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Synthesis and X-ray analysis of butyl and glycosyl (2-arylamino-4,4-dimethyl-6-oxocyclohex-1-ene)carbodithioates and their possible cyclization to 2-thioxo-6,7-dihydro-1*H*-benzo[*d*][1,3]thiazin-5(2*H*)-one derivatives

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ABSTRACT

Variety of butyl [2-arylamino-4,4-dimethyl-6-oxo-cyclohex-1-ene]carbodithioates (**3a–c**), 2-thioxo-6,7-dihydro-1*H*-benzo[*d*][1,3]thiazin-5(2*H*)-one derivatives (**5a–c**), and the glucosyl carbodithioates **6a–c** as well as galactosyl carbodithioates **7a–c** have been synthesized from the reaction of enaminone derivatives **1a–c** with carbon disulfide followed by the alkylation with *n*-butyl bromide and α-D-glycosyl bromides, respectively. The amount of carbon disulfide plays a great role in the mode of reaction. The structures of the synthesized compounds were elucidated by spectral data and X-ray crystallography.

1. Introduction

Much attention has been focused on compounds functionalized with the – CSS-group because of their diversity as represented by industrial chemicals, such as rodent repellents, vulcanization additives in rubber manufacturing, lubricants, and polymers in addition to their metal chelating properties, which are used in analytical chemistry and waste management. These compounds exhibit a wide spectrum of biological activities[1–4] and are used as fungicides in pesticides and fumigants.[4,5] They modulate the function of a number of key proteins involved in apoptosis, oxidative stress, transcription, and proteosome function.[6] Thus, they are of potential therapeutic value for cancer,[7–10] viral infection,[11] antitumor activity,[12] inflammation,[13] immunosuppressive agents,[14] and antioxidants, as well as inhibition of the replication of rhinovirus, influenza virus, and polio virus.[11–15] Their biological effects are dependent on their structural characteristics that influence the stability decomposition and their metabolic products in vivo.[16–20]

A great demand for significant amounts of oligosaccharides and glycoconjugates for biological, medicinal, and pharmacological studies has been generated because of the important roles played by these compounds in biological processes.[21] Therefore, tremendous effort has been made to develop new procedures for the synthesis of glycosides and developing strategies for the formation of glycosidic bonds.[21–24] However, efforts are still directed toward the synthesis of glycosidic bonds, particularly in a stereoselective manner. Glycosyl sulfanyl heterocycles have been regarded as good glycosyl donors in addition to their biological activities such as the inhibition of enzyme activity.[25] Having the above aspects in mind and in addition to the paucity of work that has been reported on the glycosyl carbodithioates and their biological value[26–28] as well as their value as glycosyl donors for glycosyl bond formation, we became interested in the synthesis of new members in this class of compounds. We are also investigating their spectra and X-ray crystallographic data as a continuation of our work,[23,24] and our interest[29–32] in elucidating structures by X-ray crystallography.

2. Results and discussion

The reactivity of enaminones toward some electrophilic reagents was investigated in order to synthesize carbodithioates and benzothiazine derivatives. Thus, the reaction of **1a–c**[33] with carbon disulfide in dimethyl sulfoxide (DMSO) containing sodium hydroxide followed by addition of *n*-butyl bromide afforded butyl [2-arylamino-4,4-dimethyl-6-oxo-cyclohex-1-ene]carbodithioates

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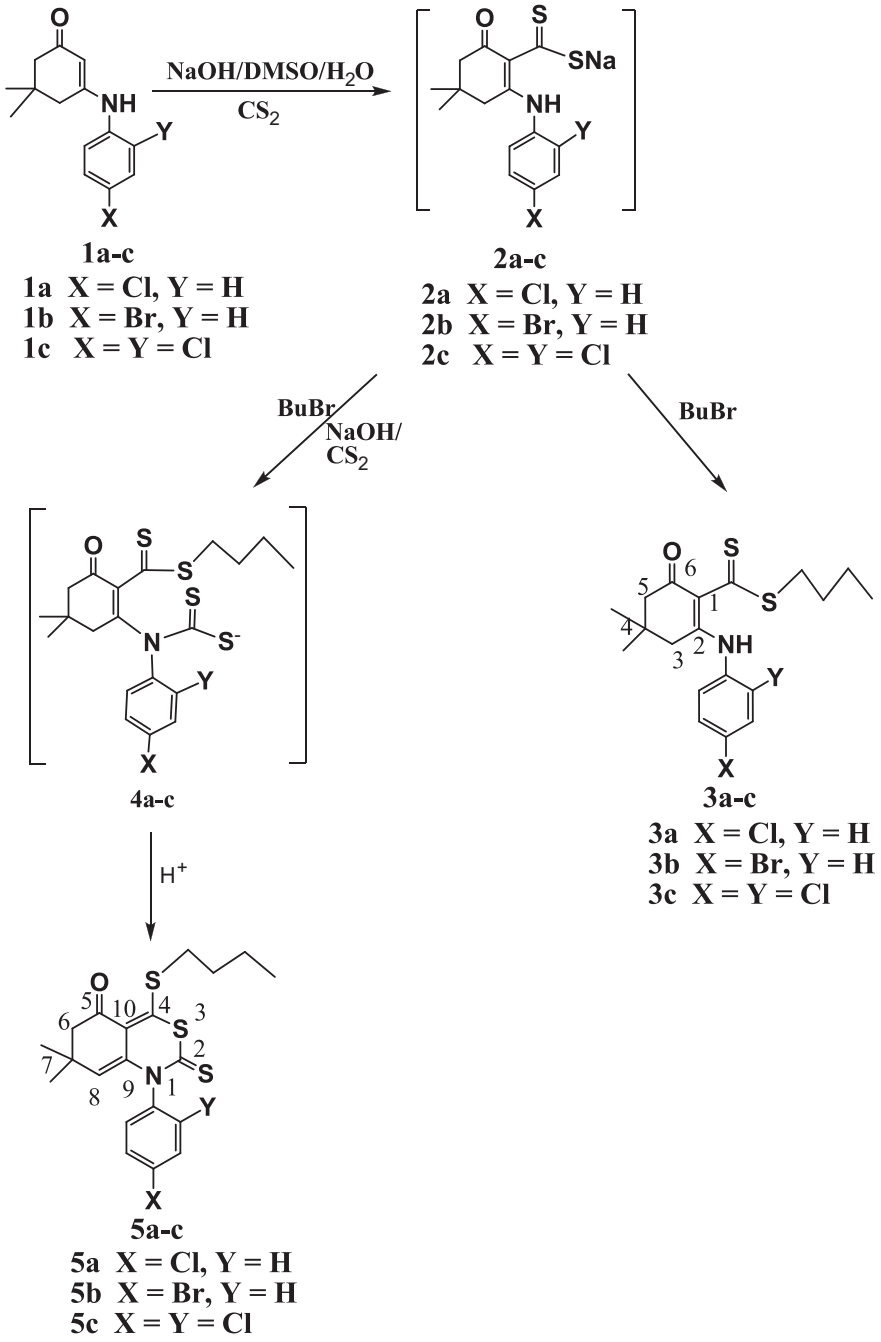
(**3a–c**) via the loss of a molecule of HBr from the nonisolable intermediates **2a–c**.

On the other hand, the reaction of enaminones **1a–c** with an excess of carbon disulfide in DMSO containing a catalytic amount of NaOH followed by addition of *n*-butyl bromide furnished benzothiazine derivatives **5a–c**, (Scheme 1). These thiazinones have been presumably formed via the heterocyclization of the nonisolable intermediates **4a–c**. The conditions for the reactions are critical, probably due to the ready loss of carbon disulfide from the reaction mixture whose amount has a great role in the formation of an intermediate such as **4a–c**. The introduction of a carbodithioate on the nitrogen of **2** before alkylation may be unlikely. The reported[34] methylation of similar analogs did not give good results in our hands. The structural assignments of the butyl derivatives have been considered as model study to be used in assigning the glycosyl derivatives as alkylating agents.

The structures of **3** or **5** can be readily differentiated by their ^{1}H NMR spectra where **3** shows a signal at the low-field region at δ 14.73–15.44 that is exchangeable with D_2O and is due to the NH proton. Such a signal at low field does not appear in the spectra of compounds **5**. On the other hand, the ^{13}C NMR spectra of **3** showed a C=S resonance at δ_c 191.3, whereas the C=S of **5** appeared at δ_c 182.5–183.6. Moreover the H-8 appeared at δ_c 4.49–4.55, which is in agreement with an olefinic proton rather than a methylene group.

Applying the above synthetic scheme, we further explored the synthesis of thioglycoside analogs from the enaminones. Thus, the reaction of enaminones **1a–c** with carbon disulfide in the



Scheme 1.

presence of sodium hydroxide and then glycosylation with α-D-glycosyl bromides, namely 2′,3′,4′,6′-tetra-*O*-acetyl-α-D-glucopyranosyl bromide and 2′,3′,4′,6′-tetra-*O*-acetyl-α-D-galactopyranosyl bromide, gave (2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl) [2-(arylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]carbodithioates **6a–c** and (2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl) [2-(arylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]carbodithioates (**7a–c**), respectively. No products could be isolated having structure **8** (Scheme 2). The ^{1}H NMR spectra of the glycosyl derivatives showed signals in the range of δ 15.23–16.02 indicating that the products have structures **6** and **7** rather than **8**. The anomeric protons appeared in the range of δ 5.72–5.76 with large coupling constants ($J_{1',2'}$ = 10.5–10.8 Hz) confirming the diaxial orientation of H-1 and H-2 and indicating that the reaction of the donor with the acceptor gave the β-glycoside.

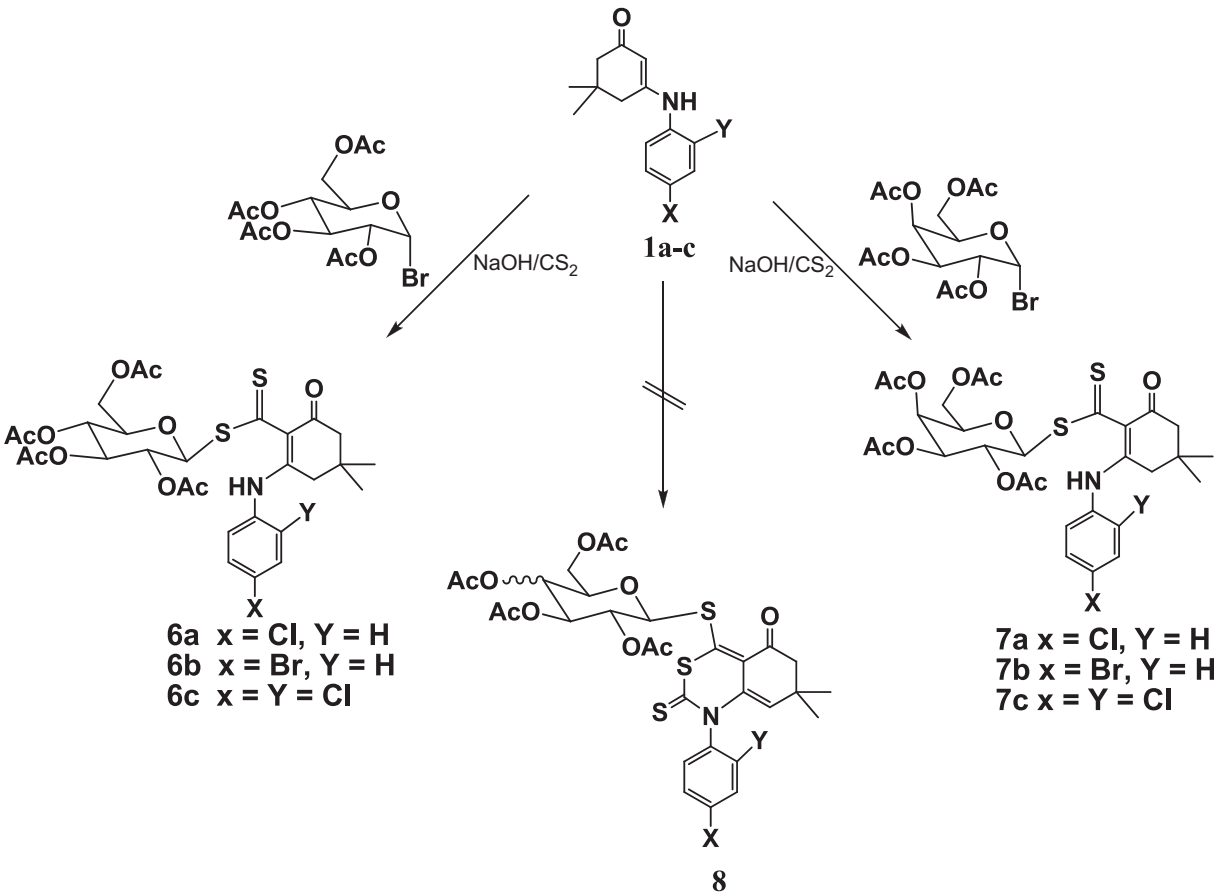
The structures of **5a** and **7a** were confirmed by X-ray crystallography as it will be shown in the following section.

3. X-ray analysis

Generally, calculated positions (C–H 0.93–0.99 Å) were adopted for carbon-bound H-atoms and were included in the refinement in the riding model approximation, with *U*(H) set to 1.2–1.5 *U*(C). The amino H-atom was refined by keeping a distance restraint of N–H at 0.88 ± 0.01 Å; its temperature factor was freely refined and was located in a difference Fourier map. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles, and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes refinement of F^2 against all reflections. The weighted *R*-factor w*R* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative F^2. The threshold expression of F^2 2sigma (F^2) is used only for calculating *R*-factors (gt) etc. and is not relevant to the choice of reflections for refinement. *R*-Factors based on F^2 are statistically about twice as large as those based on *F* and *R*-factors based on all data will be even larger.[35–38]

The single-crystal diffraction analysis of **5a** showed the compound has a bicyclic structure (Fig. 1, Table 1 and Supplementary data Tables S1–S5) rather than the expected monocyclic structure **3a**. The crystal data revealed that the C11–S3 bond length (1.817(3) Å) is typical of a single bond, while the other C9–S1 bond length (1.753(3) Å), suggesting a degree of conjugation in the 4-(butylsulfanyl)-1-(4-chlorophenyl)-7,7-dimethyl-2-thioxo-6,7-dihydro-1*H*-benzo[*d*][1,3]thiazin-5(2*H*)-one.

On the other hand, C10–S2 displayed a bond length of 1.658 Å, reflecting double bond character. The bond lengths C4–C5 and C6–C9 are 1.361(7) Å and 1.358(5) Å, respectively, which revealed the presence of unsaturation. A deviation of the methyl group C7 from the mean path of benzothiazin-5-one was observed having torsion angle of 83.0(4)° (C5–C4–C3–C7). The cyclohexene ring has an envelope conformation, with atom C3 deviating from the plane of the remaining five ring atoms (Fig. 1). The deviation of C3 from the plane of the rest of the molecule caused reduction in the angle formed between C2, C3, and C4 (C4–C3–C2, 108.4 (3)°). Intermolecular S–S interactions link the molecules into a two-dimensional network as shown in Figure 2.



Scheme 2.

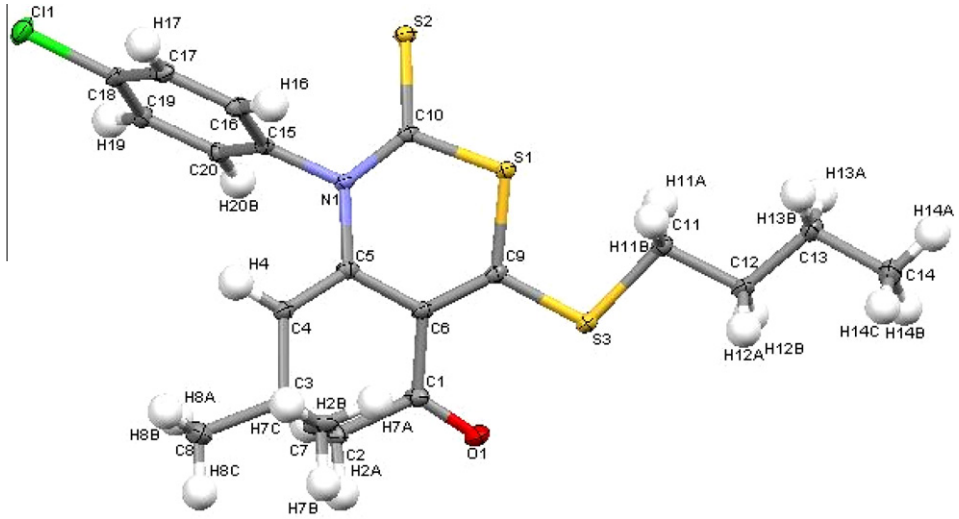


Figure 1. Displacement ellipsoids of **5a** at the 50% probability level are shown along with labeling.

Table 1
Crystal data, collection and refinement for **5a**

$C_{20}H_{22}ClNOS_3$	$F000$ = 444
M_r = 424.02	Dx = 1.360 Mg m^{-3}
Monoclinic, $P21$	Mo Kα radiation, λ = 0.71073 Å
Hall symbol: P 2yb	Cell parameters from 2674 reflections
a = 12.0457 (3) Å	θ = 2.6–26.2°
b = 6.4534 (2) Å	μ = 0.50 mm^{-1}
c = 13.7375 (3) Å	T = 100 K
β = 104.198 (2)°	Prism, yellowish orange
V = 1035.27 (5) Å^3	0.30 × 0.03 × 0.03 mm
Z = 2	
Bruker SMART APEX diffractometer	4730 Independent reflections
Radiation source: fine-focus sealed tube	4065 Reflections with $I > 2\sigma(I)$
Monochromator: graphite	R_{int} = 0.035
T = 100 K	θ_{max} = 27.5°
ω Scans	θ_{min} = 1.5°
Absorption correction: Multi-scan SADABS (Sheldrick, 1996)	h = −15→15
T_{min} = 0.776, T_{max} = 0.985	k = −8→8
9856 Measured reflections	l = −17→17
Refinement on F^2	Hydrogen site location: inferred from neighboring sites
Least-squares matrix: full	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.041	$w = 1/[\sigma^2(F_o^2) + (0.0578P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F2)$ = 0.106	(Δ/σ)max = 0.001
S = 1.05	$\Delta\rho_{max}$ = 0.44 e Å^{-3}
4730 Reflections	$\Delta\rho_{min}$ = −0.29 e Å^{-3}
239 Parameters	Extinction correction: none
1 Restraint	Absolute structure: Flack (Flack, 1983) parameter from 2133 Friedel pairs
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.26 (8)
Secondary atom site location: difference Fourier map	

The crystallographic analysis revealed that the sugar molecule in (2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl) [2-(4-chloroanilino)-4,4-dimethyl-6-oxocyclohex-1-ene]carbodithioate exists in galactopyranose form Table 2. Examinations of bond lengths, angles, and torsion angles demonstrate that the values conform to those observed in other galactopyranose and carbodithioate analogs.[29–32] Intramolecular bond angles, lengths, and torsion angles indicated that the galactopyranose ring is in the usual $^4C_1$ conformation, and the anomeric center of the sugar has β configuration. No significant hydrogen bonds exist in the crystal except intermolecular hydrogen bonding between NH–S. The acetyl group attached to the primary hydroxyl group in the title compound is in the *gt* position, which is known to be the favored orientation for pyranose with the *galacto* configuration. The cyclohexene ring of (2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl) [2-(4-chloroanilino)-4,4-dimethyl-6-oxocyclohex-1-ene]carbodithioate adopts an envelope conformation, with the C-9 atom bearing the two methyl groups representing the flap. The acetoxymethyl group is equatorially bonded to the C17 ring atom by making a torsion angle of O3–C17–C21–O4, of 60.6(4)°. The acetoxymethyl group was found to be running parallel with respect to cyclohexene ring as shown in Figure 3. The acetyl group bonded to C18 was found to be axially oriented with a torsion angle of 131.5(4)°, C17–C18–O6–C24 with respect to sugar moiety. The acetyl groups attached to C19 and C20 are equatorially oriented bearing torsion angles C18–C19–O8–C26 136.9(4)° and C19–C20–O10–C28, −139.3(4)°, respectively. The 2-(4-chloroanilino)-4,4-dimethyl-6-oxocyclohex-1-enecarbodithioate group is axially bonded to C16 atom of the galactose sugar with a torsion angle O3–C16–S1–C15, of −78.6(3)°. The 4-chloroaniline ring is experiencing a torsion angle of 3.7(7)°, for C8–C7–N1–C1, thus indicating a slight deviation in planarity with respect to the cyclohexene ring (Tables S6–S9).

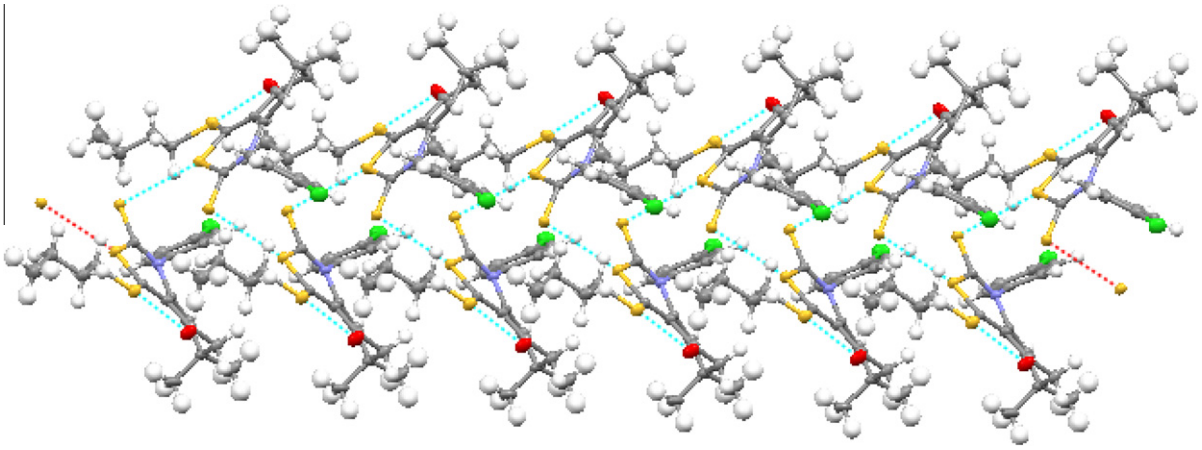


Figure 2. Packing diagram of **5a** showing S–S connectivities.

Table 2
Crystal data, collection, and refinement for **7a**

$C_{29}H_{33}ClNO_{10}S_2$	V = 1616.05 (16) Å^3
M_r = 655.13	Z = 2
a = 13.4331 (8) Å	Dx = 1.346 Mg m^{-3}
b = 8.6843 (5) Å	Mo Kα radiation, λ = 0.71073 Å
c = 13.9745 (8) Å	μ = 0.30 mm^{-1}
α = 90°	T = 123 K
β = 97.560 (3)°	0.36 × 0.04 × 0.04 mm
γ = 90°	
Radiation source: fine-focus sealed tube	R_{int} = 0.075
Monochromator: graphite	θ_{max} = 27.5°
T = 123 K	θ_{min} = 1.5°
	h = −17→17
11,306 Measured reflections	k = −11→11
6693 Independent reflections	l = −18→17
4129 Reflections with $I > 2\sigma(I)$	
Refinement on F^2	Hydrogen site location: inferred from neighboring sites
Least-squares matrix: full	H atoms treated by a mixture of independent and constrained refinement
$R[F^2 > 2\sigma(F^2)]$ = 0.062	$w = 1/[\sigma^2(F_o^2) + (0.038P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
wR (F^2) = 0.131	(Δ/σ)max = 0.001
S = 0.96	$\Delta\rho_{max}$ = 0.39 e Å^{-3}
6693 Reflections	$\Delta\rho_{min}$ = −0.37 e Å^{-3}
394 Parameters	Extinction correction: none
1 restraint	Absolute structure: Flack, H. D., *Acta Crystallogr., Sect. A* **1983**, *39*, 876–881
Primary atom site location: structure-invariant direct methods	Flack parameter: 0.03 (9)
Secondary atom site location: difference Fourier map	

4. Experimental

4.1. General methods and materials

Melting points were determined with a Mel-Temp apparatus (SMP10) in open capillaries and are uncorrected. TLC was performed on E. Merck Silica Gel 60 F_{254} with detection by UV light absorption. ^{1}H NMR spectra were recorded on Bruker Avance AV NMR spectrometer at 300 or 400 MHz, whereas the ^{13}C NMR were recorded on the same instrument at 75 or 100 MHz, respectively, with TMS as the internal standard. Mass spectra were recorded on a Finnigan (MAT312) or Jeol (JMS.600H) instrument, HRMS were recorded with a Thermo Finnegan (MAT 95XP) instrument. Solvents used were purified by simple distillation.

4.2. General procedure for preparation the carbodithioates 3a–c

To a cooled solution of enaminones **1a–c** (0.01 mol) and NaOH (0.4 g, 0.01 mol) in a mixture of DMSO (20 mL) and water (1 mL) was added CS_2 (0.03 mol). The reaction mixture was stirred for 20 min at room temperature and then *n*-butyl bromide (0.012 mol) was added. The reaction mixture was stirred for 24 h at room temperature, then poured onto cold water (100 mL), and acidified with 10% HCl. The product that separated out was filtered off, dried, and purified by silica gel column chromatography (3:7 EtOAc–*n*-hexane) and recrystallized from MeOH to give **3a–c**.

4.2.1. *n*-Butyl [2-(4-chlorophenylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]carbodithioate (3a)

Yield (52.5%, yellow crystals), mp 162–164 °C, TLC (8:2 *n*-hexane–EtOAc): R_f 0.42, ^{1}H NMR ($CDCl_3$, 300 MHz) : δ 0.93 (t, 3H, J = 7.2 Hz, CH_3-4′), 1.01 (s, 6H, $2CH_3$), 1.44–1.51 (m, 2H, CH_2-3′), 1.66–1.74 (m, 2H, CH_2-2′), 2.14 (s, 2H, CH_2-5), 2.45 (s, 2H, CH_2-3), 3.13 (t, 2H, J = 7.5 Hz, SCH_2), 7.08 (d, 2H, ArH), 7.39 (d, 2H, ArH), 15.44 (s, 1H, NH). FABMS: m/z = 382 [M$^+$+1], ESIMS: Calcd for $C_{19}H_{25}ClNOS_2$ (M$^+$+H), m/z 382.1066, Found 382.1067.

4.2.2. *n*-Butyl [2-(4-bromophenylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]carbodithioate (3b)

Yield (49%, yellow crystals), mp 130–132 °C, TLC (6:4 *n*-hexane–EtOAc): R_f 0.77, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.95 (t, 3H, J = 7.5 Hz,

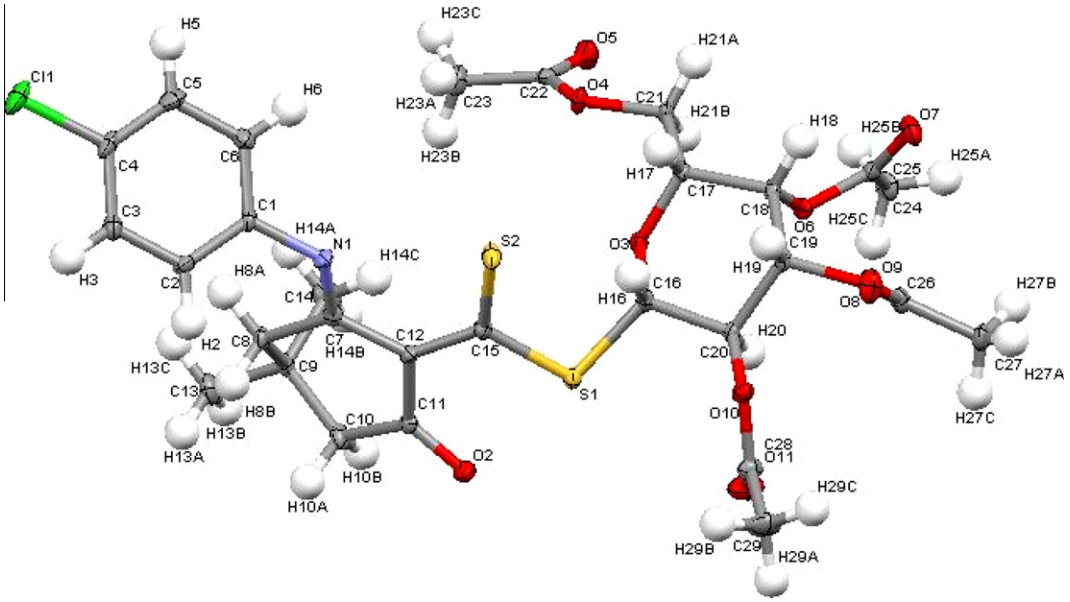


Figure 3. Displacement ellipsoid of **7a** at 50% probability level are shown along with labeling.

CH_3-4′), 1.00 (s, 6H, $2CH_3$), 1.44–1.54 (m, 2H, CH_2-3′), 1.66–1.74 (m, 2H, CH_2-2′), 2.41 (s, 2H, CH_2-5), 2.45 (s, 2H, CH_2-3), 3.12 (t, 2H, SCH_2), 7.02 (d, 2H, ArH), 7.54 (d, 2H, ArH), 15.40 (s, 1H, NH). EIMS: *m*/*z* (%) = 425 (2), 370 (47), 338 (24), 306 (4), 55 (100). ESIMS: Calcd for $C_{19}H_{24}BrNOS_2$ (M^++H), *m*/*z* 426.0561, Found 426.0558.

4.2.3. *n*-Butyl [2-(2,4-dichlorophenylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]carbodithioate (3c)

Yield (34.5%, yellow crystals), mp 128–130 °C, TLC (8:2 *n*-hexane–EtOAc): R_f 0.41, ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.93 (t, 3H, *J* = 7.2 Hz, CH_3-4′), 1.01 (s, 6H, $2CH_3$), 1.45–1.56 (m, 2H, CH_2-3′), 1.67–1.75 (m, 2H, CH_2-2′), 2.31 (s, 2H, CH_2-5), 2.40 (s, 2H, CH_2-3), 3.14 (t, 2H, *J* = 7.6 Hz, SCH_2), 7.51(d, 1H, *J* = 8.4 Hz, ArH), 7.31 (m, 1H, ArH), 7.51 (d, 1H, ArH), 14.73 (s, 1H, NH).^{13}C NMR (DMSO-d_6, 125 MHz): δ 13.5 (CH_3-4′), 21.9 (CH_2-3′), 27.3 ($2CH_3$), 28.5 (CH_2-2′), 30.9 (C-4), 35.7 (SCH_2), 41.2 (C-5), 50.8 (C-3), 118.4 (C-1), 128.1, 129.4, 130.5, 131.5, 132.5, 133.9 (ArH), 162.7 (C-2), 191.3 (C=S), 223.0 (C=O). EIMS: *m*/*z* (%) = 415 (12), 358 (100), 326 (12), 291 (20), 186 (6), 145 (6). HREIMS (M^+): Calcd for $C_{19}H_{23}Cl_2NOS_2$: *m*/*z* 415.0598, Found 415.0556.

4.3. General procedure for the preparation of benzothiazine derivatives 5a–c

To a cooled solution of enaminones **1a–c** (0.01 mol) and NaOH (0.8 g, 0.02 mol) in a mixture of DMSO (20 mL) and water (2 mL) was added CS_2 (0.06 mol). The reaction mixture was stirred for 20 min at room temperature, and then *n*-butyl bromide (0.012 mol) was added. The reaction mixture was stirred for 24 h at room temperature, then poured into cold water (100 mL), and acidified with 10% HCl. The product that separated out was filtered off, dried, and purified on silica gel column chromatography (3:7 EtOAc–*n*-hexane) and recrystallized from EtOH to give **5a–c**.

4.3.1. 4-(Butylthio)-1-(4-chlorophenyl)-7,7-dimethyl-2-thioxo-6,7-dihydro-1*H*-benzo[*d*][1,3]thiazin-5(2*H*)-one (5a)

Yield (29%, yellow crystals), mp 178–180 °C, TLC (*n*-hexane–EtOAc 8:2): R_f 0.38, ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.91 (m, 9H, $3CH_3$), 1.38–1.45 (m, 2H, CH_2-3′), 1.56–1.63 (m, 2H, CH_2-2′), 2.33 (s, 2H, CH_2-6), 3.01 (t, 2H, SCH_2), 4.55 (s, 1H, CH-8), 7.36 (d, 2H, ArH), 7.61 (d, 2H, ArH).^{13}C NMR (DMSO-d_6, 75 MHz) :δ13.4 (CH_3-4′), 21.4 (C-3′), 28.2 ($2CH_3$), 29.9 (C-2′), 30.8 (SCH_2), 32.1 (C-7), 50.7 (C-6), 116.4 (C-8), 122.1, 130.4, 130.5, 133.6 (ArH), 133.5 (C-10), 139.4 (C-9), 145.1 (C-S), 182.6 (C=S), 193.8 (C=O). EIMS: *m*/*z* (%) = 423 (10), 408 (100), 366 (3), 276 (13), 170 (20), 123 (18), 57 (46). HREIMS (M^+): Calcd for $C_{20}H_{22}ClNOS_3$: *m*/*z* 423.0552, Found 423.0559.

4.3.2. 4-(Butylthio)-1-(4-bromophenyl)-7,7-dimethyl-2-thioxo-6,7-dihydro-1*H*-benzo[*d*][1,3]thiazin-5(2*H*)-one (5b)

Yield (35%, yellowish crystals), mp 173–175 °C, TLC (6:4 *n*-hexane–EtOAc): R_f 0.75, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.92 (t, 9H, $3CH_3$), 1.40–1.50 (m, 2H, CH_2-3′), 1.63–1.73 (m, 2H, CH_2-2′), 2.34 (s, 2H, CH_2-6), 2.99 (t, 2H, *J* = 7.5 Hz, SCH_2), 4.55 (s, 1H, CH-8), 7.03–7.08 (m, 2H, ArH), 7.63–7.68 (m, 2H, ArH). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 13.4 (CH_3-4′), 21.3 (CH_2-3′), 28.1 ($2CH_3$), 29.9 (CH_2-2′), 30.8 (SCH_2), 32.0 (C-7), 50.6 (C-6), 116.4 (C-8), 122.1, 130.8, 133.3, 139.8 (ArH), 136.7 (C-10), 141.8 (C-9), 145.1 (C-S), 182.5 (C=S), 193.8 (C=O). EIMS: *m*/*z* (%) = 467 (22), 452 (66), 412 (4), 320 (11), 214 (13), 123 (21), 57 (100). HREIMS (M^+): Calcd for $C_{20}H_{22}BrNOS_3$: *m*/*z* 467.0047, Found 467.0027. Anal. Calcd for $C_{20}H_{22}BrNOS_3$: C, 51.27; H, 4.73; N, 2.99. Found: C, 51.77; H, 4.64; N, 3.0.

4.3.3. 4-(Butylthio)-1-(2,4-dichlorophenyl)-7,7-dimethyl-2-thioxo-6,7-dihydro-1*H*-benzo[*d*][1,3]thiazin-5(2*H*)-one (5c)

Yield (25%, yellow crystals), mp 183–185 °C, TLC (8:2 *n*-hexane–EtOAc): R_f 0.35, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.93 (t, 3H, *J* = 7.5 Hz, CH_3-4′), 0.97 (s, 6H, $2CH_3$), 1.43–1.54 (m, 2H, CH_2-3′), 1.63–1.73 (m, 2H, CH_2-2′), 2.35 (d, 2H, *J* = 1.5 Hz, CH_2-6), 2.99 (t, 2H, *J* = 7.5 Hz, SCH_2), 4.49 (s, 1H, CH-8), 7.19–7.24 (m, 1H, ArH), 7.38–7.42 (m, 1H, ArH), 7.57 (d, 1H, *J* = 2.1 Hz, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.6 (C-4′), 22.0 (C-3′), 28.6, 28.9 ($2CH_3$), 30.9 (C-2′), 31.0 (SCH_2), 32.4 (C-7), 51.4 (C-6), 115.9 (C-8), 120.3, 128.9, 131.2, 131.5, 132.9, 135.6 (ArH), 135.8 (C-10), 136.5 (C-9), 147.6 (C-S) 183.6 (C=S), 194.2 (C=O). EIMS: *m*/*z* (%) 457 (44), 442 (50), 400(2), 366 (8), 334 (4), 185 (5).

HREIMS (M^+): Calcd for $C_{20}H_{21}Cl_2NOS_3$: *m/z* 457.0162, Found 457.0174.

4.4. General procedure for the preparation of thioglycosides 6a–c and 7a–c

To a cooled solution of enaminones **1a–c** (0.01 mol) and NaOH (0.4 g, 0.01 mol) in mixture of DMSO (20 mL) and water (1 mL) was added CS_2 (0.03 mol). The reaction mixture was stirred for 20 min at room temperature and then α-D-glycosyl bromides (0.012 mol) were added. The reaction mixture was stirred for 24 h at room temperature, then poured onto cold water (100 mL), and acidified with 10% HCl. The product that separated out was filtered off, dried, and purified by silica gel column chromatography (3:7 EtOAc–*n*-hexane) and recrystallized from EtOH to give **6a–c** and **7a–c**.

4.4.1. (2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyl) [2-(4-chlorophenylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]-carbodithioate (6a)

Yield (30%, yellow crystals), mp 119–121 °C, TLC (6:4 *n*-hexane–EtOAc): R_f 0.28, ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.91, 0.92 (2s, 6H, $2CH_3$), 1.94, 1.95, 1.98 (3s, 12H, 4OAc), 2.35 (s, 2H, CH_2-5), 2.67 (s, 2H, CH_2-3), 3.92 (dd, 1H, H-6″), 3.96–4.0 (m, 1H, H-5′), 4.11 (dd, 1H, H-6′), 4.94 (t, 1H, $J_{4',3'} = J_{4',5'}$ = 9.6 Hz, H-4′), 5.11 (t, 1H, $J_{2',3'}$ = 9.2 Hz, $J_{2',1'}$ = 10.5 Hz, H-2′), 5.41 (t, 1H, H-3′), 5.76 (d, 1H, $J_{1',2'}$ = 10.5 Hz, H-1′), 7.40 (d, 2H, ArH), 7.57 (s, 2H, ArH), 15.60 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 20.2, 20.3, 20.5 (4Ac), 27.3 ($2CH_3$), 30.5 (C-4), 41.9 (C-5), 50.8 (C-3), 61.5 (C-6′), 68.0 (C-2′), 68.4 (C-4′), 73.7 (C-3′),74.5 (C-5′), 81.6 (C-1′), 118.0 (C-1), 127.7, 129.6, 132.5, 134.6 (ArH), 168.9 (C-2), 169.0, 169.2, 169.5, 169.8 (4C═O), 192.9 (C═S), 210.5 (C═O). FABMS: *m/z* = 656 [M^++1], ESIMS: Calcd for $C_{29}H_{35}ClNO_{10}S_2$ (M^++H) *m/z* 656.1391, Found 656.1357.

4.4.2. (2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyl) [2-(4-bromophenylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]-carbodithioate (6b)

Yield (29%, yellow crystals), mp 125–127 °C, TLC (7:3 *n*-hexane–EtOAc): R_f 0.45, ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.92 (s, 6H, $2CH_3$), 1.94, 1.95, 1.98 (3s, 12H, 4OAc), 2.35 (s, 2H, CH_2-5), 2.67 (s, 2H, CH_2-3), 3.93 (dd, 1H, H-6″), 4.0–4.03 (m, 1H, H-5′), 4.12 (dd, 1H, H-6′), 4.94 (t, 1H, $J_{4',3'} = J_{4',5'}$ = 9.6 Hz, H-4′), 5.11 (t, 1H, H-2′), 5.41 (t, 1H, H-3′), 5.76 (d, 1H, $J_{1',2'}$ = 10.5 Hz, H-1′), 7.32 (d, 2H, ArH), 7.70 (d, 2H, ArH), 15.50 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 20.2, 20.3, 20.4 (4Ac), 27.3 ($2CH_3$), 30.5 (C-4), 41.9 (C-5), 50.8 (C-3), 61.6 (C-6′), 68.1 (C-2′), 68.4 (C-4′), 73.7 (C-3′),74.6 (C-5′), 81.7 (C-1′), 118.0 (C-1), 120.9, 127.9, 132.6, 135.1 (ArH), 168.9 (C-2), 169.2, 169.5, 169.9 (4C═O), 192.9 (C═S), 210.6 (C═O). FABMS: *m/z* = 700 [M^++1], ESIMS: Calcd for $C_{29}H_{35}BrNO_{10}S_2$ (M^++H), *m/z* 700.0886, Found 700.0870.

4.4.3. (2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyl) [2-(2,4-dichlorophenylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]-carbodithioate (6c)

Yield (32%, yellow crystals), mp 202–204 °C, TLC (6:4 *n*-hexane–EtOAc): R_f 0.61, ^{1}H NMR (DMSO-d_6, 300 MHz): δ 0.91 (s, 6H, $2CH_3$), 1.95, 1.96, 1.97, 1.98 (4s, 12H, 4OAc), 1.98 (s, 2H, CH_2-5), 2.35 (s, 2H, CH_2-3), 4.93 (d, 1H, H-6″), 4.0–4.05 (m, 1H, H-5′), 4.13 (dd, 1H, H-6′), 4.94 (t, 1H, $J_{4',3'} = J_{4',5'}$ = 9.6 Hz, H-4′), 5.12 (t, 1H, H-2′), 5.41 (t, 1H, H-3′), 5.74 (d, 1H, $J_{1',2'}$ = 10.5 Hz, H-1′), 7.53–7.60 (m, 2H, ArH), 7.89 (s, 1H, ArH), 15.23 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.6, 20.63, 20.7, 20.8 (4Ac), 27.9, 28.0 ($2CH_3$), 30.8 (C-4), 42.9 (C-5), 51.6 (C-3), 62.0 (C-6′), 68.4, 68.7 (C-2′, C-4′), 74.9 (C-3′), 75.7 (C-5′), 82.4 (C-1′), 118.5 (C-1), 128.4, 129.1, 130.6, 132.2, 132.8, 135.1 (ArH), 169.2 (C-2), 169.4, 169.44, 170.3, 170.7 (4C═O), 193.2 (C═S), 213.2 (C═O). FABMS: *m/z* 690 [M^++1]. Anal. Calcd for $C_{29}H_{33}Cl_2NO_{10}S_2$: C, 50.44; H, 4.82; N, 2.03. Found: C, 50.43; H, 4.77; N, 2.09.

4.4.4. (2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl) [2-(4-chlorophenylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]-carbodithioate (7a)

Yield (30%, yellow crystals), mp 211–213 °C, TLC (6:4 *n*-hexane–EtOAc): R_f 0.20, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.98, 0.99 (2s, 6H, $2CH_3$), 1.97, 1.99, 2.01, 2.12 (4s, 12H, 4OAc), 2.39 (s, 2H, CH_2-5), 2.47 (s, 2H, CH_2-3), 4.03–4.10 (m, 3H, H-6″, H-5′, H-6′), 5.16 (dd, 1H, H-3′), 5.46 (d, 1H, H-4′), 5.56 (t, 1H, H-2′), 5.72 (d, 1H, $J_{1',2'}$ = 10.5 Hz, H-1′), 7.11 (dd, 2H, ArH), 7.42 (d, 2H, ArH), 16.02 (s, 1H, NH). FABMS: *m/z* 654 [M^+−1], ESIMS: Calcd for $C_{29}H_{35}ClNO_{10}S_2$ (M^++H): *m/z* 656.1391, Found 656.1380.

4.4.5. (2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl) [2-(4-bromophenylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]-carbodithioate (7b)

Yield (38%, yellow crystals), mp 209–211 °C, TLC (6:4 *n*-hexane–EtOAc): R_f 0.22, ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.99, 1.0 (2s, 6H, $2CH_3$), 1.97, 1.99, 2.00, 2.13 (4s, 12H, 4OAc), 2.39 (s, 2H, CH_2-5), 2.47 (s, 2H, CH_2-3), 4.03–4.09 (m, 3H, H-6″, H-5′, H-6′), 5.16 (dd, 1H, H-3′), 5.45 (d, 1H, H-4′), 5.54 (t, 1H, H-2′), 5.73 (d, 1H, $J_{1',2'}$ = 10.8 Hz, H-1′), 7.10 (dd, 2H, ArH), 7.42 (d, 2H, ArH), 16.00 (s, 1H, NH). FABMS: *m/z* 700 [M^++1], ESIMS: Calcd for $C_{29}H_{35}BrNO_{10}S_2$ (M^++H) *m/z* 700.0886, Found 700.0960.

4.4.6. (2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-galactopyranosyl) [2-(2,4-dichlorophenylamino)-4,4-dimethyl-6-oxocyclohex-1-ene]-carbodithioate (7c)

Yield (28%, yellowish crystals), mp 207–209 °C, TLC (6:4 *n*-hexane–EtOAc): R_f 0.61, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.52 (s, 6H, $2CH_3$), 1.97, 1.99, 2.01, 2.12 (4s, 12H, 4OAc), 2.33 (s, 2H, CH_2-5), 2.40 (s, 2H, CH_2-3), 4.05–4.11 (m, 3H, H-6″, H-5′, H-6′), 5.16 (dd, 1H, H-3′), 5.45 (d, 1H, H-4′), 5.41 (t, 1H, $J_{2',1'}$ = 10.5 Hz, $J_{2',3'}$ = 9.9 Hz, H-2′), 5.74 (d, 1H, $J_{1',2'}$ = 10.5 Hz, H-1′),7.14 (d, 1H, ArH), 7.36 (dd, 1H, ArH), 7.56 (m, 1H, ArH), 15.77 (s, 1H, NH). FABMS: *m/z* 688 [M^+−1]. ESIMS: Calcd for $C_{29}H_{34}Cl_2NO_{10}S_2$ (M^++H) *m/z* 690.1001, Found 690.0940.

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Supplementary data

Crystallographic data, excluding structure factors, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication with CCDC No. 795086 for **5a** and 795087 for **7a**. Copies of the data can be obtained free of charge on application with the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2010.11.005.

References

1. (a) Ur-Rehman, Z.; Muhammada, N.; Shuja, S.; Ali, S.; Butler, I. S.; Meetsma, A.; Khan, M. *Polyhedron* **2009**, *28*, 3439–3448; (b) Nieuwenhuizen, P. J.; Reedijk, J.; van Duin, M.; McGill, W. J. *Rubber Chem. Technol.* **1997**, *70*, 368–429; (c) Fan, D.; Afzaal, M.; Malik, M. A.; Nguyen, C. Q.; O'Brien, P.; Thomas, P. J. *Coord. Chem. Rev.* **2007**, *251*, 1878–1888; (d) Knight, E. R.; Cowley, A. R.; Hogarth, G.; Wilton-Ely, J. D. *Dalton Trans.* **2009**, 607–609.
2. Waseem, A.; Yaqoob, M.; Nabi, A. *Anal. Sci.* **2009**, 395–400.

3. Cvek, B.; Dvorak, Z. *Curr. Pharm. Des.* **2007**, *13*, 3155–3167.
4. (a) Shahzadi, S.; Ali, S.; Bhatti, M. H.; Fettouhi, M.; Athar, M. *J. Organomet. Chem.* **2006**, *691*, 1797–1802; (b) Yang, P.; Guo, M. *Coord. Chem. Rev.* **1999**, *189*, 185–186; (c) Chadha, R. K.; Kumar, R.; Tuck, D. G. *Can. J. Chem.* **1987**, *65*, 1336–1342; (d) Al-Allaf, T. A.; Mustafa, I. A.; Al-Mukhtar, S. E. *Trans. Met. Chem.* **1993**, *18*, 1–5; (e) David, P. C.; Chrislyn, M. C. *Pestic. Sci.* **2006**, *23*, 93–102; (f) Rogachev, I.; Kampel, V.; Gusis, V.; Cohen, N.; Gressel, J.; Warshawasky, A. *Pestic. Biochem. Physiol.* **1998**, *60*, 133–145; (g) Ur-Rehman, A.; Hussain, M.; Ur-Rehman, Z.; Rauf, A.; Nasim, F. H.; Tahir, A. A.; Ali, S. *J. Organomet. Chem.* **2010**, *695*, 1526–1532.
5. (a) Boers, D.; van Amelsvoort, L.; Colosio, C.; Corsini, E.; Fustinoni, S.; Campo, L.; Bosetti, C.; La Vecchia, C.; Vergieva, T.; Tarkowski, M.; Liesivuori, J.; Steerenberg, P.; van Loveren, H. *Hum. Exp. Toxicol.* **2008**, *27*, 721–727; (b) Zel, O. G.; Salman, A. *Bioorg. Med. Chem.* **2006**, *14*, 7804–7815; (c) Soledade, M.; Pedras, C.; Jha, M. *Bioorg. Med. Chem.* **2006**, *14*, 4958–4979.
6. (a) Yin, H. D.; Xue, S. C. *Appl. Organomet. Chem.* **2006**, *20*, 283–289; (b) Tabassum, S.; Pettinari, C. *J. Organomet. Chem.* **2006**, *691*, 1761–1766; (c) Pellerito, C.; D'Agati, P.; Fiore, T.; Mansueto, C.; Mansueto, V.; Stocco, G.; Nagy, L.; Pellerito, L. *J. Inorg. Biochem.* **2005**, *99*, 1294–1305; (d) Milacic, V.; Dou, Q. P. *Coord. Chem. Rev.* **2009**, *253*, 1649–1660. pubmed/20047011; (e) Zhang, X.; Frezza, M.; Milacic, V.; Ronconi, L.; Fan, Y.; Bi, C.; Fregona, D.; Dou, Q. P. *J. Cell. Biochem.* **2010**, *109*, 162–172.
7. Bach, S. P.; Chinery, R.; O'Dwyer, S. T.; Potten, C. S.; Coffey, R. J.; Watson, A. J. *Gastroenterology* **2000**, *118*, 81–89.
8. Daniel, K. G.; Chen, D.; Orlu, S.; Cui, Q. C.; Miller, F. R.; Dou, Q. P. *Breast Cancer Res.* **2005**, *7*, 897–908.
9. Trevisan, A.; Marzano, C.; Cristofori, P.; Borella Venturini, M.; Giovagnini, L.; Fregona, D. *Arch. Toxicol.* **2002**, *76*, 262–268.
10. Huang, W.; Ding, Y.; Miao, Y.; Liu, M.-Z.; Li, Y.; Yang, G.-F. *Eur. J. Med. Chem.* **2009**, *44*, 3687–3696.
11. Si, X.; McManus, B. M.; Zhang, J.; Yuan, J.; Cheung, C.; Esfandiarei, M.; Suarez, A.; Morgan, A.; Luo, H. *J. Virol.* **2005**, *79*, 8014–8023.
12. Sofuoglu, M.; Kosten, T. R. *CNS Drugs* **2005**, *19*, 13–25.
13. Fang, I. M.; Yang, C. H.; Lin, C. P.; Yang, C. M.; Chen, M. S. *Ocul. Pharmacol. Ther.* **2005**, *21*, 95–106.
14. Pyatt, D. W.; Gruntmeir, J.; Stillman, W. S.; Irons, R. D. *Toxicology* **1998**, *128*, 83–90.
15. (a) Noboru, U.; Kunio, O. *J. Antimicrob. Chemother.* **2003**, *52*, 8–10; (b) Uchide, N.; Ohyama, K.; Bessho, T.; Yuan, B.; Yamakawa, T. *Antiviral Res.* **2002**, *56*, 207–217.
16. Amarnath, V.; Amarnath, K.; Valentine, W. M. *Curr. Top. Toxicol.* **2007**, *4*, 39–44.
17. Gogoi, P. K.; Phukan, D. P.; Das, D. K. *Asian J. Chem.* **1999**, *11*, 1291–1295.
18. Chauhan, H. P. S.; Shaik, N. M. *J. Inorg. Biochem.* **2005**, *99*, 538–545.
19. Eng, G.; Song, X.; Duong, Q.; Strickman, D.; Glass, J.; May, L. *Appl. Organomet. Chem.* **2003**, *17*, 218–225.
20. Viquez, O. M.; Lai, B.; Ahn, J. H.; Does, M. D.; Valentine, H. L.; Valentine, W. M. *Toxicol. Appl. Pharmacol.* **2009**, *239*, 71–79.
21. (a) Zhu, X.; Schmidt, R. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 1900–1934; (b) Pachamuthu, K.; Schmidt, R. R. *Chem. Rev.* **2006**, *106*, 160–187; (c) Schmidt, R. R.; Castro-Palomino, J. C.; Retz, O. *Pure Appl. Chem.* **1999**, *71*, 729–744; (d) Schmidt, R. R. In *Modern Methods in Carbohydrate Synthesis*; Khan, S. H., O'Neill, R. A., Eds.; Harwood: Amsterdam, 1996; pp 20–54; (e) Abdel-Rahman, A. A.-H.; El Ashry, E. S. H.; Schmidt, R. R. *Carbohydr. Res.* **2002**, *337*, 195–206.
22. (a) Pornsuriyasak, P.; Gangadharmath, U. B.; Rath, N. P.; Demchenko, A. *Org. Lett.* **2004**, *6*, 4515–4518. doi/abs/10.1021/ol048043y; (b) Demchenko, A. V.; Kamat, M. N.; De Meo, C. *Synlett* **2003**, 1287–1290; (c) Demchenko, A. V.; Pornsuriyasak, P.; De Meo, C.; Malysheva, N. N. *Angew. Chem., Int. Ed.* **2004**, *43*, 3069–3072; (d) Gangadharmath, U. B.; Demchenko, A. V. *Synlett* **2004**, 2191–2193; (e) Demchenko, A. V.; Malysheva, N. N.; De Meo, C. *Org. Lett.* **2003**, *5*, 455–458.
23. (a) El Ashry, E. S. H.; Rashed, N.; Ibrahim, E. I. *Tetrahedron* **2008**, *64*, 10631–10648; (b) El Ashry, E. S. H.; Rashed, N.; Ibrahim, E. I. *Curr. Org. Synth.* **2005**, *2*, 175–213; (c) El Ashry, E. S. H.; Aly, M. R. E. *Pure Appl. Chem.* **2007**, *79*, 2229–2242.
24. (a) El Ashry, E. S. H.; Awad, L. F.; Atta, I. A. *Tetrahedron* **2006**, *62*, 2943–2998; (b) Rezki, N.; Rashed, N.; Awad, L. F.; Ramadan, E.; Abdel-Maggeed, S. M.; El Ashry, E. S. H. *Phosphorus, Sulfur Silicon Relat. Elem.* **2009**, *184*, 1759–1767; (c) Awad, O. M. E.; Attia, W. E.; El Ashry, E. S. H. *Carbohydr. Res.* **2004**, *339*, 469–476; (d) El Ashry, E. S. H.; Awad, L. F.; Abdel-Hamid, H.; Atta, I. A. *J. Carbohydr. Chem.* **2005**, *24*, 745–753.
25. (a) El Ashry, E. S. H.; Rashed, N.; Shobier, A. H. *Pharmazie* **2000**, *55*, 251–262; (b) El Ashry, E. S. H.; Rashed, N.; Shobier, A. H. *Pharmazie* **2000**, *55*, 331–348; (c) El Ashry, E. S. H.; Rashed, N.; Shobier, A. H. *Pharmazie* **2000**, *55*, 403–415; (d) El Ashry, E. S. H.; El Nemr, A. *Synthesis of Naturally Occurring Nitrogen Heterocycles from Carbohydrates*; Blackwell: Oxford, 2005; (e) Aly, A. A. *Phosphorus, Sulfur, Silicon Relat. Elem.* **2003**, *178*, 2415–2429.
26. (a) Fuegedi, P.; Garegg, P. J.; Oscarson, S.; Rosen, G.; Silwanis, B. A. *Carbohydr. Res.* **1991**, *211*, 157–162; (b) Elgemeie, G. H.; Zaghary, W. A.; Nasr, T. M.; Amin, K. M. *J. Carbohydr. Chem.* **2008**, *27*, 345–356; (c) Bogusiak, J.; Szeja, W. *Tetrahedron Lett.* **2001**, *42*, 2221–2223; (d) Behalo, M. S.; Aly, A. A. *J. Chem. Res., Synop.* **2009**, *12*, 753–755; (e) Bogusiak, J.; Szeja, W. *Carbohydr. Res.* **2001**, *330*, 141–144; (f) Wandzik, I.; Szeja, W. *Pol. J. Chem.* **1999**, *73*, 1163–1170; (g) Bogusiak, J.; Szeja, W. *Carbohydr. Res.* **1996**, *295*, 235–243; (h) Tejima, S.; Ishiguro, S. *Chem. Pharm. Bull.* **1967**, *15*, 255–263; (i) Byung-Hoon, L.; Barbara, B.; Peter, S.; Norbert, F.; Manfred, W. *J. Med. Chem.* **1994**, *37*, 3154–3162.
27. Pieper, G. M.; Siebeneich, W.; Olds, C. L.; Lai, C.-S. *Eur. J. Pharmacol.* **2003**, *472*, 127–134.
28. El Ashry, E. S. H.; Amer, M. R.; Shah, M. R.; Ng, S. W. *Acta Crystallogr., Sect. E* **2009**, *65*, o1106.
29. El Ashry, E. S. H.; Amer, M. R.; Shah, M. R.; Ng, S. W. *Acta Crystallogr., Sect. E* **2009**, *65*, o597.
30. El Ashry, E. S. H.; Amer, M. R.; Shah, M. R.; Ng, S. W. *Acta Crystallogr., Sect. E* **2009**, *65*, o599.
31. El Ashry, E. S. H.; Amer, M. R.; Shah, M. R.; Ng, S. W. *Acta Crystallogr., Sect. E* **2009**, *65*, o600.
32. Yamasaki, T.; Nishida, K.; Okawara, T.; Furukawa, M. *Heterocycles* **1998**, *47*, 315–327.
33. Tominaga, Y.; Okuda, H.; Kohra, S.; Mazume, H. *J. Heterocycl. Chem.* **1991**, *28*, 1245–1255.
34. Barbour, L. J. *J. Supramol. Chem.* **2001**, *1*, 189–191.
35. *Bruker, APEX2 software (v2008.6-1) and* SAINT *(Version 7.60A)*; Bruker AXS Inc.: Madison, WI, USA, 2008.
36. Flack, H. D. *Acta Crystallogr., Sect. A* **1983**, *39*, 876–881.
37. Sheldrick, G. M. SADABS. *Program for Empirical Absorption Correction of Area Detector Data*; University of Göttingen: Germany, 1996.
38. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **2008**, *64*, 112–122.