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Design, synthesis and antimicrobial evaluation of novel N- , O- and S- glycosides based 3,5-Pyrazolidinedione scaffolds

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Abstract: 2,3,4,6-Tetra-O-acetyl-α-D-glucopyranosyl bromide were reacted with 4-arylidene-1-phenylpyrazolidine-3,5-diones **1$_{a,b}$** under phase transfer catalysis (PTC) conditions to yield unseparated products namely; *N*-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-4-arylidene-1-phenyl-3,5-pyrazolidinediones **2** & **4** and 3-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyloxy)-4-arylidene-1-phenyl-1H-pyrazol-5-ones **3** & **5**, respectively. Also, compounds **1$_{a,b}$** were treated with a mixture of carbon disulphide and 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide to give unisolated products namely; (2`,3`,4`,6`-tetra-O-acetyl-β-D-glucopyranosyl)[*N*-(1-phenyl-4-arylidene)-pyrazolidin-3,5-dione]-carbodithioates **6**&**8** and (2`,3`,4`,6`-tetra-O-acetyl-β-D-glucopyranosyl)[3-oxy-(1-phenyl-4-arylidene)-pyrazol-5-one]-carbodithioates **7**&**9**, respectively.

Keywords: 1-phenylpyrazolidine-3,5-dione, PTC, β-D-glucopyranosyl, glycosides.

1 Introduction

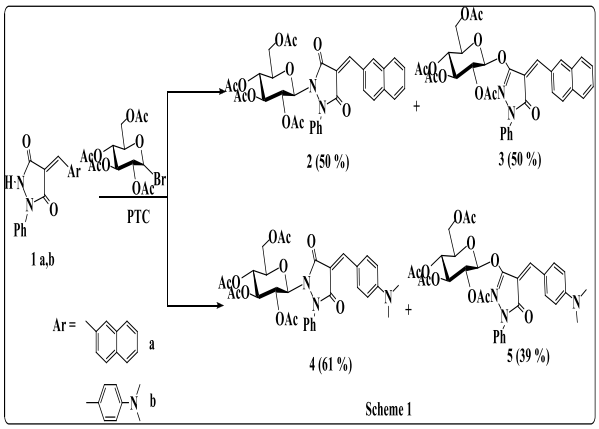
The biological and pharmacological activities of pyrazoles as important class of heterocycles owing as anti-inflammation [1–5], antitumor [6,7], antimicrobial [8,9], antiviral [10], antimalarial activities [11], anticancer agents [12] and treating Alzheimer's disease [13] have reported. Glycosyl sulfanyl heterocycles have been regarded as good glycosyl donors in addition to their biological activities such as the inhibition of enzyme activity [14], fungicides in pesticides and fumigants [15,16] and anti corona virus[17,18]. On the basis of above mentioned findings, the purpose of the present work was to design,synthesize and investigate the antimicrobial activity of some novel 3,5-Pyrazolidinedione Scaffolds carrying carbohydrate residues through N-,O- and S-glycosidic bond formation.

2 Results and Discussion

I- Chemistry part:

4-(Arylidene)-1-phenylpyrazolidine-3,5-diones **1$_{a,b}$** [19] were reacted with 2,3,4,6-tetra-O-acetyl-α-D-gluco-pyranosyl bromide under PTC conditions [dioxane / anhydrous K_2CO_3 /tetrabutyl ammonium bromide (TBABr)] at room temperature to yield *N*-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-4-arylidene-1-phenyl-3,5-pyrazolidinediones **2** & **4** and 3-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyloxy)-4-arylidene-1-phenyl-1H-pyrazol-5-ones **3 & 5**, respectively **(Scheme 1).**

Their IR spectra showed υ 1758 cm^{-1} corresponding to $C{=}O_{acetyl}$ groups. ^{1}H NMR spectrum of a mixture of compound **2 + 3** showed the following signals: 2.02 (s, 24H, 8C$\underline{H}_3$CO), 4.11-4.23 (dd, 4H,H-6a, H-6b,H-6a*, H6b*), 4.38 (t, 2H, H-4, H-4*), 5.1(d, 2H, H-3, H-3*) 5.25 (q, 2H, H-5, H-5*)5.58 (t, 2H, H-2, H-2*), 6.30 (d, 1H, H-1,J=8.00 Hz), 6.46 (d,1H, H-1*,J=8.00 Hz), 7.23-8.65 (m,, 24H, Ar-H) and, 9.03 (s, 2H,2=CH). It was shown from ^{1}H NMR spectrum that; two unseparated compounds **2** & **3** with their anomeric protons (H-1) ,(H-1*) as a doublets at δ = 6.30 and δ = 6.46 ppm with a $J_{1,2}$ = 8 Hz, which corresponds to the diaxial orientation of the H-1 and H-2 protons indicating the β-configuration.



Scheme 1

Similary, A mixture of carbon disulphide and 2,3,4,6-

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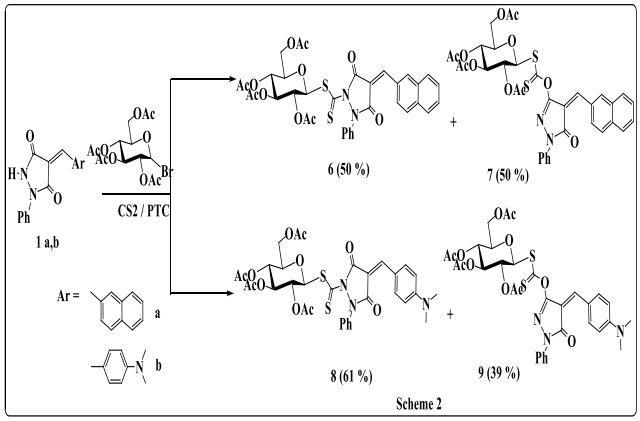
tetra-O-acetyl-α-D-glucopyranosyl bromide was reacted with compounds $\mathbf{1_{a,b}}$ to yield also unisolated products namely; (2`,3`,4`,6`-tetra-O-acetyl-β-D-glucopyranosyl) [*N*-(1-phenyl-4-arylidene)-pyrazolidin-3,5-dione]-carbodithioates **6**&**8** and (2`,3`,4`,6`-tetra-O-acetyl-β-D-glucopyranosyl)[3-oxy-(1-phenyl-4-arylidene)-pyrazol-5-one]-carbodithioates **7** & **9** , respectively **(Scheme 2).**

^{1}H NMR spectrum of a mixture of compounds **8 + 9** showed the following signals: 1.92,1.99,2.03(s, 24H, 8C$\underline{H}_3$CO),3.15(s,12H,4CH_3) 4.08-4.25 (m, 4H,H-6a, H-6b,H-6a*, H-6b*), 4.30-4.33 (t, 2H, H-4, H-4*), 5.04-5.31(m, 4H, H-3, H-3*, H-5, H-5*)5.52-5.57 (m, 2H, H-2, H-2*), 6.19 (d, 1H, H-1,*J*=8.00 Hz), 6.35 (d, 1H, H-1*,*J*=8.00 Hz), 6.8-8.01 (m,18H, Ar-H), 8.54(s, 2H,2 =CH).



Scheme 2

From ^{1}H NMR spectrum of **8 + 9** it was shown that; two unseparated compounds with their anomeric protons (H-1) ,(H-1*) as a doublet signals at δ = 6.19 and δ = 6.35 ppm with a $J_{1,2}$ = 8 Hz, which corresponds to the diaxial orientation of the H-1 and H-2 protons indicating the β-configuration.

^{13}C NMR spectrum of a mixture of compounds **8 + 9** exhibited a two signals at δ 95.31 and 96.05 corresponding to two anomeric carbons (C-1),(C-1*).also, showed two C=S group signals at δc: 170.05, 170.48, whereas the three C=O groups appeared at δc 160.98 and 163.29.

Column chromatography separation of products **8 & 9** mixture by using (ethyl acetate/ hexane) has been done to yield the separated compounds **8** and **9** in low yields.

IR spectrum of compound **8** showed a new absorption band corresponding to (CH_3**CO**) at υ 1758.58; Its ^{1}H NMR spectrum showed the following signals : 1.96, 1.99(s, 12H, 4C$\underline{H}_3$CO), 3.08(s,6H,2CH_3), 5.06-5.10 (m, 2H,H-6a, H-6b), 5.14-5.17 (t, 1H, H-4), 5.28-5.31(m, 2H, H-3, H-5), 5.48-5.52 (m, 1H, H-2), 6.10 (d, 1H, H-1, *J*=8.00 Hz), 6.77-7.90 (m,9H, Ar-H), 8.46(s, 1H, =CH).

IR spectrum of compound **9** showed a new absorption band corresponding to (CH_3**CO**) at υ 1758.58. Its ^{1}H NMR spectrum showed the following signals at: 1.99,2.03(s, 12H, 4C$\underline{H}_3$CO), 3.16(s,6H,2CH_3), 4.11-4.18 (m, 2H,H-6a*, H-6b*), 4.20-4.23 (t, 1H, H-4*), 5.07-5.17(m, 2H, H-3*, H-5*),5.54-5.57 (m, 1H, H-2*), 6.19-6.21 (d, 1H, H-1*,*J*=8.00 Hz), 6.85-7.97 (m,9H, Ar-H), 8.56(s, 1H, =CH).

II- Biological Activity:

II- 1 In Vitro Antimicrobial Activity of some prepared glycoside derivatives :

The antimicrobial potential of some prepared compounds were performed against four isolates belonging to four species of bacteria and fungi (each, two isolates). The bacterial isolates were, *Escherichia coli* (ATCC6538, Gram –ve, pathogen) and *Staphylococcus aureus* (ATCC9027, Gram+ve, pathogen). Whereas, the fungal isolates were: *Candia albicans* (ATCC10231, pathogen) and *Aspergillus fumigatus* (local isolates, saprophyte). The isolates of bacteria (*E.coli* and *S. aureus*) were pregerminated and grown on nutrient agar, whreas, *C.albicans* on sabouraud and *A. fumigatus* on 1% glucose-Czapek's agar media, respectively.

Method:

The pregermination was done on the suitable media to have a mass of cells (bacteria) or conidia and mycelia (fungi) at 37°C, 37°C and 28°C of bacteria, *C.albicans* and *A. fumigatus* isolates, respectively. At the end of incubation period, distilled water (10 ml) was added onto the surface of organism growth, carefully crushed by needle with loop and transferred to Erlenmeyer flask (100 ml) containing distilled water (50 ml) to have approx.1×10^{10} - 1×10^{11} cells and 1×10^{5} - 1×10^{6} conidia of bacteria and fungi, respctively.The final dilution (1 ml) was used to inoculate the medium in petri dish (9 cm), carefully moved with swabbed on the solidified medium.

The titled compounds and standard (Ciprofloxacine and clotrimazole as antibacterial and antifungal, respectively) were dissolved in dimethylsulfoxide (DMSO, 10 ml). the discs (10mm) of filter paper (Whatman No.1) were sterilized by dry heat at 140°C for 1h, soaked in dissolving compounds for 10-12 sec., air dried (4-5h) to exclude the effect of DMSO. The loaded discs were fixed on the surface of cultured (4 discs per Petri dish), kept at 40°C for 2h to allow the diffusion of dissolved compounds into agar media, and incubated under suitable conditions as previously described **.**

II–2 In Vitro Antimicrobial Activity of separated compounds 8& 9 :

II – 3 Antimicrobial evaluation:

All tested glycoside derivatives had a clear activities against both the Gram-positive (*S. aureus***)** and the Gram-negative (*E. Coli*) bacteria and some of them had a good activities against the fungal strains **(Table 1,2)**. Compound **8** showed the highest inhibition zone 28 and 30 mm, and lowest MIC 1.6 and 2.2 μg ml^{-1} against both the Gram-positive (*S. aureus*) and the Gram-negative (*E.coli*)

bacteria respectively, with comparable values to the standard Ciprofloxacin drug. In addition to its low antifungal activity
against *C.albicans* strain with inhibition zone of 10 mm. However it showed no reactivity against the *A. fumigatus*. Compound **9** showed strong antibacterial effect against the Gram-negative (*E.coli*) and Gram-positive (*S. aureus*) bacteria with inhibition zone of 26 and 28 mm, respectively and low MIC 2.4 and 2.8 µg ml^{-1} against both the Gram-positive (*S. aureus*) and the Gram-negative (*E.coli*) bacteria respectively. However it showed no antifungal activity against *C.albicans* strain nor *A. fumigatus*.

III- Molecular docking study: *E. coli* DNA gyrase B

Docking simulations were performed to study the binding pattern of the newly synthesized compounds in *E. coli* DNA gyrase B active site to predict their binding pattern and to investigate their ability to satisfy the required structural features for binding interactions [20]. The docking setup was first validated by performing self-docking of the co-crystalized thiazole inhibitor in the active site of *E. coli* DNA gyrase B (PDB ID: 4DUH) [21]. The self-docking validation reproduced the co-crystallized thiazole indicating that the docking protocol used is suitable for the intended docking study. This is shown by the small RMSD between the experimental co-crystallized inhibitor pose and the docked pose of 1.00 Å; and by the capability of the docking pose to reproduce all the key interactions achieved by the co-crystallized ligands in the active site. the docking energy score was S = -9.25 kcal/mol. Arg73, Arg136 interact with Ph-COO^- through H-bonding. Lys103 interacts with thiazole moiety by arene-cation interaction. Gly101 interact with Ph-NH and sulfur atom by H-bonding. Asp73 interact with NH of NHCOEt by H-bonding. Gly77 with Asp73, and Thr165 with N of thiazole by H-bonding through water bridge (**Table 3** & **Figure 1a, b**). Analysis of the molecular docking results showed that compound **8** and **9** could fit into the *E. coli* DNA gyrase B binding site with docking energy scores -8.3 and -7.85 kcal/mol, respectively. The two most active compounds **8** and **9** achieve hydrogen bonding and hydrophobic interaction with the key amino acids Arg76, Arg136,His55 and Gly101. In compound **8**, Arg136 interacts by H-bonding interaction with Sulfur atom of carbodithioate and Oxygen atom of CO of pyrazole ring. Also, Arg76 and His55 interact with Oxygen atom of Pyrane ring of sugar and Oxygen atom of CO of O-Acetyl group through H-bonding , respectively. (**Table 3** & **Figure 2a, b**).

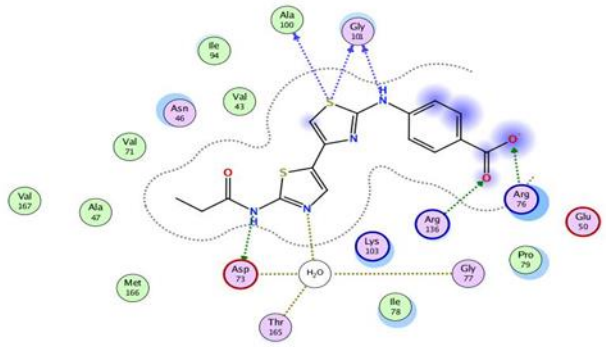


Figure 1a: 2D diagram representation of thiazole inhibitor docked into *E coli* DNA gyrase B active site showing his binding interactions with the amino acids binding site

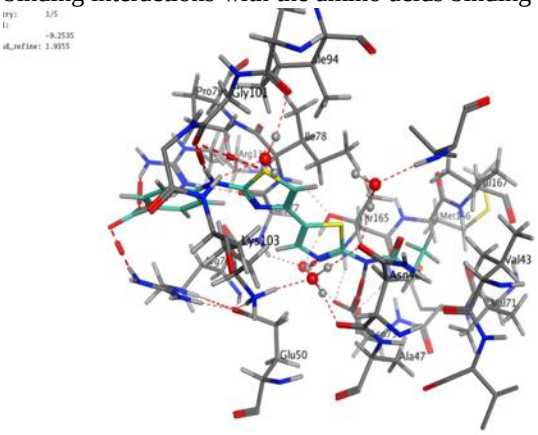


Figure 1b: 3D diagram representation of thiazole inhibitor docked into *E coli* DNA gyrase B active site.

Table (1): The inhibitory effect (inhibition Zone, mm) of some prepared glycoside derivatives in addition to standard (antibiotics) compounds (100mg) against isolate of bacteria and fungi (each, 2 isolate of 2 species), where [a, b are atndaed drugs] .

Compound	Concentration (µg ml^{-1})	Inhibition Zone (mm)			
		Bacteria		Fungal Strains	
		***S. aureus* Grm(+Ve)**	***E. coli* Gram-Ve**	***C. albicans***	*A.fumigatus*
8	100	28	30	10	N. A.
9	100	26	28	N. A.	N. A.
[a]Ciprofloxacin	100	25	15	N. A.	N. A.
[b]Clotrimazole	100	N. A.	N. A.	17	20

Experimental:

Melting points were determined with an electronic melting point apparatus(Stuart) in open capillaries and are uncorrected. TLC was performed on E. Merck Silica Gel 60 F254 with detection by UV light absorption. IR spectra were recorded with a Bruker infrared spectro- photometer

Table (2): The inhibitory effect (minimum inhibitory concentration (MIC), µg ml^{-1}) of the most active glycoside derivatives 8&9 in addition to standard (antibiotics) compounds against isolate of bacteria and fungi (each, 2 isolate of 2 species), where [a, b are atndaed drugs] .

Compound	Minimum inhibitory concentration (MIC) (µg ml-1)			
	Bacterial Strains		Fungal Strains	
	S. aureus	*E. coli*	*C. albicans*	*A. fumigatus*
8	1.6	2.2	75	N.A.
9	2.4	2.8	N.A.	N.A.
Ciprofloxacin	7.81	62.5	-	-
Clotrimazole	-	-	2.5	2.1

Table: 3

Compound	Binding scores (kcal/mol^{-1})	Ligand atom	Residue	Interaction
8	-8.3	Sulfur atom of carbodithioate	Arg136	H-bond
		O of CO of pyrazole ring	Arg136	H-bond
		O of Pyrane ring of sugar	Arg76	H-bond
		O of CO of O-Acetyl group	His55	H-bond
9	-7.85	Sulfur atom of carbodithioate	Arg76	H-bond
		Benzene ring of pyrazole	Gly101	Arene-cation
		O of CO of O-Acetyl group	H_2O-	H-bond
Legand inhibitor	-9.25	O- of Ph-COO-	Arg76	H-bond
		O- of Ph-COO-	Arg136	H-bond
		NH of Ph-NH	Gly101	H-bond
		S of Thiazole	Gly101	H-bond
		Thiazole	Lys103	Arene-cation
		NH of NHCOEt	Asp73	H-bond
		NH of Thiazole	H_2O -	H-bond

(KBr technique). ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance NMR spectrometer at 400 and 100 MHz, with TMS as the internal standard. Solvents used were purified by simple distillation.

Synthesis of compounds 2-5 :

To a solution of the corresponding compound **1$_{a,b}$** (0.05, mol) in dioxane (40 ml), anhydrous potassium carbonate (3 g) and tetrabutylammonum bromide (TBABr)(0.02 g) were added. The reaction mixture was stirred at room temperature for 30 mints, and then 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide was added portion wise (5 mints). Continues the stirring for the mixture at same temperature for overnight (TLC). Filtered the carbonate layer and the filtrate was evaporated, the residue was treated with water, dried and crystallized from ethanol.

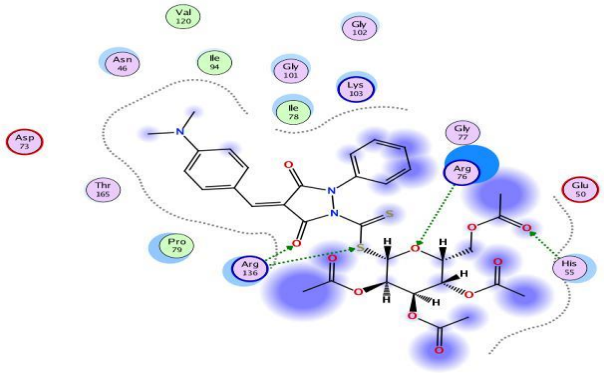


Figure 2a: 2D diagram representation of glycoside **8** docked into *E coli* DNA gyrase B active site.

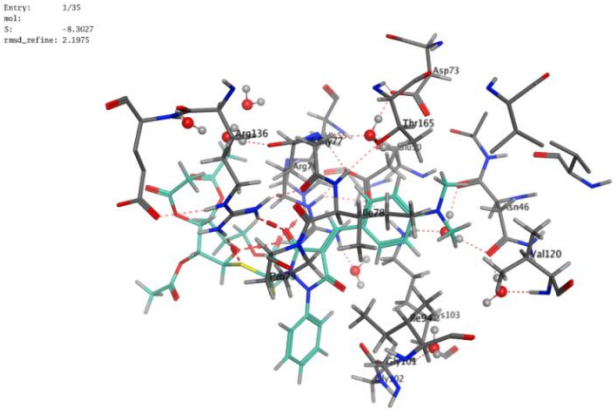


Figure 2b: 3D diagram representation of glycoside **8** docked into *E coli* DNA gyrase B active site.

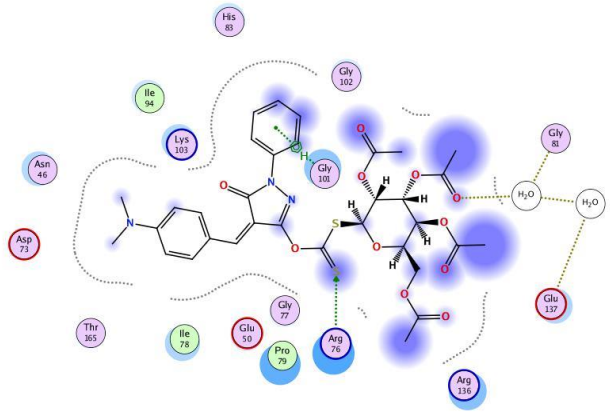


Figure 3a: 2D diagram representation of glycoside **9** docked into *E coli* DNA gyrase B active site.

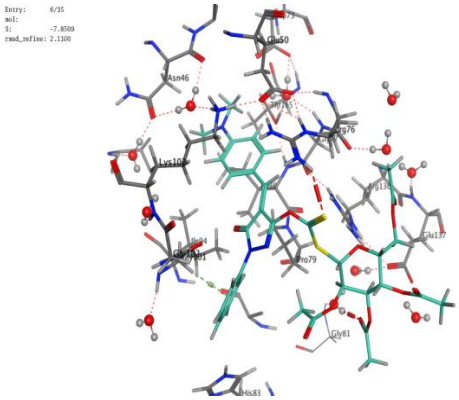


Figure 3b: 3D diagram representation of glycoside **9** docked into *E coli* DNA gyrase B active site.

Amixture of:
***N*-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-4-(2-naphthylidene)-1-phenyl-3,5-pyrazolidinedione (2)**
& 3-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyloxy)-4-(2-naphthylidene)-1-phenyl-1H-pyrazol-5-one (3)
Brown solid , m.p 208-212 ^{o}C, IR (KBr,cm^{-1}) :υ 1758 (CH_3CO); ^{1}H NMR (400 MHz, DMSO) :2.02 (s, 24H, 8C$\underline{H}_3$CO),4.11-4.23 (dd, 4H,H-6a, H-6b,H-6a*, H6b*), 4.38 (t, 2H, H-4, H-4*), 5.1(d, 2H, H-3, H-3*) 5.25 (q, 2H, H-5, H-5*)5.58 (t, 2H, H-2, H-2*), 6.30 (d, 1H, H-1,J=8.00), 6.46 (d,1H, H-1*,J=8.00), 7.23-8.65 (m,24H, Ar-H), 9.03 (s, 2H, 2=CH).

Amixture of:
***N*-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyl)-4-(4-*N*,*N*-dimethylaminobenzylidene)-1-phenyl-3,5-pyrazolidinedione (4)**
& 3-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranosyloxy)-4-(4-*N*,*N*-dimethylaminobenzylidene)-1-phenyl-1H-pyrazol-5-one (5)
Orange solid , m.p 168-170 ^{o}C, IR (KBr,cm^{-1}) :υ 1758.51 (CH_3CO); ^{1}H NMR (400 MHz, DMSO): 1.92,1.99,2.03(s, 24H,8C$\underline{H}_3$CO),3.14(s,12H,4CH3) 4.09-4.22 (m, 4H,H-6a, H-6b,H-6a*, H-6b*), 4.33 (t, 2H, H-4, H-4*), 5.05-5.33(m, 4H, H-3, H-3*, H-5, H-5*)5.52-5.59 (m, 2H, H-2, H-2*), 6.19 (d, 1H, H-1,*J*=8.00), 6.36 (d, 1H, H-1*,*J*=8.00),6.8-8.00 (m,, 18H, Ar-H), 8.55(s, 2H,2 =CH).

Synthesis of compounds 6-9 :
To a solution of the corresponding compounds $\mathbf{1_{a,b}}$ (0.0 5 mol) in dioxane (40 ml), anhydrous potassium carbonate (3g), carbondisulphide (0.05mol,3ml) and tetrabutyl ammonium bromide (TBABr)(0.02 g) were added and was stirred at 0-5 ^{o}c for 30 mints.to the reaction mixture, 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide was added portion wise (5 mints). Continues the stirring for the mixture at room temperature for overnight (TLC). Filtered the carbonate layer and the filtrate was evaporated, the residue was treated with water, the precipitated product was filtered, dried and crystallized from ethanol**.**

A mixture of:
(2`,3`,4`,6`-tetra-O-acetyl-β-D-glucopyranosyl)[*N*-(1-phenyl-4-(2-naphthylidene))-pyrazolidin-3,5-dione]-carbodithioate (6)
& (2`,3`,4`,6`-tetra-O-acetyl-β-D-glucopyranosyl)[3-oxy-(1-phenyl-4-(2-naphthylidene))-pyrazol-5-one]-carbodithioate (7)
Brown solid ,m.p 216-218 ^{o}C , IR (KBr,cm^{-1}) :υ 1761 (CH_3CO); ^{1}H NMR: 1.90,1.95,1.98,1.99,2.01,2.03 (s, 24H, 8C$\underline{H}_3$CO), 4.09-4.24 (m, 4H,H-6a, H-6b,H-6a*, H-6b*), 4.38 (t, 2H, H-4, H-4*), 5.07-5.09(m, 2H, H-3, H-3*) 5.22-5.28 (m, 2H, H-5, H-5*)5.55-5.6 (m, 2H, H-2, H-2*), 6.28 (d, 1H, H-1,J=8.00 Hz), 6.44 (d, 1H, H-1*,J=8.00 Hz), 7.23-8.11,8.7(m, 24H, Ar-H), 8.66 (s, 1H, =CH), 9.05 (s, 1H, =CH*).

Amixture of :
(2`,3`,4`,6`-tetra-O-acetyl-β-D-glucopyranosyl)[*N*-(1-phenyl-4-(4-*N*,*N*-dimethylaminobenzylidene))-pyrazolidin-3,5-dione]-carbodithioate (8)
& (2`,3`,4`,6`-tetra-O-acetyl-β-D-glucopyranosyl)[3-oxy-(1-phenyl-4-(4-*N*,*N*-dimethylaminobenzylidene))-pyrazol-5-one]-carbodithioate (9)
Orange solid ,m.p182-184 ^{o}C ,IR (KBr,cm^{-1}) :υ 1758.82 (CH_3CO); ^{1}H NMR 1.92,1.99,2.03(s, 24H, 8C$\underline{H}_3$CO),3.15(s,12H,4CH3) 4.08-4.25 (m, 4H,H-6a, H-6b,H-6a*, H-6b*), 4.30-4.33 (t, 2H, H-4, H-4*), 5.04-5.31(m, 4H, H-3, H-3*, H-5, H-5*)5.52-5.57 (m, 2H, H-2, H-2*), 6.19 (d, 1H, H-1,*J*=8.00 Hz), 6.35 (d, 1H, H-1*,*J*=8.00 Hz), 6.8-8.01 (m,18H, Ar-H), 8.54(s, 2H,2 =CH). ^{13}CNMR: 20.75(8$\underline{C}$H$_3$CO),40.52(4N$\underline{C}$H3),62.09(C-6,6*), 68.48 (C-4,4*), 71.04 (C-3), 71.35 (C-3*), 72.08 (C-2), 72.25 (C-2*), 72.71(C-5,5*), 95.31 (C-1), 96.05 (C-1*)

,108.55, 109.32, 112.12, 112.32 ,118.24, 118.71, 119.82, 120.98, 124.36 ,129.12, 129.22, 137.76, 138.26, 139.12 , 139.32 , 147.19 , 154.52 , 154.67 , 155.01, 156.77(Ar-C,C=),160.98 , 163.29(3C=O), 169.88 (8CH_3CO),170.05 ,170.48 (2C=S).

(2`,3`,4`,6`-tetra-O-acetyl-β-D-glucopyranosyl)[*N*-(1-phenyl-4-(4-*N*,*N*-dimethylaminobenzylidene))-pyrazolidin-3,5-dione]-carbodithioate (8)

Orangesolid, m.p182-184^{o}C, IR(KBr,cm^{-1}):υ1758.58 (CH_3CO);^{1}HNMR:1.96,1.99(s,12H,4CH_3CO),3.08(s,6H,2 CH3), 5.06-5.10 (m, 2H,H-6a, H-6b), 5.14-5.17 (t, 1H, H-4), 5.28-5.31(m, 2H, H-3, H-5),5.48-5.52 (m, 1H, H-2), 6.10 (d, 1H, H-1,*J*=8.00 Hz), 6.77-7.90 (m,9H, Ar-H), 8.46(s, 1H, =CH).

(2`,3`,4`,6`-tetra-O-acetyl-β-D-glucopyranosyl)[3-oxy-(1-phenyl-4-(4-*N*,*N*-dimethylaminobenzylidene))-pyrazol-5-one]-carbodithioate (9)

Orange solid ,m.p182-184 ^{o}C ,IR (KBr,cm^{-1}) :υ 1758.88 (CH_3CO);^{1}H NMR:1.99,2.03(s,12H,4CH_3CO),3.16(s, 6H, 2CH_3), 4.11-4.18 (m, 2H,H-6a*, H-6b*), 4.20-4.23 (t, 1H, H-4*), 5.07-5.17(m, 2H, H-3*, H-5*),5.54-5.57 (m, 1H, H-2*), 6.19-6.21 (d, 1H, H-1*,*J*=8.00 Hz), 6.85-7.97 (m,9H, Ar-H), 8.56(s, 1H, =CH).

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