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Synthesis and antimicrobial of some new substituted tetrazolomethylbenzo[*d*]-[1,2,3]triazole derivatives using 1H-benzo[*d*][1,2,3]triazole as starting material

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Abstract A series of tetrazolomethylbenzo[*d*][1,2,3]triazole derivatives (**2–14**) have been synthesized and evaluated as antimicrobial agents from 1H-benzo[*d*][1,2,3]triazole (**1**) as starting material. The reaction of benzotriazole **1** with chloroacetonitrile afforded 2-(1*H*-benzo[*d*][1,2,3]-triazol-1-yl)acetonitrile **2**, which was reacted with sodium azide to give tetrazole derivative **3**. Esterification of benzotriazole **1** with ethyl bromoacetate in the presence of anhydrous potassium carbonate afforded ester **4**, which was treated with hydrazine hydrate to afford the corresponding hydrazide **5**. Reaction of **3** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide afforded the nitro-glycoside derivative **6**, which was deacetylated using methanolic ammonia to deprotected nitroglycoside **7**. The hydrazide **5** was reacted with 4,5,6,7-tetrachlorophthalic anhydride or 1,2,4,5-benzenetetracarboxylic dianhydride in refluxing glacial acetic acid to give the corresponding imides **8** and **9**, respectively. Also, the hydrazide **5** was reacted with carbon disulphide in ethanol to give potassium salt **10**, which was reacted with hydrazine hydrate to afford aminotriazole derivative **11**. The latter compound was reacted with carbon disulphide to

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afford thiadiazole derivative **12**, which was treated with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide to give the thioglycoside derivative **13**. Deacetylation of the thioglycoside **13** using methanolic ammonia solution at room temperature afforded the deprotected thioglycoside **14**. The antimicrobial screening of some synthesized compounds showed that many of these compounds have good antimicrobial activities comparable to streptomycin and fusidic acid as reference drugs.

Keywords 1H-Benzo[*d*][1,2,3]triazole · Tetrazolomethylbenzo[*d*][1,2,3]triazole · Sugar · Antimicrobial agents

Introduction

The heterocyclic group is of great importance in treating biological systems. Anti-inflammatory, analgesic and antipyretic activities are observed in some heterocyclic derivatives [1–5]. Some of synthetic compounds have exhibited a range of biological activities, such as antitumor, antifilarial, antibiotic, antibacterial, antifungal, and anti-inflammatory [6–9]. Also, heterocyclic derivatives have been reported to possess diverse biological activities, such as antibacterial [10–16] and anti-inflammatory [17–19] activities. In addition, several substituted pyridines and their derivatives were reported to exhibit significant antimicrobial [20], anti-inflammatory [21], and anticancer activities [22]. In continuation of our interest in the heterocyclic chemistry and disubstituted pyridine derivatives [23–26], we report here on the synthesis of a new series of some substituted tetrazolomethylbenzo[*d*][1,2,3]triazole derivatives as antimicrobial agents.

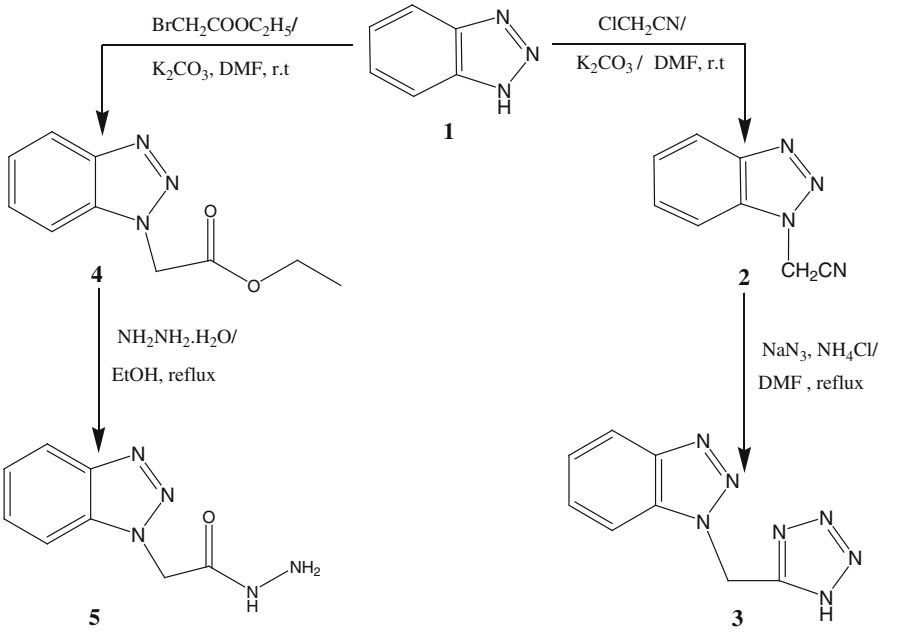
Results and discussion

2-(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)acetonitrile **2** was synthesized by the reaction of benzotriazole **1** with chloroacetonitrile in the presence of anhydrous potassium carbonate in DMF at room temperature. When, compound **2** reacted with sodium azide in DMF in the presence of ammonium chloride at reflux temperature, it afforded 1((1*H*-tetrazol-5-yl)methyl)-1*H*-benzo[*d*][1,2,3] triazole **3**. The IR spectra of **3** showed the presence of a characteristic absorption band corresponding to the NH group in the region 3220 cm^{-1} and the disappearance of the CN group present in compound **2**. On the other hand, esterification of benzotriazole **1** with ethyl bromoacetate in the presence of anhydrous potassium carbonate in DMF at room temperature afforded ethyl 2-(1H-benzo[*d*][1,2,3]triazol-1-yl)acetate **4**, which was treated with hydrazine hydrate to afford the corresponding hydrazide **5** (Scheme 1). The IR spectrum of **4** showed the presence of a characteristic absorption band corresponding to the carbonyl group in the region 1747 cm^{-1} and the disappearance of the NH group present in benzotriazole **1.** The IR spectrum of **5** showed the presence of a characteristic absorption band corresponding to the NH group in the region 3746 cm^{-1} and the NH_2 group in the region 3328 and 3424 cm^{-1}, and the amide group in the region 1696 cm^{-1}.

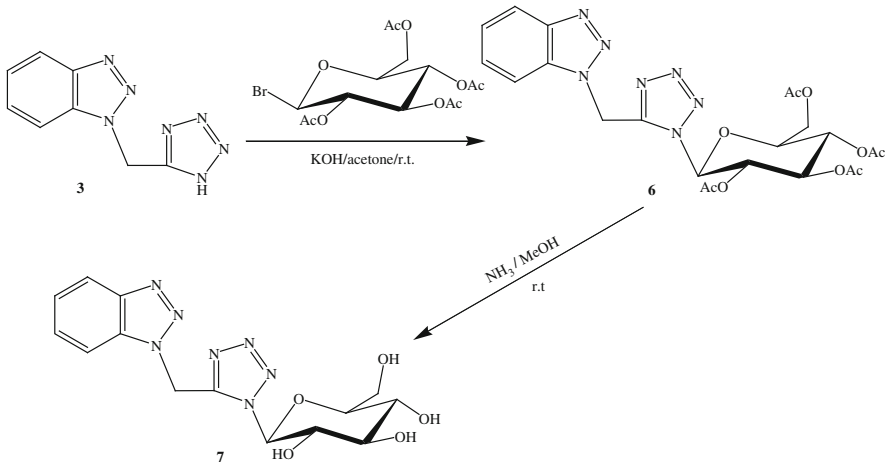
Reaction of **3** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in dry acetone at room temperature afforded the nitro-glycoside derivative **6,** which was deacetylated using methanolic ammonia solution at room temperature to the corresponding deprotected nitroglycoside **7** (Scheme 2). The IR spectrum of **6** showed the characteristic absorption bands at 1745 cm^{-1} corresponding to the carbonyl group. Its ^1H NMR spectrum revealed the presence of the *O*-acetyl-methyl groups at δ 2.02–2.20 ppm, the signals of the sugar protons were at δ 4.07–6.20 ppm. The IR spectrum of **7** showed the characteristic absorption bands at 3390 cm^{-1} corresponding to the hydroxyl groups.

Treatment of hydrazide **5** with 4,5,6,7-tetrachlorophthalic anhydride or 1,2,4,5-benzenetetracarboxylic dianhydride in refluxing glacial acetic acid afforded the corresponding imide derivatives **8** and **9**, respectively (Scheme 3). The IR spectrum of **8** showed the characteristic absorption bands at 3166 cm^{-1} corresponding to the NH group, at 1748 cm^{-1} corresponding to the carbonyl group, and at 1613 cm^{-1} corresponding to the amide group. Also, the IR spectrum of **9** showed the characteristic absorption bands at 3455 cm^{-1} corresponding to the NH group, at 1699 cm^{-1} corresponding to the carbonyl group, and at 1654 cm^{-1} corresponding to the amide group.

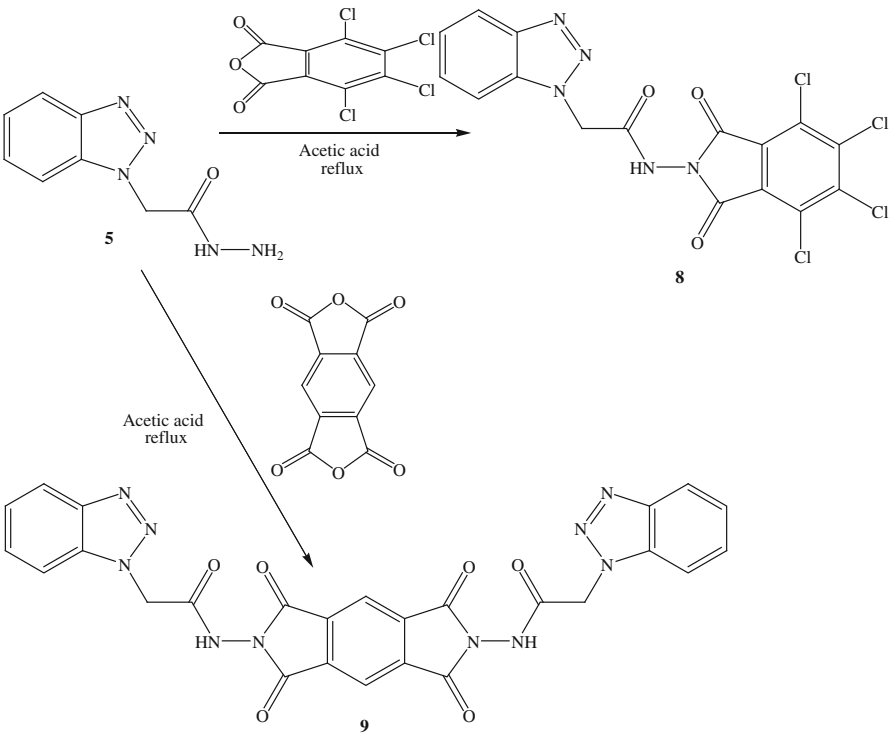
Finally, treatment of hydrazide **5** with carbon disulphide in ethanol in the presence of potassium hydroxide at water bath temperature, afforded potassium salt **10**, which was reacted with hydrazine hydrate in water at refluxed temperature with stirring to afford the corresponding aminotriazole derivative **11**. The latter compound **11** was reacted with carbon disulphide in ethanol in the presence of potassium hydroxide at refluxed temperature to give 3-((1*H*-benzo[*d*][1,2,3] triazole-1-yl)methyl-[1,2,4]



Scheme 1 Synthetic pathway for compounds 2–5



Scheme 2 Synthetic pathway for compounds 6 and 7



Scheme 3 Synthetic pathway for compounds 8 and 9

triazolo[3,4-b][1,3,4]thiadiazole-6-thiol **12**, which was treated with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide to give the thioglycoside derivative **13.** Deacetylation of the thioglycoside **13** using methanolic ammonia solution at room

temperature afforded the deprotected thioglycoside **14** (Scheme 4). The IR spectrum of **13** showed the characteristic absorption bands at 1741 cm^{-1} corresponding to the carbonyl group. Its ^1H NMR spectrum revealed the presence of the *O*-acetyl-methyl groups at δ 2.06–2.24 ppm and the signals of the sugar protons at δ 4.11–6.23 ppm. The IR spectrum of **14** showed the characteristic absorption bands at 3,405 cm^{-1} corresponding to the hydroxyl groups.

Antimicrobial activity

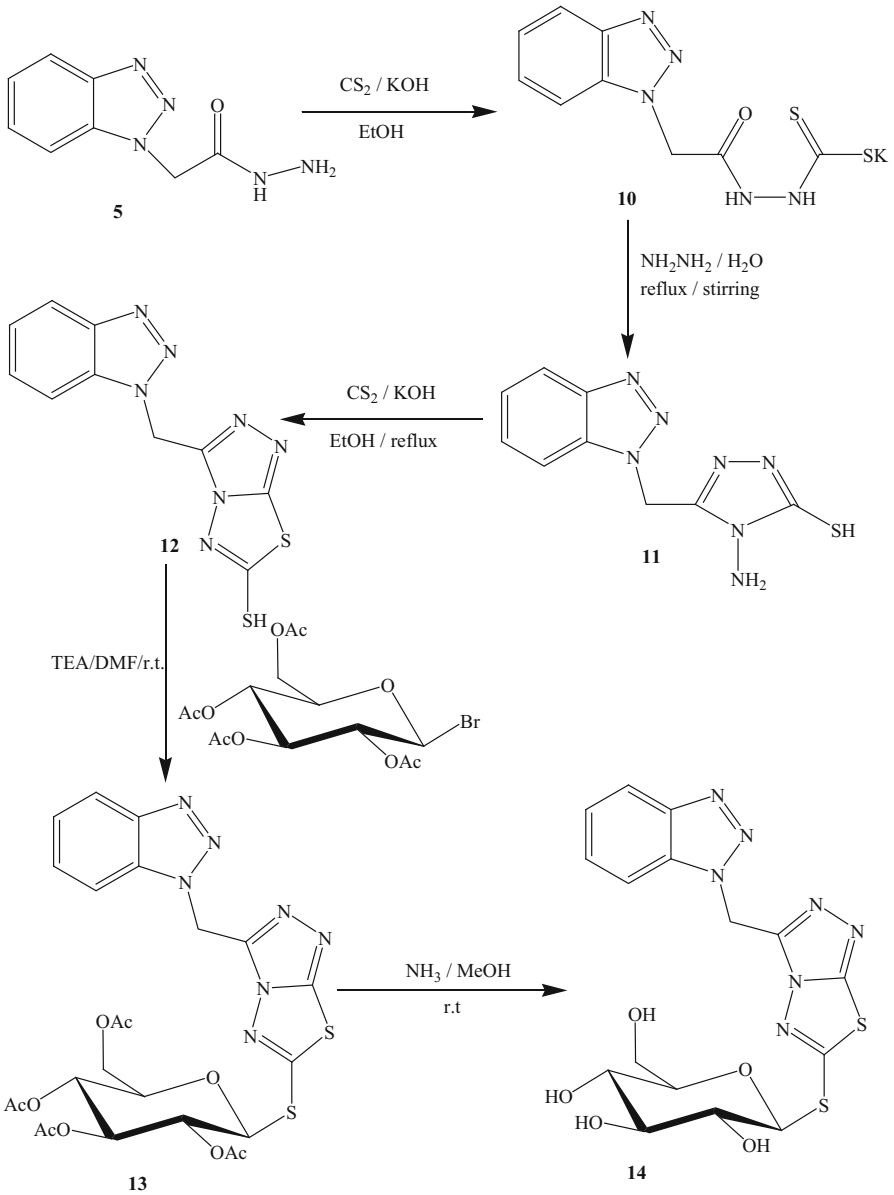
The antimicrobial activities of the synthesized compounds **2–14** were determined by the agar diffusion method as recommended by the national committee for clinical laboratory standards (NCCLS) [27]. The compounds **2–14** were evaluated for antimicrobial activity against bacteria, i.e. *Streptomyces* sp., *Bacillus subtilis, Streptococcus lactis, Escherichia coli,* and *Pseudomonas* sp. and antifungal activity against various fungi, i.e. (*Aspergillus niger*, and *Penicillium* sp.) and yeast (*Candida albicans* and *Rhodotorula ingeniosa*).

The concentrations of the tested compounds (10 μg/mL) were used according to modified Kirby–Bauer's disk diffusion method [28]. The sterile discs were impregnated with 10 μg/disc of the tested compound. Each tested compound was performed in triplicate. The solvent DMSO was used as a negative control and streptomycin/fusidic acid were used as standard calculated average diameters (for triplicates) of the zone of inhibition (in mm) for tested samples with that produced by the standard drugs.

Some of the synthesized compounds exhibited potent antibacterial and antifungal bioactivity compared with standard drug used. The other tested compounds were found to exhibit a moderate of low antibacterial activity (Table 1). On the other hand, when different concentrations of the compound that exhibited a moderate antibacterial activity (**6**, **12**, **13**) were used, this compound exhibit very good antibacterial activity at higher concentration (3× and 4×) (Table 2), while the different concentrations of compounds (**3** and **7**) exhibited a very good antifungal activity (2× and 3×) (Table 3).

Experimental

Melting points were measured with a Büchi apparatus and are uncorrected. TLC was performed on plastic plates Silica Gel 60 F_{254} (layer thickness 0.2 mm; Merck). IR spectra (KBr) were recorded on Bruker-Vector22 instrument (Bruker, Bremen, Germany). ^1H NMR spectra were recorded on Varian Gemini spectrometer at 300 MHz and 200 MHz with TMS as internal standard. Chemical shifts were reported in δ scale (ppm) relative to TMS as a standard, and the coupling constants (J values) are given in Hz. The progress of the reactions was monitored by TLC using aluminium silica gel plates 60 F_{245}. EI-mass spectra were measured on HP D5988 A 1,000 MHz spectrometer (Hewlett–Packard, Palo Alto, CA, USA). Elemental analyses were carried out at the Microanalytical center of Cairo University. Compounds **2** and **3** have been synthesized according to the reported procedures [29].



Scheme 4 Synthetic pathway for compounds 10–14

2-(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)acetonitrile (**2**)

To a solution of benzotriazole **1** (5.59 g, 0.05 mol) and anhydrous potassium carbonate (7 g, 0.05 mol) in dimethylformamide (20 mL), chloroacetonitrile (3.8 g, 0.05 mol) was added dropwise. The reaction mixture was stirred overnight at room temperature, and then poured onto water. The obtained crude product was extracted

Table 1 Antimicrobial activities of the newly compounds

Comp. No.	Inhibition zone (mm)								
	Bacteria strains				Str. sp.	Fungi strains			
	Gram−		Gram+			A.n.	Pen. sp.	Cand. alb.	R.i.
	B.s.	S.l.	E.c.	P. sp.					
2	13	12	10	9	11	19	20	19	19
3	11	12	12	13	11	14	13	16	15
6	17	16	15	17	16	13	12	11	12
7	14	15	13	11	11	14	15	14	13
8	21	23	23	22	21	19	20	19	21
9	14	15	13	12	14	12	13	11	12
11	7	8	10	9	8	11	12	11	10
12	20	21	20	19	20	21	21	22	21
13	18	16	18	17	16	13	12	11	12
14	10	11	12	13	13	19	18	19	17
Streptomycin	21	22	21	22	21	–	–	–	–
Fusidic acid	–	–	–	–	–	17	17	18	18

B.s. *Bacillus subtilis*, S.l. *Streptococcus lactis*, E.c. *Escherichia coli*, P. sp. *Pseudomonas* sp., Str. sp. *Streptomyces* sp., A.n. *Aspergillus niger*, Pen. sp. *Penicillium* sp. Cand. alb *Candida albicans,* R.i. *Rhodotorula ingeniosa*

Table 2 Effect of different concentrations of the selected compounds **6**, **12** and **13**

Comp. No.	Conc.	Str. sp.	Bacteria strains			
			Gram−		Gram+	
			B. s	S. l	E.c	P. sp.
6	1×	16	17	16	15	17
	2×	19	20	19	18	20
	3×	22	22	21	20	22
	4×	23	24	23	22	23
12	1×	20	20	21	20	19
	2×	22	23	22	22	22
	3×	23	25	24	25	24
	4×	24	25	26	25	24
13	1×	16	18	16	18	17
	2×	20	20	19	21	20
	3×	22	22	21	23	24
	4×	22	23	23	23	24

× = 10 μg

Species abbreviations as in Table 1

from the reaction mixture by ethyl acetate, dried over anhydrous potassium carbonate, and evaporated under reduced pressure. The obtained residue was triturated with diethyl ether, filtered off, dried, and crystallized from ethanol to give

Table 3 Effect of different concentrations of selected compounds **3** and **7**

Comp. No	Conc.	Fungi strains			
		A.n	Pen. sp.	Cand. alb.	R.i
3	1×	14	13	16	15
	2×	15	15	18	17
	3×	18	17	20	20
	4×	20	19	20	21
7	1×	14	15	14	13
	2×	16	16	17	16
	3×	18	19	20	20
	4×	20	19	20	20

× = 10 μg

Species abbreviations as in Table 1

compound **2** as colorless crystals. Yield 7.5 g (94 %), m.p. = 86–88 °C; MS, *m*/*z* (%): 158 [M^+, 100] corresponding to the molecular formula $C_8H_6N_4$. Anal. Calcd. For $C_8H_6N_4$ (158.16): C, 60.75; H, 3.82; N, 35.42. Found: C, 60.70; H, 3.78; N, 35.37.

1((1*H*-Tetrazol-5-yl)methyl)-1*H*-benzo[*d*][1,2,3]triazole (**3**)

A mixture of compound **2** (2.2 g, 0.01 mol), sodium azide (0.91 g, 0.014 mol) and ammonium chloride (0.75 g, 0.014 mol) in dimethylformamide (7 mL) was heated under reflux for 1 h. The reaction mixture was evaporated under reduced pressure, the obtained residue was solidified with water (20 mL) and the resulting precipitate (first portion) was collected by filtration. The filtrate was acidified with dilute hydrochloric acid to pH ~2, after cooling; the obtained solid (second portion) was filtered off, washed with water, and dried. The two portions were combined and crystallized from methanol to give compound **3** as white powder. Yield 2.5 g (92.5 %); m.p. = 180–182 °C; IR (KBr) cm^{-1}; 3220 (NH). MS, *m*/*z* (%): 201 [M^+, 12] corresponding to the molecular formula $C_8H_7N_7$. Anal. Calcd. For $C_8H_7N_7$ (201.18): C, 47.76; H, 3.51; N, 48.73. Found: C, 47.71; H, 3.48; N, 48.68.

Ethyl 2-(1H-benzo[*d*][1,2,3]triazol-1-yl)acetate (**4**)

To a stirred solution of compound **1** (1.19 g, 0.01 mol) and anhydrous potassium carbonate (1.4 g, 0.01 mol) in dimethylformamide (8 mL), ethyl bromoacetate (2.2 g, 0.01 mol) was added dropwise at room temperature. The reaction mixture was continued at the same condition for 24 h, then poured into ice water. The obtained precipitate was filtered off, washed with water, dried, and crystallized from ethanol to afford the corresponding compound **4** as white powder. Yield 1.98 g (96 %); m.p. = 242–244 °C. IR (KBr, cm^{-1}): 1747 (C=O); MS, *m*/*z* (%): 205 [M^+, 8] corresponding the molecular formula $C_{10}H_{11}N_3O_2$. Anal. Calcd. For $C_{10}H_{11}N_3O_2$ (205.21): C, 58.53; H, 5.40; N, 20.48. Found: C, 58.45; H, 5.35; N, 20.42.

2-(1H-Benzo[*d*][1,2,3]triazol-1-yl)acetohydrazide (**5**)

A mixture of the ester **4** (2.05 g, 0.01 mol) and hydrazine hydrate (1.5 g, 0.03 mol) in absolute ethanol (15 mL) was refluxed for 5 h. The reaction mixture was diluted with cold water (5 mL); the obtained precipitate was filtered off, washed with water, dried, and crystallized from ethanol to afford the corresponding hydrazide **5** as white crystals. Yield 1.9 g (57 %), m.p. = 186–188 °C; IR (KBr, cm^{-1}): 3746 (NH), 3424 and 3328 (NH_2), 1696 (C=O); MS, *m*/*z* (%): 191 [M^+, 15] corresponding to the molecular formula $C_8H_9N_5O$. Anal. Calcd. For $C_8H_9N_5O$ (191.18): C, 50.26; H, 4.74; N, 36.63. Found: C, 50.20; H, 4.69; N, 36.58.

2-(5-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)methyl-1*H*-tetrazol-1-yl)-6-(acetoxymethyl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (**6**)

To a solution of compound **3** (2.01 g, 0.01 mol) in aqueous potassium hydroxide [0.56 g, 0.01 mol in distilled water (2 mL)], a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (4.25 g, 0.01 mol) in acetone (20 mL) was added. The reaction mixture was stirred at room temperature for 7 days. The solvent was evaporated under reduced pressure at 40 °C and the residue was washed with distilled water to remove potassium bromide formed. The product was dried, and crystallized from ethanol to obtain compound **6** as white powder. Yield 3.35 g (70.82 %), m.p. = 98–100 °C. IR (KBr, cm^{-1}): 1745 (C=O). ^{1}H NMR (DMSO-d_6): δ = 2.02–2.20 (s, 12H, 4-$COCH_3$), 4.07–4.19 (m, 2H, H-5′), 5.04 (m, 1H, H-4‘), 5.07 (m, 1H, H-5‘), 5.20 (m, 1H, H-2‘), 5.37 (s, 2H, CH_2CN), 5.52 (m, 1H, H-3‘), 6.20 (m, 1H, H-1‘), 7.09–8.13 (m, 4H, Ar–H) ppm; MS, *m*/*z* (%): 531 [M^+, 6] corresponding to the molecular formula $C_{22}H_{25}N_7O_9$. Anal. Calcd. For $C_{22}H_{25}N_7O_9$ (531.47): C, 49.72; H, 4.74; N, 18.45. Found: C, 49.66; H, 4.70; N, 18.38.

2-(5-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)methyl)-1*H*-tetrazol-1-yl)-tetrahydro-6-(hydroxymethyl)-2*H*-pyran-3,4,5-triol (**7**)

A solution of compound **6** (0.47 g, 0.001 mol) in methanolic ammonia was stirred at room temperature for 4 days. The reaction mixture was evaporated under reduced pressure, the obtained residue was extracted with ethyl acetate, dried over anhydrous sodium sulphate, and evaporated to dryness to give compound **7** as an oily product in pure form. Yield 0.18 g (50 %); IR (KBr, cm^{-1}): 3390 (broad band, OH). Anal. Calcd. For $C_{14}H_{17}N_7O_5$ (353.32): C, 46.28; H, 4.72; N, 26.99. Found: C, 46.23; H, 4.66; N, 26.93.

2-(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)-*N*-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl)acetamide (**8**)

To a suspension of the benzotriazole hydrazide **5** (0.19 g, 1 mmol) and 2,3,4,5-tetrachlorophthalic anhydride (1 mmol) in acetic acid (50 mL) was refluxed for 7 h. The solid was collected by filtration by filtration, washed with acetic acid, and crystallized from methanol to give compound **8** as white powder.

Yield = 0.32 g (69.7 %), m.p. > 300. IR (KBr) cm^{-1}: 3166 (NH), 1748 (C=O), 1613 (amide); MS, *m/z* (%): 459 [M^+, 4] corresponding to the molecular formula $C_{16}H_7Cl_4N_5O_3$. Anal. Calcd. For $C_{16}H_7Cl_4N_5O_3$ (459.07): C, 41.86; H, 1.54; Cl, 30.89; N, 15.26. Found: C, 41.80; H, 1.50; Cl, 30.84; N, 15.22.

N,*N*′-(1,3,5,7-tetraoxopyrrolo[3,4,*f*]isoindole-2,6(1*H*,3*H*,5*H*,7*H*)-diyl)bis(2-(1*H*-benzo[*d*]-[1,2,3]triazol-1-yl)acetamide) (**9**)

To a suspension of the benzotriazole hydrazide **5** (0.19 g, 1 mmol) and 1,2,4,5-benzenetetracarboxylic dianhydride (2 mmol) in acetic acid (50 mL) was refluxed for 7 h. The solid was collected by filtration by filtration, washed with acetic acid and crystallized from methanol to give compound **9** as gray powder. Yield = 0.38 g (67.3 %), m.p. > 300; IR (KBr, cm^{-1}): 3455 (NH), 1699 (C=O), 1654 (amide); MS, *m/z* (%): 564 [M^+, 12] corresponding to the molecular formula $C_{26}H_{16}N_{10}O_6$. Anal. Calcd. For $C_{26}H_{16}N_{10}O_6$ (4564.46): C, 55.32; H, 2.86; N, 24.81. Found: C, 55.26; H, 2.80; N, 24.76.

Potassium 2-(2-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)acetyl)hydrazinecarbodithioate (**10**)

A solution of potassium hydroxide (0.57 g, 0.01 mol), benzotriazol hydrazide **5** (1.91 g, 0.01 mol) and carbon disulphide (1.52, 0.02 mol) in absolute ethanol (20 mL) was heated on a water bath for 15 h. The reaction mixture was evaporated under reduced pressure to give a gum material **10** in pure form. Yield = 2 g (65.5 %), Anal. Calcd. For $C_9H_8KN_5OS_2$ (305.42): C, 35.39; H, 2.64; N, 22.93; S, 21.00. Found: C, 35.35; H, 2.60; N, 22.87; S, 20.95.

5-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)methyl)-4-amino-4*H*-1,2,4-triazol-3-thiol (**11**)

To suspension of (3.05 g, 0.01 mol) potassium salt **10** in water (1 mL), hydrazine hydrate (0.02 mol) was added. The reaction mixture was refluxed with stirring for about 6 h, until the evaluation of hydrogen sulphide, diluted with water (30 mL) and acidified with HCl. The formed solid was filtered off, washed with cold water, and crystallized from ethanol to give compound **11**. Yield = 1.8 g, (72 %), m.p. = 228–230 °C; MS, *m/z* (%): 247 [M^+, 24] corresponding to the molecular formula $C_9H_9N_7S$. Anal. Calcd. For $C_9H_9N_7S$ (247.27): C, 43.71; H, 3.67; N, 39.65; S, 12.97. Found: C, 43.65; H, 3.60; N, 39.60; S, 12.92.

3-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)methyl)[1,2,4]tiazolo[3,4-*b*][1,3,4]thia diazaole-6-thiol (**12**)

To a mixture of compound **11** (2.47 g, 0.01 mol) and potassium hydroxide (0.57 g, 0.01 mol) in ethanol (30 mL), carbon disulphide (1.52 g, 0.02 mol) was added. The reaction mixture was refluxed for 40 h, then evaporated under reduced pressure, and the obtained residue was dissolved in 10 % KOH. The solution was acidified with

dil. HCl to pH 3, the obtained solid was filtered off, washed with water, dried, and crystallized from methanol to give compound **12** as a pale-brown powder, Yield = 1.8 g (62.2 %), m.p. = 190–192 °C; MS, *m/z* (%): 289 [M^+, 65] corresponding to the molecular formula $C_{10}H_7N_7S_2$. Anal. Calcd. For $C_{10}H_7N_7S_2$ (289.33): C, 41.51; H, 2.44; N, 33.89; S, 22.16. Found: C, 41.44; H, 2.40; N, 33.83; S, 22.12.

2-(3-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)methyl)[1,2,4]triazolo[3,4,*b*][1,3,4]thiadiazol-6-ylthio)-6-acetoxymethyl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (**13**)

To a solution of compound **12** (2.89 g, 0.01 mol) in DMF (10 mL), triethylamine (1 mL) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (4.25 g, 0.01 mol) were added. The reaction mixture was stirred at room temperature for 7 days, then poured onto ice water. The obtained solid was filtered off, washed with water, dried, and crystallized from methanol to obtain compound **13** as a page powder. Yield = 3.5 g (56.5 %), m.p. = 114–116 °C; IR (KBr) cm^{-1}: 1741 (C=O); ^1H NMR (DMSO-d_6): δ = 2.06–2.24(s, 12H, 4-Ac), 4.11–4.23 (m, 2H, H-5'), 5.04 (m, 1H, H-4'), 5.08 (m, 1H, H-5'), 5.11 (m, 1H, H-2'), 5.24 (s, 2H, CH_2CN), 5.40 (m, 1H, H-1'), 6.23 (m, 1H, H-3'), 7.54–8.13(m, 4H, Ar–H) ppm; MS, *m/z* (%): 620 [M^++1, 5] corresponding the molecular formula $C_{24}H_{25}N_7O_9S_2$. Anal. Calcd. For $C_{24}H_{25}N_7O_9S_2$ (619.62): C, 46.52; H, 4.07; N, 15.82; S, 10.35. Found: C, 46.45; H, 4.00; N, 15.76; S, 10.30.

2-(3-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)methyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazol-6-ylthio)-tetrahydro-6-(hydroxymethyl)-2*H*-Pyran-3,4,5-triol (**14**)

A solution of compound **13** (0.619 g, 0.001 mol) in methanolic ammonia solution (15 mL) was stirred at room temperature for 4 days. The reaction mixture was evaporated under reduced pressure to dryness to give compound **14** as an oily material in pure form. Yield = 0.25 g (55.5 %); IR (KBr) cm^{-1}: 3405 (broad band, OH); MS, *m/z* (%): 451 [M^+, 24] corresponding to the molecular formula $C_{16}H_{17}N_7O_5S_2$. Anal. Calcd. For $C_{16}H_{17}N_7O_5S_2$ (451.48): C, 42.56; H, 3.80; N, 21.72; S, 14.20. Found: C, 42.50; H, 3.75; N, 21.68; S, 14.15.

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