, 85.4, 72.6, 65.8, 63.4, 52.0, 32.3, 17.5; MS m/z ($\text{M}^+ + \text{H}$) 483. Anal. calcd. for $\text{C}_{24}\text{H}_{23}\text{ClN}_4\text{O}_3\text{S}$: C, 59.68; H, 4.80; N, 11.60. Found: C, 59.48; H, 4.55; N, 11.49.

(R)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-*p*-tolylthiazolidin-4-one (9e). M.p. 195–198 °C. Yield 79% (0.270 g). ^1H NMR (300 MHz, CDCl_3) δ 8.05 (s, 1H, Ar-H), 7.51 (d, J = 9.2 Hz, 2H, Ar-H), 7.45 (d, J = 8.7 Hz, 2H, Ar-H), 7.25 (d, J = 8.2 Hz, 2H, Ar-H), 6.84 (d, J = 9.4 Hz, 2H, Ar-H), 5.72–5.68 (m, 2H, =CH), 4.95 (s, 1H, CHS), 4.59 (s, 2H, OCH_2), 4.04–3.99 (m, 2H, CH), 3.98 (t, 2H, OCH_2), 3.90 (s, 2H, CH_2), 2.32 (s, 3H, CH_3); ^{13}C NMR (75

MHz, CDCl₃) δ 170.5, 144.2, 138.6, 136.2, 14.1, 133.2, 129.4, 127.5, 122.5, 119.5, 85.4, 72.0, 66.4, 63.5, 51.5, 34.0, 21.4; MS m/z ($M^+ + H$) 483. Anal. calcd. for C₂₄H₂₃ClN₄O₃S: C, 59.68; H, 4.80; N, 11.60. Found: C, 59.58; H, 4.65; N, 11.43.

(R)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(3-hydroxyphenyl)thiazolidin-4-one (9f). M.p. 218–219 °C. Yield 85% (0.360 g). ¹H NMR (300 MHz, CDCl₃) δ 9.40 (brs, 1H, Ph-OH), 8.08 (s, 1H, Ar-H), 7.58 (d, J = 9.3 Hz, 2H, Ar-H), 7.49 (d, J = 8.6 Hz, 2H, Ar-H), 6.83–6.76 (m, 4H, Ar-H), 5.72–5.68 (m, 2H, =CH), 4.94 (d, J = 5.2 Hz, 1H, CHS), 4.64 (s, 2H, OCH₂), 4.12 (t, 2H, OCH₂), 4.01–3.94 (m, 2H, CH), 3.92 (s, 2H, CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 170.5, 158.2, 143.8, 134.5, 130.4, 128.6, 125.6, 122.4, 119.5, 114.8, 106.5, 85.4, 72.5, 66.4, 63.4, 51.5, 34.1; MS m/z ($M^+ + Na$) 507. Anal. calcd. for C₂₃H₂₁ClN₄O₄S: C, 59.96; H, 4.36; N, 11.55. Found: C, 59.28; H, 4.65; N, 11.43.

(R)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-hydroxyphenyl)thiazolidin-4-one (9g). M.p. 273–275 °C. Yield 82% (0.282 g). ¹H NMR (300 MHz, CDCl₃) δ 9.42 (brs, 1H, Ph-OH), 8.05 (s, 1H, Ar-H), 7.56 (d, J = 9.2 Hz, 2H, Ar-H), 7.46 (d, J = 8.4 Hz, 2H, Ar-H), 7.32 (d, J = 8.6 Hz, 2H, Ar-H), 7.02 (d, J = 8.8 Hz, 2H, Ar-H), 5.89–5.80 (m, 2H, =CH), 4.96 (d, J = 5.4 Hz, 1H, CHS), 4.66 (s, 2H, OCH₂), 4.09 (d, J = 2H, OCH₂), 4.04–3.98 (m, 2H, CH), 3.94 (s, 2H, CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 170.9, 154.1, 144.4, 134.9, 134.8, 128.8, 127.2, 125.6, 123.2, 119.4, 116.4, 85.4, 72.6, 66.5, 64.0, 51.6, 34.5; MS m/z ($M^+ + H$) 485. Anal. calcd. for C₂₃H₂₁ClN₄O₄S: C, 59.96; H, 4.36; N, 11.55. Found: C, 59.38; H, 4.75; N, 11.33.

General Procedure for the Synthesis of 10a–g

In anhydrous glacial acetic acid (20 mL), a mixture of compound **9a** (0.235 g, 0.501 mmol), *para*-fluorobenzaldehyde (0.065 g, 0.524 mmol) and sodium acetate (0.01 mol) was refluxed for about 3 h. The reaction mixture was concentrated and then poured into ice cold water, the solid thus separated, then it was filtered, and washed with water and crystallized from glacial acetic acid, to afford pure **10a** as a yellow solid.

(R,Z)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-5-(4-fluorobenzylidene)-3-phenylthiazolidin-4-one (10a). M.p. 235–237 °C. Yield 85% (0.244 g). ¹H NMR (300 MHz, CDCl₃) δ 8.07 (s, 1H, Ar-H), 7.80 (s, 1H, CH=C), 7.72 (d, J = 9.6 Hz, 2H, Ar-H), 7.40 (d, J = 9.2 Hz, 2H, Ar-H), 7.45 (d, J = 8.9 Hz, 2H, Ar-H), 7.19 (d, J = 8.2 Hz, 2H, Ar-H), 7.02–6.80 (m, 5H, Ar-H), 5.80–5.74 (m, 2H, =CH), 4.90 (d, J = 5.2 Hz, 1H, CH-S), 4.52 (s, 2H, OCH₂), 4.09–3.94 (m, 2H, 2 $\times$ CH), 3.79 (d, J = 6.6 Hz, 2H, OCH₂); ¹³C NMR (75 MHz, CDCl₃) δ 170.4, 162.1, 144.1, 141.8, 139.8, 134.1, 130.4, 128.2, 125.6, 124.6, 122.4, 119.4, 115.5, 85.6,

72.6, 66.4, 64.0, 51.5; MS m/z ($M^+ + H$) 575. Anal. calcd. for C₃₀H₂₄ClFN₄O₃S: C, 62.66; H, 4.21; N, 9.74. Found: C, 62.48; H, 4.15; N, 9.56.

Similarly all the compounds (**10b–e**) prepared according to above procedure

(R,Z)-3-(4-Chlorophenyl)-2-((2S,3S)-3-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-5-(4-fluorobenzylidene)thiazolidin-4-one (10b). M.p. 216–218 °C. Yield 72% (0.207 g). ¹H NMR (300 MHz, CDCl₃) δ 8.09 (s, 1H, Ar-H), 7.75 (s, 1H, CH=C), 7.62 (d, J = 9.5 Hz, 2H, Ar-H), 7.52 (d, J = 9.4 Hz, 4H, Ar-H), 7.40 (d, J = 8.6 Hz, 4H, Ar-H), 7.19 (d, J = 8.1 Hz, 2H, Ar-H), 5.84–5.75 (m, 2H, =CH), 4.94 (d, J = 5.2 Hz, 1H, CHS), 4.52 (s, 2H, OCH₂), 4.06–3.94 (m, 2H, 2 $\times$ CH), 3.80 (t, 2H, OCH₂); ¹³C NMR (75 MHz, CDCl₃) δ 170.5, 162.1, 144.2, 139.2, 134.2, 130.4, 129.2, 125.5, 124.1, 122.2, 119.4, 85.4, 72.8, 65.4, 63.4, 51.2; MS m/z ($M^+ + Na$) 632. Anal. calcd. for C₃₀H₂₃Cl₂FN₄O₃S: C, 59.12; H, 3.80; N, 9.19. Found: C, 59.01; H, 3.45; N, 8.96.

(R,Z)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-5-(4-fluorobenzylidene)-3-(4-nitrophenyl)thiazolidin-4-one (10c). M.p. 221–223 °C. Yield 75% (0.216 g). ¹H NMR (300 MHz, CDCl₃) δ 8.29 (d, J = 8.7 Hz, 2H, Ar-H), 8.09 (s, 1H, Ar-H), 7.69 (d, J = 9.1 Hz, 2H, Ar-H), 7.65 (s, 1H, CH=C), 7.61 (d, J = 9.4 Hz, 2H, Ar-H), 7.46 (d, J = 8.5 Hz, 2H, Ar-H), 7.18 (d, J = 8.3 Hz, 2H, Ar-H), 6.84 (d, J = 9.8 Hz, 2H, Ar-H), 5.86–5.79 (m, 2H, =CH), 4.96 (d, J = 5.2 Hz, CH-S), 4.55 (s, 2H, OCH₂), 4.05–3.95 (m, 2H, 2 $\times$ CH), 3.85 (d, J = 6.9 Hz, 2H, OCH₂); ¹³C NMR (75 MHz, CDCl₃) δ 171.5, 162.1, 144.0, 141.8, 134.2, 130.4, 128.5, 125.4, 119.5, 115.4, 85.4, 72.4, 65.9, 63.6, 51.5; MS m/z ($M^+ + H$) 620. Anal. calcd. for C₃₀H₂₃ClFN₄O₅S: C, 58.11; H, 3.74; N, 11.29. Found: C, 57.98; H, 3.55; N, 11.09.

(R,Z)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-5-(4-fluorobenzylidene)-3-*o*-tolylthiazolidin-4-one (10d). M.p. 201–203 °C. Yield 85% (0.217 g). ¹H NMR (300 MHz, CDCl₃) δ 8.08 (s, 1H, Ar-H), 7.69 (d, J = 8.5 Hz, 2H, Ar-H), 7.62 (s, 1H, CH=C), 7.56 (d, J = 9.2 Hz, 2H, Ar-H), 7.49 (d, J = 8.7 Hz, 2H, Ar-H), 7.45–7.39 (m, 4H, Ar-H), 7.10 (d, J = 9.1 Hz, 2H, Ar-H), 5.76 (m, 2H, =CH), 4.93 (d, J = 5.2 Hz, 1H, CHS), 4.60 (s, 2H, OCH₂), 4.05–3.96 (m, 2H, CH), 3.90 (t, 2H, OCH₂), 2.1 (s, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 170.8, 162.9, 144.6, 137.2, 133.2, 130.6, 130.4, 128.2, 125.9, 122.7, 119.2, 116.2, 115.4, 84.4, 72.1, 65.3, 63.1, 52.5, 32.0, 17.5; MS m/z ($M^+ + H$) 589. Anal. calcd. for C₃₁H₂₆ClFN₄O₃S: C, 63.21; H, 4.45; N, 9.51. Found: C, 62.75; H, 4.25; N, 9.29.

(R,Z)-2-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-5-(4-fluorobenzylidene)-3-*p*-tolylthiazolidin-4-one (10e).

M.p. 205–215 °C. Yield 66% (0.209 g). ^1H NMR (300 MHz, CDCl_3) δ 8.02 (s, 1H, Ar-H), 7.69 (s, 1H, CH=C), 7.65 (d, J = 9.1 Hz, 2H, Ar-H), 7.54 (d, J = 9.2 Hz, 2H, Ar-H), 7.42 (d, J = 8.7 Hz, 2H, Ar-H), 7.35 (d, J = 8.2 Hz, 2H, Ar-H), 7.18 (d, J = 8.8 Hz, 2H, ArH), 6.80 (d, J = 9.4 Hz, 2H, ArH), 5.70–5.69 (m, 2H, =CH), 4.94 (s, 1H, CHS), 4.55 (s, 2H, OCH_2), 4.04–3.98 (m, 2H, CH), 3.96 (t, 2H, OCH_2), 2.32 (s, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) d 170.1, 162.5, 144.1, 139.5, 137.6, 135.2, 133.2, 130.4, 129.1, 127.5, 124.1, 122.5, 119.5, 115.3, 85.1, 72.5, 66.1, 63.2, 51.2, 21.6; MS m/z ($\text{M}^+ + \text{H}$) 589. Anal. calcd. for $\text{C}_{31}\text{H}_{26}\text{ClFN}_4\text{O}_3\text{S}$: C, 63.21; H, 4.45; N, 9.51. Found: C, 62.98; H, 4.25; N, 9.33.

(*R,Z*)-2-((2*S*,3*S*)-3-((1-(4-Chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2*H*-pyran-2-yl)-5-(4-fluorobenzylidene)-3-(3-hydroxyphenyl)thiazolidin-4-one (10f). M.p. 218–219 °C. Yield 82% (0.219 g). ^1H NMR (300 MHz, CDCl_3) δ 9.42 (brs, 1H, PhOH), 8.08 (s, 1H, ArH), 7.71 (d, J = 9.7 Hz, 2H, ArH), 7.65 (s, 1H, CH=C), 7.59 (d, J = 9.3 Hz, 2H, Ar-H), 7.44 (d, J = 8.6 Hz, 2H, Ar-H), 7.15 (d, J = 8.4 Hz, 2H, ArH), 6.80–6.78 (m, 4H, Ar-H), 5.70–5.68 (m, 2H, =CH), 4.92 (d, J = 5.2 Hz, 1H, CHS), 4.64 (s, 2H, OCH_2), 4.10 (t, 2H, OCH_2), 4.01–3.98 (m, 2H, CH); ^{13}C NMR (75 MHz, CDCl_3) d 170.5, 162.1, 158.2, 143.8, 139.8, 134.5, 130.8, 128.6, 125.6, 124.1, 122.4, 119.5, 115.7, 114.8, 106.5, 85.4, 72.5, 66.4, 63.4, 51.5; MS m/z ($\text{M}^+ + \text{H}$) 591. Anal. calcd. for $\text{C}_{30}\text{H}_{24}\text{ClFN}_4\text{O}_4\text{S}$: C, 60.96; H, 4.09; N, 9.48. Found: C, 60.58; H, 3.85; N, 9.13.

(*R,Z*)-2-((2*S*,3*S*)-3-((1-(4-Chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2*H*-pyran-2-yl)-5-(4-fluorobenzylidene)-3-(4-hydroxyphenyl)thiazolidin-4-one (10g). M.p. 283–285 °C. Yield 62% (0.203 g). ^1H NMR (300 MHz, CDCl_3) δ 9.42 (brs, 1H, Ph-OH), 8.05 (s, 1H, Ar-H), 7.85 (d, J = 9.3 Hz, 2H, Ar-H), 7.65 (s, 1H, CH=C), 7.56 (d, J = 9.2 Hz, 2H, Ar-H), 7.46 (d, J = 8.4 Hz, 2H, Ar-H), 7.32 (d, J = 8.6 Hz, 2H, Ar-H), 7.19 (d, J = 8.3 Hz, 2H, ArH), 7.02 (d, J = 8.8 Hz, 2H, ArH), 5.89–5.80 (m, 2H, =CH), 4.96 (d, J = 5.4 Hz, 1H, CHS), 4.66 (s, 2H, OCH_2), 4.09 (d, J = 2H, OCH_2), 4.04–3.98 (m, 2H, CH); ^{13}C NMR (75 MHz, CDCl_3) d 170.9, 162.5, 154.1, 144.4, 139.8, 134.9, 134.8, 130.4, 128.8, 127.2, 125.6, 123.2, 119.4, 116.4, 115.9, 85.4, 72.6, 66.5, 64.0, 51.6; MS m/z ($\text{M}^+ + \text{H}$) 591. Anal. calcd. for $\text{C}_{30}\text{H}_{24}\text{ClFN}_4\text{O}_4\text{S}$: C, 60.96; H, 4.09; N, 9.48. Found: C, 60.58; H, 3.95; N, 9.23.

General Procedure for the Synthesis of 11a–g

To the anhydrous sodium acetate (0.191 mmol) a mixture of compound **10a** (0.191 mmol), phenyl hydrazine (0.191 mmol), in glacial acetic acid (10 mL), was refluxed for about 7 h. Then the reaction mixture was concentrated and cooled at room temperature, the solid was separated and filtered off, then it was washed thoroughly with water, the crude product was obtained and it was purified by column chromatography on silica gel with hexane–ethyl acetate as the eluent to afford pure compounds **11**.

(5*R*)-5-((2*S*,3*S*)-3-((1-(4-Chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2*H*-pyran-2-yl)-3-(4-fluorophenyl)-2,6-diphenyl-3,3*a*,5,6-tetrahydro-2*H*-pyrazolo[3,4-*d*]thiazole (11a). M.p. 245–247 °C. Yield 85% (0.107 g). IR (KBr) ν 3090, 3010, 1620, 1604, 1480, 1369, 1240, 1132, 764 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.08 (s, 1H, Ar-H), 7.74 (d, J = 9.6 Hz, 2H, Ar-H), 7.46 (d, J = 9.2 Hz, 2H, Ar-H), 7.45 (d, J = 8.9 Hz, 2H, Ar-H), 7.18 (d, J = 8.2 Hz, 2H, Ar-H), 7.05–6.99 (m, 5H, Ar-H), 6.83–7.10 (m, 5H, Ar-H), 5.80–5.79 (m, 2H, =CH), 5.62 (d, J = 2.2 Hz, 1H, S-CH), 5.25 (d, J = 2.2 Hz, 1H, CH-N), 4.95 (d, J = 5.2 Hz, 1H, CH-S), 4.50 (s, 2H, OCH_2), 4.09–3.97 (m, 2H, 2 $\times$ CH), 3.79 (d, J = 6.6 Hz, 2H, OCH_2); ^{13}C NMR (75 MHz, CDCl_3) d 170.8, 162.5, 144.4, 143.4, 141.2, 134.5, 130.1, 129.8, 128.7, 125.6, 122.4, 120.8, 119.4, 115.5, 116.5, 85.6, 72.6, 66.4, 64.0, 51.0; MS m/z ($\text{M}^+ + \text{H}$) 665. Anal. calcd. for $\text{C}_{36}\text{H}_{30}\text{ClFN}_6\text{O}_2\text{S}$: C, 65.0; H, 4.45; N, 12.63. Found: C, 64.58; H, 4.15; N, 12.46.

Similarly, all the compounds **11b–g** were prepared according to the above procedure.

(5*R*)-6-(4-Chlorophenyl)-5-((2*S*,3*S*)-3-((1-(4-chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2*H*-pyran-2-yl)-3-(4-fluorophenyl)-2-phenyl-3,3*a*,5,6-tetrahydro-2*H*-pyrazolo[3,4-*d*]thiazole (11b). M.p. 216–218 °C. Yield 65% (0.071 g). IR (KBr) ν 3080, 3014, 1632, 1609, 1462, 1359, 1250, 1228, 1140, 742 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.04 (s, 1H, Ar-H), 7.60 (d, J = 9.5 Hz, 2H, Ar-H), 7.55 (d, J = 9.4 Hz, 4H, Ar-H), 7.42 (d, J = 8.6 Hz, 4H, Ar-H), 7.16 (d, J = 8.1 Hz, 2H, Ar-H), 6.90–7.02 (m, 5H, Ar-H), 5.82–5.78 (m, 2H, =CH), 5.62 (d, J = 2.2 Hz, 1H, S-CH), 5.25 (d, J = 2.2 Hz, 1H, CH-N), 4.94 (d, J = 5.2 Hz, 1H, CHS), 4.52 (s, 2H, OCH_2), 4.06–3.94 (m, 2H, 2 $\times$ CH), 3.80 (t, 2H, OCH_2); ^{13}C NMR (75 MHz, CDCl_3) d 170.5, 162.1, 144.2, 143.8, 134.2, 130.4, 129.2, 125.5, 122.2, 120.8, 119.4, 116.8, 85.1, 72.5, 65.3, 63.2, 51.0; MS m/z ($\text{M}^+ + \text{H}$) 699. Anal. calcd. for $\text{C}_{36}\text{H}_{29}\text{Cl}_2\text{FN}_6\text{O}_2\text{S}$: C, 61.80; H, 4.18; N, 12.01. Found: C, 61.61; H, 3.95; N, 11.86.

(5*R*)-5-((2*S*,3*S*)-3-((1-(4-Chlorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2*H*-pyran-2-yl)-3-(4-fluorophenyl)-6-(4-nitrophenyl)-2-phenyl-3,3*a*,5,6-tetrahydro-2*H*-pyrazolo[3,4-*d*]thiazole (11c). M.p. 231–233 °C. Yield 85% (0.096 g). IR (KBr) ν 3098, 3019, 1611, 1601, 1540, 1472, 1359, 1262, 1121, 694 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.20 (d, J = 8.7 Hz, 2H, Ar-H), 8.05 (s, 1H, Ar-H), 7.68 (d, J = 9.1 Hz, 2H, Ar-H), 7.61 (d, J = 9.4 Hz, 2H, Ar-H), 7.42 (d, J = 8.5 Hz, 2H, Ar-H), 7.28 (d, J = 8.3 Hz, 2H, Ar-H), 7.10–6.88 (m, 5H, Ar-H), 6.74 (d, J = 9.8 Hz, 2H, Ar-H), 5.86–5.79 (m, 2H, =CH), 5.58 (d, J = 2.2 Hz, 1H, S-CH), 5.21 (d, J = 2.2 Hz, 1H, CH-N), 4.96 (d, J = 5.2 Hz, CH-S), 4.55 (s, 2H, OCH_2), 4.05–3.95 (m, 2H, 2 $\times$ CH), 3.85 (d, J = 6.9 Hz, 2H, OCH_2); ^{13}C NMR (75 MHz, CDCl_3) d 171.5, 162.1, 144.0, 144.9, 134.2, 130.4, 129.5, 128.5, 125.4, 120.8, 119.5, 116.4, 115.4, 85.4, 72.4, 65.9, 63.6,

51.5; MS m/z ($M^+ + H$) 710. Anal. calcd. for $C_{36}H_{29}ClFN_7O_4S$: C, 60.88; H, 4.12; N, 13.81. Found: C, 60.58; H, 4.01; N, 13.59.

(5R)-5-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-2-phenyl-6-*o*-tolyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (11d). M.p. 211–213 °C. Yield 89% (0.105 g). IR (KBr) ν 3084, 3013, 2928, 1621, 1609, 1462, 1374, 1239, 1129, 712 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1H, Ar-H), 7.65 (d, J = 8.5 Hz, 2H, Ar-H), 7.52 (d, J = 9.2 Hz, 2H, Ar-H), 7.47 (d, J = 8.7 Hz, 2H, Ar-H), 7.42–7.40 (m, 4H, Ar-H), 7.12 (d, J = 9.1 Hz, 2H, Ar-H), 6.89–6.80 (m, 5H, ArH), 5.73 (m, 2H, =CH), 5.62 (d, J = 2.2 Hz, 1H, S-CH), 5.25 (d, J = 2.2 Hz, 1H, CH-N), 4.91 (d, J = 5.2 Hz, 1H, CHS), 4.50 (s, 2H, OCH_2), 4.02–3.99 (m, 2H, CH), 3.92 (t, 2H, OCH_2), 2.14 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 162.9, 144.6, 137.2, 133.2, 130.6, 130.4, 128.2, 125.9, 122.7, 119.2, 116.2, 115.4, 84.4, 72.1, 65.3, 63.1, 52.5, 32.0, 17.5; MS m/z ($M^+ + Na$) 701. Anal. calcd. for $C_{37}H_{32}ClFN_6O_2S$: C, 65.43; H, 4.75; N, 12.37. Found: C, 65.15; H, 4.45; N, 12.09.

(5R)-5-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-2-phenyl-6-*p*-tolyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (11e). M.p. 205–215 °C. Yield 67% (0.078 g). IR (KBr) ν 3099, 3018, 2875, 1635, 1614, 1459, 1371, 1229, 1130, 745 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 1H, Ar-H), 7.62 (d, J = 9.1 Hz, 2H, Ar-H), 7.53 (d, J = 9.2 Hz, 2H, Ar-H), 7.40 (d, J = 8.7 Hz, 2H, Ar-H), 7.32 (d, J = 8.2 Hz, 2H, Ar-H), 7.15 (d, J = 8.8 Hz, 2H, Ar-H), 6.92–6.87 (m, 5H, ArH), 6.84 (d, J = 9.4 Hz, 2H, Ar-H), 5.70–5.69 (m, 2H, =CH), 5.62 (d, J = 2.2 Hz, 1H, S-CH), 5.25 (d, J = 2.2 Hz, 1H, CH-N), 4.94 (s, 1H, CHS), 4.55 (s, 2H, OCH_2), 4.04–3.98 (m, 2H, CH), 3.96 (t, 2H, OCH_2), 2.32 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 162.5, 143.8, 137.6, 135.2, 133.2, 130.4, 129.1, 127.9, 122.8, 120.2, 119.0, 116.6, 115.3, 85.4, 72.8, 66.5, 63.4, 51.5, 21.8; MS m/z ($M^+ + H$) 679. Anal. calcd. for $C_{37}H_{32}ClFN_6O_2S$: C, 65.43; H, 4.75; N, 12.37. Found: C, 65.28; H, 4.45; N, 12.03.

3-((5R)-5-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-2-phenyl-3,3a-dihydro-2H-pyrazolo[3,4-*d*]thiazol-6(5H)-yl)phenol (11f).

M.p. 218–219 °C. Yield 85% (0.097 g). IR (KBr) ν 3546, 3100, 1640, 1609, 1471, 1359, 1252, 1110, 779 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 9.40 (brs, 1H, Ph-OH), 8.05 (s, 1H, Ar-H), 7.61 (d, J = 9.7 Hz, 2H, Ar-H), 7.56 (d, J = 9.3 Hz, 2H, Ar-H), 7.42 (d, J = 8.6 Hz, 2H, Ar-H), 7.14 (d, J = 8.4 Hz, 2H, Ar-H), 6.98–6.91 (m, 5H, ArH), 6.80–6.78 (m, 4H, Ar-H), 5.70–5.67 (m, 2H, =CH), 5.65 (d, J = 2.2 Hz, 1H, S-CH), 5.28 (d, J = 2.2 Hz, 1H, CH-N), 4.92 (d, J = 5.2 Hz, 1H, CHS), 4.66 (s, 2H, OCH_2), 4.13 (t, 2H, OCH_2),

4.02–3.99 (m, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 162.1, 158.2, 143.8, 134.5, 130.8, 129.5, 128.6, 125.6, 122.4, 120.7, 119.5, 116.8, 115.7, 114.8, 106.5, 85.4, 72.5, 66.4, 63.4, 51.5; MS m/z ($M^+ + H$) 681. Anal. calcd. for $C_{36}H_{30}ClFN_6O_3S$: C, 63.48; H, 4.44; N, 12.34. Found: C, 63.18; H, 4.15; N, 12.13.

4-((5R)-5-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-2-phenyl-3,3a-dihydro-2H-pyrazolo[3,4-*d*]thiazol-6(5H)-yl)phenol (11g).

M.p. 283–285 °C. Yield 65% (0.074 g). IR (KBr) ν 3369, 3092, 1635, 1616, 1602, 1492, 1372, 1274, 1120, 723 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 9.40 (brs, 1H, Ph-OH), 8.08 (s, 1H, Ar-H), 7.85 (d, J = 9.3 Hz, 2H, Ar-H), 7.52 (d, J = 9.2 Hz, 2H, Ar-H), 7.48 (d, J = 8.4 Hz, 2H, Ar-H), 7.32 (d, J = 8.6 Hz, 2H, Ar-H), 7.19 (d, J = 8.3 Hz, 2H, ArH), 7.02 (d, J = 8.8 Hz, 2H, Ar-H), 6.85–6.80 (m, 5H, ArH), 5.89–5.85 (m, 2H, =CH), 4.86 (d, J = 5.4 Hz, 1H, CHS), 4.56 (s, 2H, OCH_2), 4.08 (d, J = 2H, OCH_2), 4.05–3.99 (m, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 162.3, 154.1, 144.4, 143.8, 134.9, 134.8, 130.4, 128.8, 127.2, 125.6, 123.2, 120.8, 119.4, 116.4, 115.9, 85.4, 72.6, 66.5, 64.0, 51.6; MS m/z ($M^+ + H$) 681. Anal. calcd. for $C_{36}H_{30}ClFN_6O_3S$: C, 63.48; H, 4.44; N, 12.34. Found: C, 63.18; H, 4.15; N, 12.03.

General Procedure for Synthesis of Compounds 12a–g

In anhydrous glacial acetic acid (10 mL), a mixture of compound **10a** (0.191 mol), hydroxylamine hydrochloride (0.4 mol) and sodium acetate (0.191 mol) was refluxed for about 8 h. The reaction mixture was concentrated and then poured into ice cold water, the solid thus separated, was filtered, and washed with ice water, and crystallized from ethanol to afford pure **12a** (87% yield) as a brown solid.

(5R)-5-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-6-phenyl-3,3a,5,6-tetrahydroisoxazolo[3,4-*d*]thiazole (12a). M.p. 255–257 °C. Yield 71% (0.070 g). IR (KBr) ν 3086, 3002, 1616, 1464, 1360, 1309, 1220, 1129, 759 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 8.09 (s, 1H, Ar-H), 7.70 (d, J = 9.6 Hz, 2H, Ar-H), 7.45 (s, 1H, CH-N), 7.42 (d, J = 9.2 Hz, 2H, Ar-H), 7.40 (d, J = 8.9 Hz, 2H, Ar-H), 7.32–7.20 (m, 5H, Ar-H), 7.16 (d, J = 8.2 Hz, 2H, Ar-H), 5.83–5.77 (m, 2H, =CH), 5.70 (d, J = 2.2 Hz, 1H, CH-O), 4.69 (d, J = 2.2 Hz, 1H, CH-S), 4.55 (s, 2H, OCH_2), 4.08–3.96 (m, 2H, 2 $\times$ CH), 3.89 (d, J = 6.6 Hz, 2H, OCH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 144.1, 135.8, 130.4, 127.2, 122.4, 120.0, 119.4, 115.8, 81.0, 72.6, 66.6, 64.0, 61.0, 40.1; MS m/z ($M^+ + H$) 590. Anal. calcd. for $C_{30}H_{25}ClFN_5O_3S$: C, 61.06; H, 4.27; N, 11.87. Found: C, 60.88; H, 4.05; N, 11.56.

Similarly all the compounds **12b–g** prepared according to the above procedure.

(5R)-6-(4-Chlorophenyl)-5-((2S,3S)-3-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-3,3a,5,6-tetrahydrothiazolo[4,5-c]isoxazoles (12b). M.p. 242–244 °C. Yield 85% (0.100 g). IR (KBr) ν 3076, 3011, 1620, 1459, 1342, 1320, 1264, 1219, 1151, 764 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.03 (s, 1H, Ar-H), 7.67 (d, J = 9.5 Hz, 2H, Ar-H), 7.50 (d, J = 9.4 Hz, 4H, Ar-H), 7.44 (s, 1H, CH-N), 7.40 (d, J = 8.6 Hz, 4H, Ar-H), 7.29 (d, J = 8.1 Hz, 2H, Ar-H), 5.82–5.78 (m, 2H, =CH), 5.70 (d, J = 2.2 Hz, 1H, CH-O), 4.69 (d, J = 2.2 Hz, 1H, CH-S), 4.50 (s, 2H, OCH_2), 4.08–3.96 (m, 2H, $2 \times \text{CH}$), 3.84 (t, 2H, OCH_2); ^{13}C NMR (75 MHz, CDCl_3) δ 164.5, 162.1, 144.4, 136.2, 129.6, 127.2, 126.0, 124.7, 122.0, 119.1, 117.5, 115.7, 85.4, 73.1, 66.0, 63.8, 61.0, 40.2; MS m/z ($\text{M}^+ + \text{H}$) 624. Anal. calcd. for $\text{C}_{30}\text{H}_{24}\text{Cl}_2\text{FN}_5\text{O}_3\text{S}$: C, 57.70; H, 3.87; N, 11.21. Found: C, 57.51; H, 3.49; N, 11.46.

(5R)-5-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-6-(4-nitrophenyl)-3,3a,5,6-tetrahydrothiazolo[4,5-c]isoxazoles (12c). M.p. 251–254 °C. Yield 75% (0.095 g). IR (KBr) ν 3089, 3010, 1619, 1608, 1537, 1442, 1349, 1336, 1221, 1131, 754 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.23 (d, J = 8.7 Hz, 2H, Ar-H), 8.06 (s, 1H, Ar-H), 7.55 (d, J = 9.1 Hz, 2H, Ar-H), 7.44 (s, 1H, CH-N), 7.40 (d, J = 9.4 Hz, 2H, Ar-H), 7.36 (d, J = 8.5 Hz, 2H, Ar-H), 7.15 (d, J = 8.3 Hz, 2H, Ar-H), 6.86 (d, J = 9.8 Hz, 2H, Ar-H), 5.84–5.80 (m, 2H, =CH), 5.72 (d, J = 2.2 Hz, 1H, CH-O), 4.70 (d, J = 2.2 Hz, 1H, CH-S), 4.53 (s, 2H, OCH_2), 4.07–3.98 (m, 2H, $2 \times \text{CH}$), 3.83 (d, J = 6.9 Hz, 2H, OCH_2); ^{13}C NMR (75 MHz, CDCl_3) δ 164.0, 161.8, 150.5, 144.4, 134.9, 128.5, 127.3, 126.9, 124.7, 122.0, 119.5, 115.4, 84.4, 73.4, 65.9, 63.6, 61.0, 40.5; MS m/z ($\text{M}^+ + \text{Na}$) 657. Anal. calcd. for $\text{C}_{30}\text{H}_{24}\text{ClFN}_6\text{O}_5\text{S}$: C, 56.74; H, 3.81; N, 13.23. Found: C, 56.58; H, 3.55; N, 13.09.

(5R)-5-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-6-*o*-tolyl-3,3a,5,6-tetrahydrothiazolo[4,5-c]isoxazoles (12d). M.p. 221–223 °C. Yield 81% (0.082 g). IR (KBr) ν 3091, 3008, 2918, 1630, 1426, 1396, 1347, 1232, 1146, 785 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.02 (s, 1H, Ar-H), 7.59 (d, J = 8.5 Hz, 2H, Ar-H), 7.54 (d, J = 9.2 Hz, 2H, ArH), 7.50 (d, J = 8.7 Hz, 2H, ArH), 7.45 (s, 1H, CHN), 7.40–7.35 (m, 4H, ArH), 7.10 (d, J = 9.1 Hz, 2H, ArH), 5.76 (m, 2H, =CH), 5.72 (d, J = 2.2 Hz, 1H, CH-O), 5.68 (d, J = 2.2 Hz, 1H, S-CH), 4.93 (d, J = 5.2 Hz, 1H, CHS), 4.64 (s, 2H, OCH_2), 4.05–3.98 (m, 2H, CH), 3.92 (t, 2H, OCH_2), 2.2 (s, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ 164.8, 162.9, 144.6, 141.3, 136.2, 134.2, 131.6, 128.2, 126.9, 122.2, 119.2, 116.2, 115.8, 108.8, 84.4, 81.3, 73.1, 66.3, 63.8, 61.3, 46.1, 17.9; MS m/z ($\text{M}^+ + \text{H}$) 604. Anal. calcd. for $\text{C}_{31}\text{H}_{27}\text{ClFN}_5\text{O}_3\text{S}$: C, 61.63; H, 4.50; N, 11.59. Found: C, 61.35; H, 11.55; N, 11.29.

(5R)-5-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-6-*p*-tolyl-3,3a,5,6-tetrahydrothiazolo[4,5-c]isoxazoles (12e). M.p. 221–223 °C. Yield 65% (0.066 g). IR (KBr) ν 3069, 3032, 2850, 1653, 1462, 1362, 1242, 1156, 794 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.09 (s, 1H, Ar-H), 7.62 (d, J = 9.1 Hz, 2H, Ar-H), 7.58 (d, J = 9.2 Hz, 2H, Ar-H), 7.40 (d, J = 8.7 Hz, 2H, Ar-H), 7.42 (s, 1H, CH-N), 7.33 (d, J = 8.2 Hz, 2H, Ar-H), 7.18 (d, J = 8.8 Hz, 2H, Ar-H), 6.80 (d, J = 9.4 Hz, 2H, Ar-H), 5.70 (d, J = 2.2 Hz, 1H, CH-O), 5.62 (d, J = 2.2 Hz, 1H, S-CH), 5.60–5.56 (m, 2H, =CH), 4.55 (s, 2H, OCH_2), 4.04–3.98 (m, 2H, CH), 3.96 (t, 2H, OCH_2), 2.32 (s, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ 164.9, 162.5, 144.4, 141.3, 136.2, 134.2, 129.8, 128.8, 127.5, 125.9, 122.5, 119.5, 115.3, 84.5, 73.5, 71.8, 66.5, 63.9, 61.2, 40.1, 21.3; MS m/z ($\text{M}^+ + \text{H}$) 604. Anal. calcd. for $\text{C}_{31}\text{H}_{27}\text{ClFN}_5\text{O}_3\text{S}$: C, 61.63; H, 4.50; N, 11.59. Found: C, 61.48; H, 4.35; N, 11.43.

3-((5R)-5-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-3,3a-dihydrothiazolo[4,5-c]isoxazol-6(5H)-yl)phenol (12f). M.p. 228–231 °C. Yield 83% (0.084 g). IR (KBr) ν 3426, 3109, 1662, 1495, 1395, 1272, 1156, 712 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 9.46 (brs, 1H, Ph-OH), 8.12 (s, 1H, Ar-H), 7.61 (d, J = 9.7 Hz, 2H, Ar-H), 7.59 (d, J = 9.3 Hz, 2H, Ar-H), 7.44 (d, J = 8.6 Hz, 2H, Ar-H), 7.42 (s, 1H, CH-N), 7.18 (d, J = 8.4 Hz, 2H, Ar-H), 6.80–6.78 (m, 4H, Ar-H), 5.70 (d, J = 2.2 Hz, 1H, CH-O), 5.67–5.64 (m, 2H, =CH), 5.62 (d, J = 2.2 Hz, 1H, S-CH), 4.92 (d, J = 5.2 Hz, 1H, CHS), 4.62 (s, 2H, OCH_2), 4.09 (t, 2H, OCH_2), 4.01–3.99 (m, 2H, CH); ^{13}C NMR (75 MHz, CDCl_3) δ 164.5, 162.1, 159.2, 144.8, 136.8, 130.9, 128.6, 126.9, 125.6, 124.1, 122.4, 119.1, 115.7, 112.8, 106.5, 98.2, 85.4, 84.6, 73.1, 72.5, 66.4, 63.9, 61.0, 40.5; MS m/z ($\text{M}^+ + \text{H}$) 606. Anal. calcd. for $\text{C}_{30}\text{H}_{25}\text{ClFN}_5\text{O}_4\text{S}$: C, 59.45; H, 4.16; N, 11.56. Found: C, 59.28; H, 3.95; N, 11.33.

4-((5R)-5-((2S,3S)-3-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-3,6-dihydro-2H-pyran-2-yl)-3-(4-fluorophenyl)-3,3a-dihydrothiazolo[4,5-c]isoxazol-6(5H)-yl)phenol (12g). M.p. 283–285 °C. Yield 88% (0.093 g). IR (KBr) ν 3639, 3072, 1654, 1618, 1482, 1379, 1294, 1150, 796 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 9.49 (brs, 1H, Ph-OH), 8.05 (s, 1H, Ar-H), 7.82 (d, J = 9.3 Hz, 2H, Ar-H), 7.56 (d, J = 9.2 Hz, 2H, Ar-H), 7.48 (d, J = 8.4 Hz, 2H, Ar-H), 7.30 (d, J = 8.6 Hz, 2H, Ar-H), 7.16 (d, J = 8.3 Hz, 2H, ArH), 7.05 (d, J = 8.8 Hz, 2H, ArH), 5.90–5.86 (m, 2H, =CH), 4.98 (d, J = 5.4 Hz, 1H, CHS), 4.63 (s, 2H, OCH_2), 4.12 (d, J = 2H, OCH_2), 4.02–3.96 (m, 2H, CH); ^{13}C NMR (75 MHz, CDCl_3) δ 164.7, 161.8, 146.4, 144.4, 139.8, 137.0, 134.9, 134.3, 128.8, 126.9, 125.6, 122.0, 119.1, 116.7, 81.4, 73.6, 66.5, 64.0, 61.0, 40.9; MS m/z ($\text{M}^+ + \text{Na}$) 628. Anal. calcd. for $\text{C}_{30}\text{H}_{25}\text{ClFN}_5\text{O}_4\text{S}$: C, 59.45; H, 4.16; N, 11.56. Found: C, 59.18; H, 3.95; N, 11.63.

5. Conclusions

A series of novel pyranose glycosides **11a–g** and **12a–g** was prepared and evaluated for their antimicrobial activity; we found out that compounds **11b**, **12b**, **11d**, **12d**, **11g**, and **12g** possess high activity, while compounds **11a**, **12a**, **11c**, **11e**, **12e**, **11f**, and **12f** possess moderate activity against Gram positive strains. As far as Gram negative microorganisms are concerned, compounds **11a**, **12a**, **11f**, **12f**, **11b**, and **12b** showed high activity while compounds **11c**, **12c**, **11g**, and **12g** display moderate activity. Compounds **11e**, **12e**, **11g**, and **12g** also exerted high activity while compounds **11a**, **12a**, **11c**, **12c**, **11d**, **12d**, **11b**, and **12b** have moderate activity against fungi.

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Povzetek

Z reakcijo med halkonskimi derivati (*R,Z*)-2-((2*S*,3*S*)-3-((1-(4-klorofenil)-1*H*-1,2,3-triazol-4-il)metoksi)-3,6-dihidro-2*H*-piran-2-il)-5-(4-fluorobenziliden)-3-feniltiazolidin-4-onov **10a–g** s fenilhidrazinom ali hidroksilamin hidrokloridom smo pripravili serijo novih (5*R*)-5-((2*S*,3*S*)-3-((1-(4-klorofenil)-1*H*-1,2,3-triazol-4-il)metoksi)-3,6-dihidro-2*H*-piran-2-il)-3-(4-fluorofenil)-2,6-difenil-3,3a,5,6-tetrahidro-2*H*-pirazolo[3,4-*d*]tiazolov **11a–g** in (5*R*)-5-((2*S*,3*S*)-3-((1-(4-klorofenil)-1*H*-1,2,3-triazol-4-il)metoksi)-3,6-dihidro-2*H*-piran-2-il)-3-(4-fluorofenil)-6-fenil-3,3a,5,6-tetrahidroizoksazolo[3,4-*d*]tiazolov **12a–g**. Kemijske strukture novih pripravljenih spojin smo določili z IR, NMR, MS in elementno analizo. Za spojine **11a–g** in **12a–g** smo določili tudi učinkovitost delovanja proti bakterijam in glivam.

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