Scientific paper

Synthesis, Nematicidal and Antifungal Properties of Hybrid Heterocyclics

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Received: 28-08-2017

Abstract

A new series of 5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2,6-diphenyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-d]thiazoles **10a–r** was synthesized by the reaction of chalcone derivatives of 2-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-phenylthiazolidin-4-one **9** with aryl/alkyl hydrazines. The chemical structures of newly synthesized compounds were elucidated by IR, NMR, MS and elemental analysis. The compounds **10a–r** were evaluated for their nematicidal activity against *Dietylenchus myceliophagus* and *Caenorhabditis elegans* by aqueous *in vitro* screening technique. Among them, compounds containing *N*-benzylpyrazole moiety (**10d**, **10j**, **10p**), and *N*-methylpyrazole moiety (**10f**, **10i**, **10r**) showed significant nematicidal activity against both tested nematodes with LD₅₀ 160–210 ppm, almost equal to oxamyl standard. Further, these compounds **10a–r** were screened for their antifungal (MZI, MIC, and MFC) activity against four fungal organisms viz, *Candida albicans* (ATCC 10231), *Aspergillus fumigatus* (HIC 6094), *Trichophyton rubrum* (IFO 9185) and *Trichophyton mentagrophytes* (IFO 40996). Most of the new compounds showed appreciable activity against the tested fungi, and emerged as potential molecules for further development.

Keywords: Hybrid heterocyclics, click reaction, Knoevenagel condensation, cyclisation, nematicidal activity, antifungal activity

1. Introduction

1,2,3-Triazoles are one of the most important classes of heterocyclic organic compounds, which are reported to be present in a plethora of biological activities in diverse therapeutic areas.¹ The 1,2,3-triazole motif is associated with diverse pharmacological activities, such as antibacterial, antifungal, hypoglycemic, antihypertensive and analgesic properties. Polysubstituted five-membered aza heterocycles rank as the most potent glycosidase inhibitors.² Further, this nucleus in combination (or linked) with various other classes of compounds, such as amino acids, steroids, aromatic compounds, carbohydrates *etc.*, became prominent in having various pharmacological properties.³ 1,2,3-Triazole modified carbohydrates have become easily available after the discovery of the Cu(I) catalyzed azide-alkynes 1,3-dipolar cycloaddition reaction⁴ and quickly became a pronounced class of non-nat-

ural sugars. The chemistry and biology of triazole modified sugars is dominated by triazole glycosides.⁵ Therefore, the synthesis and investigation of biological activity of 1,2,3-triazole glycosides is an important objective, which also received a considerable attention by the medicinal chemists.

Thiazoles are familiar group of heterocyclic compounds possessing a wide variety of biological activities and their utility as medicine is very much established.⁶ Thiazole nucleus is also an integral part of all the available penicillins which have revolutionized the therapy of bacterial diseases.⁷ Furthermore, there has been considerable interest in the chemistry of thiazolidine-4-one ring system which is the core structure in various synthetic pharmaceuticals displaying a broad spectrum of biological activities.^{8–10} The thiazolidine-4-one ring also occurs in nature; thus actithiazic acid isolated from *Streptomyces* strains exhibits highly specific *in vitro* activity against mycobacteri-

um *Tuberculosis*.¹¹ Thiazolidine-4-ones are known to exhibit diverse bioactivities, such as antiplatelet activating factor,¹² antihistaminic,¹³ COX inhibitor,¹⁴ Ca²⁺ channel blocking,¹⁵ PAF antagonist,¹⁶ cardioprotective,¹⁷ anti-ischemic¹⁸ and nematocidal activities.¹⁹ Moreover, pyrazoles and their derivatives could be considered as possible antimicrobial agents.²⁰ The other derivatives display antidepressant,²¹ antiarthritic²² and cerebroprotecting²³ properties. Some aryl pyrazoles were reported to be non-nucleoside human immunodeficiency virus (HIV-1) reverse transcriptase inhibitor,²⁴ COX-2 inhibitor,^{25–27} activator of the nitric oxide receptor and to have soluble guanylate cyclase activity.²⁸

Nematodes are tiny worms, some of them are plant parasites, and can play an important role in the predisposition of the host plant to the invasion by secondary pathogens.²⁹ Plants attacked by nematodes show retarded growth and development, as well as loss in the quality and quantity of the harvest. The nematocides currently still in use are slated for reduction due to the environmental problems, and human and animals health concerns. For example, effective nematocides, such as dibromochloropropane (DBCD) and ethylene dibromide (EDB) have been withdrawn from the market due to their deleterious effects on humans and the environment. Methyl bromide, the most effective and widely used fumigant for soil-borne pests including nematodes, has already been banned.

The use of nonfumigant nematocides, based on organophosphates and carbamates, is expected to increase concomitantly with the withdrawal of methyl bromide, which will bring about new environmental concerns. In fact, the highly toxic Aldicarb used to control insects and nematodes has been detected in ground water.³⁰ Therefore, alternative nematode control methods or less toxic nematocides need to be developed.³¹ One way of searching for such nematocidal compounds is to screen naturally occurring compounds in plants. Several such compounds, e.g. alkaloids, sesquiterpenes, diterpenes, polyacetylenes have nematocidal activity.^{32–33} For example, *a*-terthienyl is a highly effective nematocidal compound. Other compounds with nematocidal activity have been isolated from plants, mainly from the family *Asteraceae*.^{32–33} However, compounds of plant origin and their analogs have not been developed into commercial nematocides yet; hence there is a need to develop commercial syntheses.

Following the successful introduction of antimicrobial and nematocidal agents, inspired by the biological profile of triazoles, thiazolidinones, pyrazoles and their increasing importance in pharmaceutical and biological fields and in continuation of our work on biologically active molecules^{34–48} and in order to enhance the biological activity of triazoles, thiazolidinones and pyrazole moieties, it was thought to be of interest to accommodate triazole, thiazolidinones and pyrazole moieties in single molecular framework. In this article we report the synthesis of a new class of hybrid heterocycles **10a–g** in good yields

and their evaluation for *in vitro* antifungal and nematocidal activity.

2. Results and Discussion

The key intermediate **8** required for the synthesis of title compound was prepared according to the procedure outlined in the Scheme 1. Diacetone D-glucose (**1**) prepared from D-(+)-glucose by treating with acetone in the presence of a catalytic amount of sulphuric acid according to the literature procedure,⁴⁹ reduction of **2** (prepared by Swern oxidation of **1**) with NaBH₄ in aq. ethanol at 0 °C for 1 h gave **3** (77%), which on subsequent propargylation in DMF in the presence of NaH for 1 h afforded propargyl ether **4** (80%). Now the propargyl ether converted into triazole **5** (82%) by using 1,3-dipolar cycloaddition with *p*-chlorophenyl azide was carried out at ambient temperature in the presence of CuSO₄ and sodium ascorbate in a mixture of 1:1 *t*-BuOH–H₂O as reported by Sharpless. Acid hydrolysis of 5,6-acetonide **5** in 60% AcOH furnished the diol **6** (85%), which on oxidative cleavage with NaIO₄ gave the aldehyde **7**. Subsequently one-pot synthesis of triazole linked to thiazolidenone glycosides was carried out by the condensation reaction between **7**, primary aromatic amine and a thioglycolic acid in the presence of ZnCl₂ under microwave irradiation/conventional heating (Scheme 2). In the classical method, the reactions were performed in dry toluene at reflux for a long time (2–4 h), often leading to degradation processes and consequent low yields of isolated products, whereas the application of microwave assisted technology, the reaction is completed in only 5–10 minutes and the compounds, isolated by conventional work-up, are obtained in satisfactory yields, often higher

Table 1. Synthesis of compounds **10a–r**

Compound	R	R ^I	Yield (%)
10a	<i>p</i> -Me-C ₆ H ₄ -	C ₆ H ₅ -	69
10b	<i>p</i> -Me-C ₆ H ₄ -	<i>p</i> -MeOC ₆ H ₄ -	70
10c	<i>p</i> -Me-C ₆ H ₄ -	<i>p</i> -Cl-C ₆ H ₄ -	67
10d	<i>p</i> -Me-C ₆ H ₄ -	C ₆ H ₅ -CH ₂ -	72
10e	<i>p</i> -Me-C ₆ H ₄ -	(CH ₃) ₂ -CH-	76
10f	<i>p</i> -Me-C ₆ H ₄ -	CH ₃ -	66
10g	<i>p</i> -Cl-C ₆ H ₄ -	C ₆ H ₅ -	68
10h	<i>p</i> -Cl-C ₆ H ₄ -	<i>p</i> -MeOC ₆ H ₄ -	70
10i	<i>p</i> -Cl-C ₆ H ₄ -	<i>p</i> -Cl-C ₆ H ₄ -	76
10j	<i>p</i> -Cl-C ₆ H ₄ -	C ₆ H ₅ -CH ₂ -	69
10k	<i>p</i> -Cl-C ₆ H ₄ -	(CH ₃) ₂ -CH-	67
10l	<i>p</i> -Cl-C ₆ H ₄ -	CH ₃ -	71
10m	<i>p</i> -NO ₂ -C ₆ H ₄ -	C ₆ H ₅ -	74
10n	<i>p</i> -NO ₂ -C ₆ H ₄ -	<i>p</i> -MeOC ₆ H ₄ -	76
10o	<i>p</i> -NO ₂ -C ₆ H ₄ -	<i>p</i> -Cl-C ₆ H ₄ -	72
10p	<i>p</i> -NO ₂ -C ₆ H ₄ -	C ₆ H ₅ -CH ₂ -	74
10q	<i>p</i> -NO ₂ -C ₆ H ₄ -	(CH ₃) ₂ -CH-	71
10r	<i>p</i> -NO ₂ -C ₆ H ₄ -	CH ₃ -	67

Scheme 1

Scheme 2

R = a) 4-CH₃-C₆H₅; b) 4-Cl-C₆H₅; c) 4-NO₂-C₆H₅

Reagents and conditions: a) COCl₂, CH₂Cl₂, Et₃N, -78 °C → rt, 1.5 h, 83%; b) NaBH₄, EtOH, H₂O, (19:1), 0 °C → rt, 78%; c) Propargyl bromide, NaH, DMF, 0 °C → rt; d) *p*-Chlorophenylazide, sodium ascorbate, CuSO₄ · 5H₂O, *t*-BuOH/H₂O, 0 °C → rt, 75%; e) 60%, AcOH, rt, 69%; f) NaIO₄, CH₂Cl₂, 0 °C → rt, 75%; g) Ar-NH₂, SHCH₂COOH, ZnCl₂, toluene, 80 °C, 85%; h) 4-F-C₆H₄-CHO, AcOH / NaOAc, reflux, 82–88%; i) R'-NHNH₂ · HCl, AcOH/NaOAc reflux, 76–67%.

than those achieved by traditional methods.³⁵ Compound **8** was then reacted with *p*-fluorobenzaldehyde in the presence of anhydrous NaOAc in glacial AcOH at reflux temperature to give chalcone derivatives of triazole linked thiazolidenone glycosides **9**. Furthermore, the compounds upon cyclocondensation with alkyl/aryl hydrazines in the presence of anhydrous NaOAc in glacial AcOH at reflux temperature gave **10a–r** in good yields. The versatility of the reaction is demonstrated by the fact that both aromatic hydrazines, such as phenyl hydrazines, and aliphatic hydrazines, such as benzylhydrazine, isopropylhydrazine, methylhydrazine, afforded their corresponding **10a–r** in good yields. The structures of synthesized compounds

were confirmed by IR, NMR, MS and elemental analysis. Furthermore, the compounds were subjected to nematocidal and anti bacterial testing.

3. Antifungal Activity

The newly prepared compounds **10a–r** were screened for their antifungal activity against four fungal organisms, viz *Candida albicans* (ATCC 10231), *Aspergillus fumigatus* (HIC 6094), *Trichophyton rubrum* (IFO 9185) and *Trichophyton mentagrophytes* (IFO 40996) in dimethyl sulfoxide (DMSO) by agar diffusion method.⁵⁰ Amphotericin B was

used as the standard drug and the zones of fungal inhibition values are reported in Table 3. In addition, the MIC and MFC values determined by the broth dilution method⁵¹ are recorded in Table 4.

4. Nematicidal Activity

The compounds synthesized **10a–g** in this study were also screened for their nematicidal activity against *Dietylenchus myceliophagus* and *Caenorhabditis elegans* by aqueous *in vitro* screening technique⁵² at various concentrations. The nematicidal activity of each tested compound was compared with the standard drug Levamisole. The results have been expressed in terms of LD₅₀ *i.e.* median le-

thal dose at which 50% of nematodes became immobile (dead). The screened data reveal that compounds **10e** and **10f** are the most effective against *Dietylenchus myceliophagus* and *Caenorhabditis elegans* with LD₅₀ 190 and 220 × 10⁻⁶ respectively, whereas the other tested compounds showed moderate activity. The LD₅₀ values of the compounds screened are presented in Table 2.

5. Experimental

Commercial grade reagents were used as supplied. Solvents except analytical reagent grade were dried and purified according to literature when necessary. Reaction progress and purity of the compounds were checked by

Table 2. Median lethal dose LD₅₀ (ppm) of compounds **10a–r**

Compd.	<i>D. myceliophagus</i>	<i>C. elegans</i>	Compd.	<i>D. myceliophagus</i>	<i>C. elegans</i>
10a	850	670	10j	180	200
10b	950	870	10k	520	670
10c	240	360	10l	190	210
10d	190	210	10m	800	620
10e	550	600	10n	920	810
10f	160	200	10o	230	350
10g	810	650	10p	190	190
10h	900	820	10q	510	600
10i	290	380	10r	180	200
Oxamyl	150	180	Oxamyl	150	180

LD₅₀, median lethal dose (the concentration at which 50% nematodes became immobile)

Table 3. Inhibitory zone diameters (mm) of **10a–r** against tested fungal strains

Compound	Mean zone of inhibition (MZI) in mm ^a			
	<i>C. albicans</i>	<i>A. fumigatus</i>	<i>T. rubrum</i>	<i>T. mentagrophytes</i>
10a	11	10	–	09
10b	09	15	13	12
10c	13	11	11	10
10d	22	16	15	16
10e	–	13	–	–
10f	20	20	20	18
10g	–	–	17	–
10h	14	–	–	–
10i	–	–	15	–
10j	21	17	14	16
10k	10	–	11	12
10l	18	15	13	16
10m	08	11	10	09
10n	13	–	–	–
10o	15	–	–	–
10p	19	16	11	13
10q	–	–	09	–
10r	21	14	15	14
Amphotericin B	25	20	20	18

Amphotericin B (100 µg/disc) was used as the positive reference; compounds **10a–r** (300 µg/disc).

– indicates no sensitivity or MZI lower than 7 mm. ^a Values are mean (n = 3).

Table 4. Minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) in µg/mL of compounds **10a–r**

Compd.	<i>C. albicans</i>		<i>A. fumigatus</i>		<i>T. rubrum</i>		<i>T. mentagrophytes</i>	
	MIC	MFC	MIC	MFC	MIC	MFC	MIC	MFC
10a	–	–	25.0	25.0	25.0	50.0	25.0	25.0
10b	25.0	25.0	25.0	50.0	12.5	12.5	12.5	25.0
10c	12.5	25.0	6.25	12.5	6.25	12.5	6.25	12.5
10d	3.12	6.25	25.0	25.0	12.5	25.0	25.0	25.0
10e	12.5	25.0	–	–	–	–	–	–
10f	3.12	3.12	3.12	6.25	3.12	6.25	6.25	12.5
10g	6.25	6.25	12.5	25.0	12.5	12.5	6.25	12.5
10h	25.0	50.0	–	–	25.0	50.0	25.0	50.0
10i	12.5	12.5	25.0	25.0	12.5	12.5	25.0	50.0
10j	3.12	6.25	6.25	12.5	6.25	12.5	12.5	25.0
10k	12.5	25.0	25.0	25.0	–	–	25.0	50.0
10l	12.5	25.0	6.25	50.0	6.25	25.0	–	–
10m	12.5	25.0	12.5	50.0	6.25	25.0	12.5	12.5
10n	6.25	12.5	12.5	25.0	12.5	25.0	–	–
10o	25.0	25.0	25.0	50.0	25.0	50.0	6.25	12.5
10p	12.5	25.0	–	–	–	–	–	–
10q	25.0	25.0	25.0	50.0	12.5	25.0	12.5	25.0
10r	12.5	25.0	12.5	25.0	12.5	25.0	12.5	25.0
Amphotericin B	6.25	12.5	3.12	6.25	3.12	12.5	3.12	12.5

– Indicates fungi are resistant to the compound >100 µg/mL concentration.

thin-layer chromatography (TLC) on pre-coated silica gel F254 plates from Merck and compounds 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. Microwave reactions were carried out in mini lab microwave catalytic reactor (ZZKD, WBFY-201). Optical rotations were measured on Perkin–Elmer 141 polarimeter by using a 2 mL cell with a path length of 1 dm with CHCl₃ or CDCl₃ as solvent. All melting points are uncorrected and measured using Fisher–Johns apparatus. IR spectra were recorded as KBr disks on a Perkin–Elmer FT IR spectrometer. The ¹H NMR and ¹³C NMR spectra were recorded on a Varian Gemini spectrometer (300 MHz for ¹H and 75 MHz for ¹³C). Chemical shifts are reported as δ on ppm scale against TMS as the internal reference and coupling constants (*J*) are reported in Hz units. Mass spectra were recorded on a VG micro mass 7070H spectrometer. Elemental analyses (C, H, N) were determined by a Perkin–Elmer 240 CHN elemental analyzer and are within ±0.4% of theoretical values.

2-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-phenylthiazolidin-4-ones 8a–c. To a solution of diol **6** (0.200 g, 0.48 mmol) in CH₂Cl₂ (5 mL), NaIO₄ (0.130 g, 0.61 mmol) was added at 0 °C and stirred at room temperature for 6 h. The reaction mixture was filtered and washed with CH₂Cl₂ (2 × 10 mL). It was dried (Na₂SO₄) and evaporated to give aldehyde **7** (0.150 g) in quantitative yield as a yellow liquid, which was used as such for the next reaction.

To a stirred mixture of **7** (0.150 g, 0.395 mmol), aromatic amine (0.395 mmol) and anhydrous thioglycolic acid (0.160 g, 0.211 mmol) in dry toluene (5 mL), ZnCl₂ (0.100g, 0.751 mmol) was added after 2 min and irradiated in microwave bath reactor at 280 W for 4–7 minutes at 110 °C. After cooling, the filtrate was concentrated to dryness under reduced pressure and the residue was taken-up in ethyl acetate. The ethyl acetate layer was washed with 5% sodium bicarbonate solution and finally with brine. The organic layer was dried over Na₂SO₄ and evaporated to dryness at reduced pressure. The crude product thus obtained was purified by column chromatography on silica gel (60–120 mesh) with hexane/ethyl acetate as the eluent.

2-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-p-tolylthiazolidin-4-one (8a) m.p. 191–193 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.26 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.04 (s, 1H, Ar-H), 7.54 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.39 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.15 (d, *J* = 8.3 Hz, 2H, Ar-H), 5.76 (d, *J* = 3.6 Hz, 1H, C₁H), 4.96 (d, *J* = 5.2 Hz, 1H, CH-S), 4.66 (t, *J* = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.91 (m, 1H, C₄H), 3.76 (s, 2H, CH₂), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 2.3 (s, 3H, CH₃), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 172.6, 143.2, 137.4, 133.6, 132.3, 131.2, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 51.4, 26.1, 16.1; MS: *m/z* (M⁺+Na) 565. Anal. Calcd for C₂₆H₂₇ClN₄O₅S: C, 57.51; H, 5.51; N, 10.32. Found: C, 57.32; H, 5.35; N, 10.09.

3-(4-Chlorophenyl)-2-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-imidazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)thiazolidin-4-one (8b) m.p. 216–218 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.02 (s, 1H, Ar-H), 7.50 (d, *J* = 9.2 Hz, 4H, Ar-H), 7.41 (d, *J* = 8.9 Hz, 4H, Ar-H), 5.72 (d, *J* = 3.6 Hz, 1H, C₁H), 4.94 (d, *J* = 5.2 Hz, CH-S), 4.60 (t, *J* = 3.9 Hz, 1H, C₂H), 4.51 (s, 2H, OCH₂), 3.96–3.91 (m, 1H, C₄H), 3.76 (s, 2H, CH₂), 3.31 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 1.55 (s, 3H, CH₃), 1.32 (m, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 170.6, 139.4, 134.8, 133.2, 129.4, 128.6, 125.6, 122.2, 119.4, 111.2, 104.9, 81.5, 74.5, 66.3, 52.6, 34.6, 26.5; MS: *m/z* (M⁺+H) 563. Anal. Calcd for C₂₅H₂₄Cl₂N₄O₅S: C, 53.29; H, 4.29; N, 9.94. Found: C, 53.21; H, 4.16; N, 9.83.

2-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-(4-nitrophenyl)thiazolidin-4-one (8c) m.p. 201–205 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.26 (d, *J* = 8.7 Hz, 2H), 8.04 (s, 1H, Ar-H), 7.51 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.42 (d, *J* = 8.5 Hz, 2H, Ar-H), 6.82 (d, *J* = 9.8 Hz, 2H, Ar-H), 5.71 (d, *J* = 3.6 Hz, 1H, C₁H), 4.96 (d, *J* = 5.2 Hz, CH-S), 4.62 (t, *J* = 3.9 Hz, 1H, C₂H), 4.53 (s, 2H, OCH₂), 3.96–3.91 (m, 1H, C₄H), 3.76 (s, 2H, CH₂), 3.28 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 1.52 (s, 3H, CH₃), 1.34 (m, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 170.6, 147.5, 144.4, 143.2, 134.8, 131.2, 128.6, 124.6, 122.4, 119.8, 111.8, 104.9, 81.5, 78.2, 74.8, 66.9, 52.4, 34.6, 26.8; MS: *m/z* (M⁺+H) 574. Anal. Calcd for C₂₅H₂₄ClN₅O₇S: C, 52.31; H, 4.21; N, 12.20. Found: C, 52.26; H, 4.19; N, 12.11.

(Z)-5-Benzylidene-2-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-phenylthiazolidin-4-ones 9a–c. A mixture of compound **8** (0.01 mol), *p*-fluorobenzaldehyde (0.02 mol) and sodium acetate (0.01 mol) in anhydrous glacial acetic acid (20 mL), was refluxed for 3 h. The reaction mixture was concentrated and then poured into ice cold water, the solid thus separated was filtered, washed with water and crystallized from glacial acetic acid to afford pure compounds.

(Z)-2-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-5-(4-fluorobenzylidene)-3-*p*-tolylthiazolidin-4-one (9a). This compound was obtained as brown solid, m.p. 231–235 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.22 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.06 (s, 1H, Ar-H), 7.84 (s, 1H, CH=C), 7.54 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.39 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.15 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.91–6.87 (m, 5H, Ar-H and CH-S), 5.76 (d, *J* = 3.6 Hz, 1H, C₁H), 4.66 (t, *J* = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.91 (m, 1H, C₄H), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 2.3 (s, 3H, CH₃), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 172.6, 143.2, 137.4,

133.6, 132.3, 131.2, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 51.4, 26.1, 16.1; MS: *m/z* (M⁺+H) 649. Anal. Calcd for C₃₃H₃₀ClFN₄O₅S: C, 61.06; H, 4.66; N, 8.63. Found: C, 60.82; H, 4.45; N, 8.43.

(Z)-3-(4-Chlorophenyl)-2-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-5-(4-fluorobenzylidene)thiazolidin-4-one (9b). The compound was obtained as dark yellow solid, m.p. 232–235 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.06 (s, 1H, Ar-H), 7.82 (s, 1H, CH=C), 7.52 (d, *J* = 9.2 Hz, 4H, Ar-H), 7.43 (d, *J* = 8.9 Hz, 4H, Ar-H), 6.91–6.87 (m, 5H, Ar-H and CH-S), 5.72 (d, *J* = 3.6 Hz, 1H, C₁H), 4.60 (t, *J* = 3.9 Hz, 1H, C₂H), 4.51 (s, 2H, OCH₂), 3.96–3.91 (m, 1H, C₄H), 3.31 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 1.55 (s, 3H, CH₃), 1.32 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 170.6, 138.4, 134.8, 133.2, 130.8, 129.4, 128.6, 124.6, 122.2, 119.4, 111.2, 104.9, 81.5, 74.5, 66.3, 52.6, 34.6, 26.5; MS: *m/z* (M⁺+H) 669. Anal. Calcd for C₃₂H₂₇Cl₂FN₄O₅S: C, 57.40; H, 4.06; N, 8.37. Found: C, 57.21; H, 4.01; N, 8.03.

(Z)-2-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-5-(4-fluorobenzylidene)-3-(4-nitrophenyl)thiazolidin-4-one (9c). The compound was obtained as brown solid, m.p. 216–218 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.26 (d, *J* = 8.7 Hz, 2H), 8.04 (s, 1H, Ar-H), 7.84 (s, 1H, CH=C), 7.51 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.42 (d, *J* = 8.5 Hz, 2H, Ar-H), 6.91–6.87 (m, 5H, Ar-H and CH-S), 6.82 (d, *J* = 9.8 Hz, 2H, Ar-H), 5.71 (d, *J* = 3.6 Hz, 1H, C₁H), 4.62 (t, *J* = 3.9 Hz, 1H, C₂H), 4.53 (s, 2H, OCH₂), 3.96–3.91 (m, 1H, C₄H), 3.76 (s, 2H, CH₂), 3.28 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 1.52 (s, 3H, CH₃), 1.34 (m, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 170.6, 147.5, 144.4, 143.2, 138.4, 134.8, 130.6, 131.2, 128.6, 124.6, 122.4, 119.8, 111.8, 104.9, 81.5, 78.2, 74.8, 66.9, 52.4, 26.8; MS: *m/z* (M⁺+Na) 692. Anal. Calcd for C₃₁H₂₉ClFN₅O₇S: C, 55.56; H, 4.36; N, 10.30. Found: C, 55.26; H, 4.29; N, 10.10.

5-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2,6-diphenyl-2-alkyl-6-phenyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-d]thiazoles 10a–r. A mixture of compound **9** (5 mmol), alkyl/aryl hydrazine (5 mmol) and anhydrous sodium acetate (5 mmol) in glacial acetic acid (20 mL), was refluxed for 7 h. The reaction mixture was concentrated and cooled to room temperature, the solid thus separated was filtered, washed thoroughly with water. The crude product thus obtained was purified by column chromatography on silica gel with hexane/ethyl acetate as eluent to afford pure compounds.

5-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofu-

ro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-phenyl-6-*p*-tolyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10a). This was obtained by reacting compound **9a** (1 g) and phenylhydrazine (0.25 g) as described in the typical procedure and isolated as a brown solid, yield 72%, m.p. 248–250 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.20 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.04 (s, 1H, Ar-H), 7.51 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.40 (s, 1H, CH-S), 7.29 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.18–7.15 (m, 5H, Ar-H), 7.05 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.91–6.87 (m, 4H, Ar-H), 5.76 (d, *J* = 3.6 Hz, 1H, C₁H), 5.62 (d, *J* = 2.2 Hz, 1H, S-CH), 5.25 (d, *J* = 2.2 Hz, 1H, CH-N), 4.66 (t, *J* = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.91 (m, 1H, C₄H), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 2.3 (s, 3H, CH₃), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 172.6, 143.2, 141.4, 137.4, 133.6, 132.3, 131.2, 129.3, 125.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 51.4, 26.1, 21.3, 16.1; MS: *m/z* (*M*⁺+Na) 761. Anal. Calcd for C₃₉H₃₆ClFN₆O₄S: C, 63.36; H, 4.90; N, 11.37. Found: C, 63.12; H, 4.75; N, 11.29.

5-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-(4-methoxyphenyl)-6-*p*-tolyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10b). This was obtained by reacting compound **9a** (1 g) and *p*-methoxyphenylhydrazine (0.35 g) as described in the typical procedure and isolated as a yellow solid, yield 62%, m.p. 268–272 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.18 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.04 (s, 1H, Ar-H), 7.51 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.40 (s, 1H, CH-S), 7.29 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.12–7.10 (m, 4H, Ar-H), 7.05 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.91–6.87 (m, 4H, Ar-H), 5.76 (d, *J* = 3.6 Hz, 1H, C₁H), 5.62 (d, *J* = 2.2 Hz, 1H, S-CH), 5.25 (d, *J* = 2.2 Hz, 1H, CH-N), 4.66 (t, *J* = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.91 (s, 3H, OMe), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 2.3 (s, 3H, CH₃), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 172.6, 151.7, 143.2, 141.4, 137.4, 133.6, 132.3, 131.2, 129.3, 125.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 55.8, 51.4, 26.1, 21.3, 16.1; MS: *m/z* (*M*⁺+H) 789. Anal. Calcd for C₄₀H₃₈ClFN₆O₅S: C, 62.46; H, 4.98; N, 10.92. Found: C, 62.12; H, 4.88; N, 10.87.

2-(4-Chlorophenyl)-5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-6-*p*-tolyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10c). This was obtained by reacting compound **9a** (1 g) and *p*-chlorophenylhydrazine (0.45 g) as described in the typical procedure and isolated as a brown solid, yield 76%, m.p. 248–251 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.21 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.09 (s, 1H, Ar-H), 7.55 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.42 (s, 1H, CH-S), 7.29 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.10–7.08 (m, 4H,

Ar-H), 7.05 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.91–6.87 (m, 4H, Ar-H), 5.76 (d, *J* = 3.6 Hz, 1H, C₁H), 5.62 (d, *J* = 2.2 Hz, 1H, S-CH), 5.25 (d, *J* = 2.2 Hz, 1H, CH-N), 4.66 (t, *J* = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 2.3 (s, 3H, CH₃), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 172.6, 151.7, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 126.3, 125.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 51.4, 26.1, 21.3, 16.1; MS: *m/z* (*M*⁺+H) 773. Anal. Calcd for C₃₉H₃₅Cl₂FN₆O₄S: C, 60.54; H, 4.58; N, 10.86. Found: C, 60.32; H, 4.28; N, 10.47.

2-Benzyl-5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-6-*p*-tolyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10d). This was obtained by reacting compound **9a** (1 g) and benzylhydrazine (0.65 g) as described in the typical procedure and isolated as a brown solid, yield 66%. m.p. 288–291 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.21 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.09 (s, 1H, Ar-H), 7.55 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.42 (s, 1H, CH-S), 7.29 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.10–7.08 (m, 5H, Ar-H), 7.05 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.91–6.87 (m, 4H, Ar-H), 5.92 (s, 2H, CH₂Ph), 5.76 (d, *J* = 3.6 Hz, 1H, C₁H), 5.62 (d, *J* = 2.2 Hz, 1H, S-CH), 5.25 (d, *J* = 2.2 Hz, 1H, CH-N), 4.66 (t, *J* = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 2.3 (s, 3H, CH₃), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 171.6, 151.6, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 125.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 58.1, 51.4, 26.1, 21.3, 16.1; MS: *m/z* (*M*⁺+H) 753. Anal. Calcd for C₄₀H₃₈ClFN₆O₄S: C, 63.78; H, 5.08; N, 11.16. Found: C, 63.52; H, 4.96; N, 10.97.

5-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-isopropyl-6-*p*-tolyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10e). This was obtained by reacting compound **9a** (1 g) and isopropylhydrazine (0.35 g) as described in the typical procedure and isolated as a yellow solid, yield 76%, m.p. 248–251 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.19 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.06 (s, 1H, Ar-H), 7.55 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.42 (s, 1H, CH-S), 7.29 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.05 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.91–6.87 (m, 4H, Ar-H), 5.76 (d, *J* = 3.6 Hz, 1H, C₁H), 5.62 (d, *J* = 2.2 Hz, 1H, S-CH), 5.25 (d, *J* = 2.2 Hz, 1H, CH-N), 4.66 (t, *J* = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 2.80–2.78 (m, 1H, CH), 2.3 (s, 3H, CH₃), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃), 0.96 (d, *J* = 6.3 Hz, 6H, 2 × CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 171.6, 151.6, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 58.1, 51.4, 50.6, 26.1, 21.3, 16.1; MS: *m/z* (*M*⁺+H) 705. Anal. Calcd for

$C_{36}H_{38}ClFN_6O_4S$: C, 61.31; H, 5.43; N, 11.92. Found: C, 60.98; H, 5.26; N, 11.77.

5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-methyl-6-*p*-tolyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-d]thiazole (10f). This was obtained by reacting compound **9a** (1 g) and methylhydrazine (0.25 g) as described in the typical procedure and isolated as a yellow solid, yield 66%, m.p. 228–231 °C; 1H NMR (300 MHz, DMSO- d_6) δ 8.19 (d, J = 8.7 Hz, 2H, Ar-H), 8.06 (s, 1H, Ar-H), 7.55 (d, J = 9.2 Hz, 2H, Ar-H), 7.42 (s, 1H, CH-S), 7.29 (d, J = 8.33 Hz, 2H, Ar-H), 7.05 (d, J = 8.3 Hz, 2H, Ar-H), 6.91–6.87 (m, 4H, Ar-H), 5.76 (d, J = 3.6 Hz, 1H, C₁H), 5.62 (d, J = 2.2 Hz, 1H, S-CH), 5.25 (d, J = 2.2 Hz, 1H, CH-N), 4.66 (t, J = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.71 (s, 3H, N-CH₃), 3.26 (dd, J_1 = 9.1 Hz, J_2 = 4.2 Hz, 1H, C₃H), 2.3 (s, 3H, CH₃), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ^{13}C NMR (75 MHz, DMSO- d_6) δ 171.6, 151.6, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 58.1, 51.4, 39.3, 26.1, 16.1; MS: m/z (M^+ + Na⁺) 689. Anal. Calcd for $C_{34}H_{34}ClFN_6O_4S$: C, 60.30; H, 5.06; N, 12.42. Found: C, 60.22; H, 4.96; N, 12.22.

6-(4-Chlorophenyl)-5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-phenyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-d]thiazole (10g). This was obtained by reacting compound **9b** (1 g) and phenylhydrazine (0.25 g) as described in the typical procedure and isolated as a brown solid, yield 65%, m.p. 249–251 °C; 1H NMR (300 MHz, DMSO- d_6) δ 8.16 (d, J = 8.7 Hz, 2H, Ar-H), 8.02 (s, 1H, Ar-H), 7.49 (d, J = 9.2 Hz, 2H, Ar-H), 7.36 (s, 1H, CH-S), 7.22 (d, J = 8.33 Hz, 2H, Ar-H), 7.13–7.11 (m, 5H, Ar-H), 7.02 (d, J = 8.3 Hz, 2H, Ar-H), 6.81–6.77 (m, 4H, Ar-H), 5.66 (d, J = 3.6 Hz, 1H, C₁H), 5.58 (d, J = 2.2 Hz, 1H, S-CH), 5.21 (d, J = 2.2 Hz, 1H, CH-N), 4.62 (t, J = 3.9 Hz, 1H, C₂H), 4.51 (s, 2H, OCH₂), 3.94–3.91 (m, 1H, C₄H), 3.26 (dd, J_1 = 9.1 Hz, J_2 = 4.2 Hz, 1H, C₃H), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ^{13}C NMR (75 MHz, DMSO- d_6) δ 174.6, 143.0, 141.4, 137.4, 133.6, 132.3, 131.2, 129.3, 125.3, 128.4, 127.9, 126.1, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 51.4, 26.1, 16.1; MS: m/z (M^+ + H) 759. Anal. Calcd for $C_{39}H_{36}ClFN_6O_4S$: C, 60.08; H, 4.38; N, 11.07. Found: C, 60.02; H, 4.11; N, 10.95.

6-(4-Chlorophenyl)-5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-(4-methoxyphenyl)-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-d]thiazole (10h). This was obtained by reacting compound **9b** (1 g) and *p*-methoxyphenylhydrazine (0.35 g) as described in the typical procedure and isolated as a yellow solid, yield 68%, m.p. 274–276 °C; 1H NMR (300 MHz, DMSO- d_6) δ 8.18 (d, J = 8.7 Hz, 2H, Ar-H), 8.04 (s, 1H, Ar-H), 7.51 (d, J = 9.2 Hz, 2H, Ar-H), 7.40 (s, 1H, CH-S), 7.29 (d, J = 8.33 Hz, 2H, Ar-H), 7.12–7.10 (m, 4H, Ar-H), 7.05 (d, J = 8.3 Hz, 2H, Ar-H), 6.91–6.87 (m, 4H, Ar-H), 5.76 (d, J = 3.6 Hz, 1H, C₁H), 5.62 (d, J = 2.2 Hz, 1H, S-CH), 5.25 (d, J = 2.2 Hz, 1H, CH-N), 4.66 (t, J = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.91 (s, 3H, OMe), 3.26 (dd, J_1 = 9.1 Hz, J_2 = 4.2 Hz, 1H, C₃H), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ^{13}C NMR (75 MHz, DMSO- d_6) δ 172.6, 151.7, 143.2, 141.4, 137.4, 133.6, 132.3, 131.2, 129.3, 126.1, 125.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 55.8, 51.4, 26.1, 16.1; MS: m/z (M^+ + H) 789. Anal. Calcd for $C_{39}H_{35}Cl_2FN_6O_5S$: C, 59.32; H, 4.47; N, 10.64. Found: C, 58.92; H, 4.18; N, 10.47.

2,6-Bis(4-chlorophenyl)-5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-d]thiazole (10i). This was obtained by reacting compound **9b** (1 g) and *p*-chlorophenylhydrazine (0.45 g) as described in the typical procedure and isolated as a brown solid, yield 76%, m.p. 268–271 °C; 1H NMR (300 MHz, DMSO- d_6) δ 8.23 (d, J = 8.7 Hz, 2H, Ar-H), 8.11 (s, 1H, Ar-H), 7.58 (d, J = 9.2 Hz, 2H, Ar-H), 7.46 (s, 1H, CH-S), 7.29 (d, J = 8.33 Hz, 2H, Ar-H), 7.11–7.09 (m, 4H, Ar-H), 7.07 (d, J = 8.3 Hz, 2H, Ar-H), 6.91–6.87 (m, 4H, Ar-H), 5.76 (d, J = 3.6 Hz, 1H, C₁H), 5.62 (d, J = 2.2 Hz, 1H, S-CH), 5.25 (d, J = 2.2 Hz, 1H, CH-N), 4.66 (t, J = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.26 (dd, J_1 = 9.1 Hz, J_2 = 4.2 Hz, 1H, C₃H), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ^{13}C NMR (75 MHz, DMSO- d_6) δ 172.6, 151.7, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 126.3, 125.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 51.4, 26.1, 16.1; MS: m/z (M^+ + Na) 815. Anal. Calcd for $C_{38}H_{32}Cl_3FN_6O_4S$: C, 57.47; H, 4.08; N, 10.56. Found: C, 57.22; H, 3.95; N, 10.32.

2-Benzyl-6-(4-chlorophenyl)-5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-d]thiazole (10j). This was obtained by reacting compound **9b** (1 g) and benzylhydrazine (0.65 g) as described in the typical procedure and isolated as a brown solid, yield 71%, m.p. 258–261 °C; 1H NMR (300 MHz, DMSO- d_6) δ 8.25 (d, J = 8.7 Hz, 2H, Ar-H), 8.11 (s, 1H, Ar-H), 7.59 (d, J = 9.2 Hz, 2H, Ar-H), 7.46 (s, 1H, CH-S), 7.32 (d, J = 8.33 Hz, 2H, Ar-H), 7.12–7.10 (m, 5H, Ar-H), 7.08 (d, J = 8.3 Hz, 2H, Ar-H), 6.96–6.90 (m, 4H, Ar-H), 5.96 (s, 2H, CH₂Ph), 5.77 (d, J = 3.6 Hz, 1H, C₁H), 5.65 (d, J = 2.2 Hz, 1H, S-CH), 5.28 (d, J = 2.2 Hz, 1H, CH-N), 4.66 (t, J = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.26 (dd, J_1 = 9.1 Hz, J_2 = 4.2 Hz, 1H, C₃H), 1.53

(s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 171.6, 151.6, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 125.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 58.1, 51.4, 26.1, 16.1; MS: *m/z* (M⁺ + H) 773. Anal. Calcd for C₃₉H₃₅Cl₂FN₆O₄S: C, 60.54; H, 4.56; N, 10.86. Found: C, 60.34; H, 4.36; N, 10.37.

6-(4-Chlorophenyl)-5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-isopropyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10k). This was obtained by reacting compound **9b** (1 g) and isopropylhydrazine (0.35 g) as described in the typical procedure and isolated as a yellow solid, yield 69%, m.p. 238–239 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.32 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.16 (s, 1H, Ar-H), 7.65 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.52 (s, 1H, CH-S), 7.39 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.09 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.95–6.92 (m, 4H, Ar-H), 5.76 (d, *J* = 3.6 Hz, 1H, C₁H), 5.62 (d, *J* = 2.2 Hz, 1H, S-CH), 5.25 (d, *J* = 2.2 Hz, 1H, CH-N), 4.66 (t, *J* = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 2.80–2.78 (m, 1H, CH), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃), 0.96 (d, *J* = 6.3 Hz, 6H, 2×CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 171.6, 151.6, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 58.1, 51.4, 50.6, 26.1, 16.1; MS: *m/z* (M⁺ + H) 725. Anal. Calcd for C₃₅H₃₅Cl₂FN₆O₄S: C, 57.93; H, 4.86; N, 11.58. Found: C, 57.72; H, 4.66; N, 11.46.

6-(4-Chlorophenyl)-5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-methyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10l). This was obtained by reacting compound **9b** (1 g) and methylhydrazine (0.25 g) as described in the typical procedure and isolated as a yellow solid, yield 76%, m.p. 241–243 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.29 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.16 (s, 1H, Ar-H), 7.59 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.48 (s, 1H, CH-S), 7.39 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.09 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.91–6.88 (m, 4H, Ar-H), 5.76 (d, *J* = 3.6 Hz, 1H, C₁H), 5.62 (d, *J* = 2.2 Hz, 1H, S-CH), 5.25 (d, *J* = 2.2 Hz, 1H, CH-N), 4.66 (t, *J* = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.71 (s, 3H, N-CH₃), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 171.6, 151.6, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 58.1, 51.4, 39.3, 16.1; MS: *m/z* (M⁺ + H) 684. Anal. Calcd for C₃₂H₃₀Cl₂FN₆O₄S: C, 56.14; H, 4.42; N, 12.28. Found: C, 55.92; H, 4.26; N, 12.02.

5-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofu-

ro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-6-(4-nitrophenyl)-2-phenyl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10m). This was obtained by reacting compound **9c** (1 g) and phenylhydrazine (0.25 g) as described in the typical procedure and isolated as a brown solid, yield 75%, m.p. 241–243 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.26 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.02 (s, 1H, Ar-H), 7.49 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.22 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.08–7.05 (m, 6H, Ar-H and CH-S), 7.02 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.81–6.77 (m, 4H, Ar-H), 5.66 (d, *J* = 3.6 Hz, 1H, C₁H), 5.58 (d, *J* = 2.2 Hz, 1H, S-CH), 5.21 (d, *J* = 2.2 Hz, 1H, CH-N), 4.62 (t, *J* = 3.9 Hz, 1H, C₂H), 4.51 (s, 2H, OCH₂), 3.94–3.91 (m, 1H, C₄H), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 174.6, 143.0, 141.4, 137.4, 136.2, 133.6, 132.3, 131.2, 129.3, 128.4, 127.9, 126.1, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 51.4, 26.1, 16.1; MS: *m/z* (M⁺ + H) 770. Anal. Calcd for C₃₈H₃₃ClFN₇O₆S: C, 59.26; H, 4.32; N, 12.73. Found: C, 59.16; H, 4.10; N, 12.53.

5-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-(4-methoxyphenyl)-6-(4-nitrophenyl)-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10n). This was obtained by reacting compound **9c** (1 g) and *p*-methoxyphenylhydrazine (0.35 g) as described in the typical procedure and isolated as a yellow solid, yield 76%, m.p. 264–266 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.28 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.04 (s, 1H, Ar-H), 7.51 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.40–7.35 (m, 5H, Ar-H and CH-S), 7.29 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.05 (d, *J* = 8.3 Hz, 2H, Ar-H), 6.91–6.87 (m, 4H, Ar-H), 5.76 (d, *J* = 3.6 Hz, 1H, C₁H), 5.62 (d, *J* = 2.2 Hz, 1H, S-CH), 5.25 (d, *J* = 2.2 Hz, 1H, CH-N), 4.66 (t, *J* = 3.9 Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.91 (s, 3H, OMe), 3.26 (dd, *J*₁ = 9.1 Hz, *J*₂ = 4.2 Hz, 1H, C₃H), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 172.6, 151.7, 143.2, 141.4, 137.4, 133.6, 132.3, 131.2, 129.3, 126.1, 125.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 55.8, 51.4, 26.1, 16.1; MS: *m/z* (M⁺ + H) 800. Anal. Calcd for C₃₉H₃₅ClFN₇O₇S: C, 58.53; H, 4.41; N, 12.25. Found: C, 58.22; H, 4.16; N, 12.01.

2-(4-Chlorophenyl)-5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-6-(4-nitrophenyl)-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10 o). This was obtained by reacting compound **9c** (1 g) and *p*-chlorophenylhydrazine (0.45 g) as described in the typical procedure and isolated as a brown solid, yield 72%, m.p. 285–287 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.23 (d, *J* = 8.7 Hz, 2H, Ar-H), 8.11 (s, 1H, Ar-H), 7.58 (d, *J* = 9.2 Hz, 2H, Ar-H), 7.40–7.35 (m, 5H, Ar-H and CH-S), 7.29 (d, *J* = 8.33 Hz, 2H, Ar-H), 7.07 (d, *J* = 8.3 Hz,

2H, Ar-H), 6.91–6.87 (m, 4H, Ar-H), 5.76 (d, $J = 3.6$ Hz, 1H, C₁H), 5.62 (d, $J = 2.2$ Hz, 1H, S-CH), 5.25 (d, $J = 2.2$ Hz, 1H, CH-N), 4.66 (t, $J = 3.9$ Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.26 (dd, $J_1 = 9.1$ Hz, $J_2 = 4.2$ Hz, 1H, C₃H), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 172.6, 151.7, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 126.3, 125.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 51.4, 26.1, 16.1; MS: m/z ($M^+ + Na$) 815. Anal. Calcd for C₃₈H₃₂Cl₂FN₇O₆S: C, 56.72; H, 4.01; N, 12.81. Found: C, 56.42; H, 3.95; N, 12.72.

2-Benzyl-5-((3aR,5S,6S,6aR)-6-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-6-(4-nitrophenyl)-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10p). This was obtained by reacting compound **9c** (1 g) and benzylhydrazine (0.65 g) as described in the typical procedure and isolated as a yellow solid, yield 71%, m.p. 275–277 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.35 (d, $J = 8.7$ Hz, 2H, Ar-H), 8.11 (s, 1H, Ar-H), 7.59 (d, $J = 9.2$ Hz, 2H, Ar-H), 7.46–7.40 (m, 6H, Ar-H and CH-S), 7.32 (d, $J = 8.33$ Hz, 2H, Ar-H), 7.08 (d, $J = 8.3$ Hz, 2H, Ar-H), 6.96–6.90 (m, 4H, Ar-H), 5.96 (s, 2H, CH₂Ph), 5.77 (d, $J = 3.6$ Hz, 1H, C₁H), 5.65 (d, $J = 2.2$ Hz, 1H, S-CH), 5.28 (d, $J = 2.2$ Hz, 1H, CH-N), 4.66 (t, $J = 3.9$ Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.26 (dd, $J_1 = 9.1$ Hz, $J_2 = 4.2$ Hz, 1H, C₃H), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 171.6, 151.6, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 125.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 58.1, 51.4, 26.1, 16.1; MS: m/z ($M^+ + H$) 773. Anal. Calcd for C₃₉H₃₅ClFN₇O₆S: C, 59.73; H, 4.50; N, 12.56. Found: C, 59.66; H, 4.41; N, 12.36.

5-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-isopropyl-6-(4-nitrophenyl)-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10q). This was obtained by reacting compound **9c** (1 g) and isopropylhydrazine (0.35 g) as described in the typical procedure and isolated as a brown solid, yield 69%, m.p. 221–223 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.32 (d, $J = 8.7$ Hz, 2H, Ar-H), 8.16 (s, 1H, Ar-H), 7.65 (d, $J = 9.2$ Hz, 2H, Ar-H), 7.52–7.48 (m, 5H, Ar-H and CH-S), 7.39 (d, $J = 8.33$ Hz, 2H, Ar-H), 7.09 (d, $J = 8.3$ Hz, 2H, Ar-H), 5.76 (d, $J = 3.6$ Hz, 1H, C₁H), 5.62 (d, $J = 2.2$ Hz, 1H, S-CH), 5.25 (d, $J = 2.2$ Hz, 1H, CH-N), 4.66 (t, $J = 3.9$ Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.26 (dd, $J_1 = 9.1$ Hz, $J_2 = 4.2$ Hz, 1H, C₃H), 2.80–2.78 (m, 1H, CH), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃), 0.96 (d, $J = 6.3$ Hz, 6H, 2×CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 171.6, 151.6, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 58.1, 51.4, 50.6, 26.1, 16.1; MS: m/z ($M^+ + H$) 736. Anal. Calcd for C₃₅H₃₅ClFN₇O₆S: C, 57.10; H, 4.79; N, 13.32. Found: C, 56.98; H, 4.56; N, 12.99.

5-((3aR,5S,6S,6aR)-6-((1-(4-Chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)-3-(4-fluorophenyl)-2-methyl-6-(4-nitrophenyl)-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-*d*]thiazole (10r). This was obtained by reacting compound **9c** (1 g) and methylhydrazine (0.25 g) as described in the typical procedure and isolated as a brown solid, yield 67%, m.p. 251–253 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.29 (d, $J = 8.7$ Hz, 2H, Ar-H), 8.16 (s, 1H, Ar-H), 7.59 (d, $J = 9.2$ Hz, 2H, Ar-H), 7.48–7.44 (m, 5H, Ar-H and CH-S), 7.39 (d, $J = 8.33$ Hz, 2H, Ar-H), 7.09 (d, $J = 8.3$ Hz, 2H, Ar-H), 5.76 (d, $J = 3.6$ Hz, 1H, C₁H), 5.62 (d, $J = 2.2$ Hz, 1H, S-CH), 5.25 (d, $J = 2.2$ Hz, 1H, CH-N), 4.66 (t, $J = 3.9$ Hz, 1H, C₂H), 4.54 (s, 2H, OCH₂), 3.96–3.94 (m, 1H, C₄H), 3.71 (s, 3H, N-CH₃), 3.26 (dd, $J_1 = 9.1$ Hz, $J_2 = 4.2$ Hz, 1H, C₃H), 1.53 (s, 3H, CH₃), 1.36 (m, 3H, CH₃); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 171.6, 151.6, 143.2, 137.4, 133.6, 132.3, 131.2, 129.3, 128.4, 127.9, 124.8, 122.9, 119.2, 111.2, 103.8, 81.2, 78.1, 74.1, 65.9, 58.1, 51.4, 39.3, 16.1; MS: m/z ($M^+ + H$) 684. Anal. Calcd for C₃₃H₃₁ClFN₇O₆S: C, 55.97; H, 4.41; N, 13.85. Found: C, 55.82; H, 4.26; N, 13.72.

6. Conclusion

In conclusion, a series of a new class of hybrid heterocycles **10a–r** have been synthesized and evaluated for their nematocidal activity, most of the compounds showed appreciable nematocidal activity. The antifungal activities of these compounds were evaluated against various fungi. Many of the synthesized compounds showed good activity against the tested fungi and therefore have emerged as potential molecules for further development.

7. Acknowledgements

The authors are thankful to CSIR-New Delhi for the financial support (Project funding No: 02 (247)15/EMR-II), Director, CSIR- IICT, Hyderabad, India, for NMR and MS spectral analysis and Principal, Vaagdevi Degree & PG College Hanamkonda for his constant encouragement.

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Povzetek

Z reakcije med halkonskimi derivati 2-((3aR,5S,6S,6aR)-6-((1-(4-klorofenil)-1H-1,2,3-triazol-4-il)metoksi)-2,2-dimetiltetrahydrofuro[2,3-d][1,3]dioksol-5-il)-3-feniltiazolidin-4-onov **9** in aril/alkil hidrazini smo pripravili novo serijo 5-((3aR,5S,6S,6aR)-6-((1-(4-klorofenil)-1H-1,2,3-triazol-4-il)metoksi)-2,2-dimetiltetrahydrofuro[2,3-d][1,3]dioksol-5-il)-3-(4-fluorofenil)-2,6-difenil-3,3a,5,6-tetrahydro-2H-pirazolo[3,4-d]tiazolov **10a–r**. Strukture novih spojin smo določili na osnovi IR, NMR, MS in elementne analize. Za spojine **10a–r** smo tudi določili učinkovanje proti ploskim črvom (nematodam) *Dietylenchus myceliophagus* in *Caenorhabditis elegans* z *in vitro* metodo v vodnih raztopinah. Ugotovili smo, da spojine, ki vsebujejo N-benzilpirazolni (**10d**, **10j**, **10p**) ali N-metilpirazolni fragment (**10f**, **10i**, **10r**), izkazujejo občutno nematocidno aktivnost proti obema testiranima živalskima vrstama z LD₅₀ 160–210 ppm, kar je skoraj enako aktivnosti standarda oksamila. Za spojine **10a–r** smo tudi raziskali delovanje proti glivam (izmerili smo MZI, MIC in MFC vrednosti) in sicer: *Candida albicans* (ATCC 102331), *Aspergillus fumigates* (HIC 6094), *Trichophyton rubrum* (IFO 9185) in *Trichophyton mentagrophytes* (IFO 40996). Večina novih spojin je izkazala opazno delovanje proti testiranim glivam, kar daje možnosti nadaljnega razvoja predstavljenih spojin