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Synthesis and Characterization of 2-Tetra-O-acetyl-β-D-glucopyranosylimino-5-(Arylidinehydrazino)-1,3,4-thiadiazolidines

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ABSTRACT

A novel five-membered N-glucosylated 1, 3, 4-thiadiazolidines (7a-f) have been synthesized by the interaction of substituted N-arylidine thiocarbohydrazides (4) with N-tetra-O-acetyl-β-D-glucopyranosyl isocyanodichloride (5). The later requisite was synthesized by excessive chlorination of N-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate. The structure of all the newly synthesized 2-tetra-O-acetyl-β-D-glucopyranosylimino-5-(arylidinehydrazino)-1,3,4-thiadiazolidines (7a-h) were established on the basis of usual chemical characteristics, IR, ^{1}H NMR, ^{13}C NMR and mass spectral analyses.

Keywords: *Thiadiazolidine, thiocarbohydrazide, glucopyranosyl isocyanodichloride*.

INTRODUCTION

Thiadiazole rings showing wide interest owing to their herbicidal, antimicrobial, anticonvulsant, vasodilator, and antitubercular activity 1-5. It is known that saturated derivatives of these compounds, 1,3,4-thiadiazolidines display fungicidal activity.6 Nizovtseva and co-workers have discovered a novel method of synthesizing 2-imino-1,3,4-thiadiazolidine perchlorates by treating 1,2-di(thiocarbamoyl)hydrazine with benzoylacetylene in glacial acetic acid in the presence of HClO [1-6].

One of the most common approaches for synthesis of 1,3,4-thiadiazolidines is the cyclomethylation reaction of hydrazines with hydrogen sulfide and formaldehyde.[7-12] However, the main drawback of this method is the formation of 1,3,4-thiadiazolidines in low yield or mixed with N-amino-1,3,5-dithiazinanes. Besides, 1,3,4- and 1,2,5-thiadiazole and thiadiazolidine rings show wide spectrum biological activity and hence, the investigation of novel derivatives of these compounds is of significant interest [13-19]

We have previous reported the synthesis of N-glucosylated-1,3,4-thiadiazolidines by the interaction of 1H/aryl-4-tetra-O-acetyl-β-D-glucopyranosyl thiosemicarbazide and aryl isothiocyanates [20] Looking at the importance of glucosylated and heterocyclic compounds, we are reporting the synthesis of N-glucosylated 1,3,4-thiadiazolidines through the C-S bond formation by the interaction of N-arylidine thiocarbohydrazides with N-tetra-O-acetyl-β-D-glucopyranosylisocyanodichlorid

MATERIALS AND METHODS

All melting points are uncorrected and were measured using an electro-thermal apparatus. ^{1}H NMR spectra were recorded on Brucker Avance II 400 NMR spectrometer using DMSO-d_6 and $CDCl_3$ as solvent and tetramethylsilane as internal standard and chemical shifts being reported in parts per million (δ) relative to TMS. Mass spectra were obtained using Waters Micromass Q-Tof Micro instrument at 70eV. Optical rotations were measured by Equip-Tronics Digital Polarimeter EQ-801. Analytical thin-layer chromatography (TLC) was performed on Silica Gel $60F_{254}$ (Merck, Germany). The spots were visualized by exposure to UV light and I_2vapours.

Interaction of N-tetra-O-acetyl-β-D-glucopyranosyl isocyanodichloride and N-arylidine thiocarbohydrazide: Synthesis of 2-tetra-O-acetyl-β-D-glucopyranosylimino-5-(arylidinehydrazino)-1,3,4-thiadiazolidine (7a-h)

2-Tetra-O-acetyl-β-D-glucopyranosylimino-5-(arylidinehydrazino)-1,3,4-thiadiazolidine (7a-h) was prepared by refluxing arylidine thiocarbohydrazide (3a-h) (1 mmol) with N-tetra-O-acetyl-β-D-glucopyranosyl isocyanodichloride (1mmol) in chloroform (10ml) for 3h. A brisk reaction with evolution of hydrogen chloride gas was observed. Progress of the reaction was monitored with TLC. After completion of the reaction, the reaction mixture was cooled. The solvent was evaporated under reduced pressure to give 5a-h as crude mass. It was purified by flash chromatography on silica gel column using chloroform as eluent to afford yellow solid**.**

2-Tetra-O-acetyl-β-D-glucopyranosylimino-5-(3-hydroxybenzylidinehydrazino)-1, 3, 4-thiadiazolidine (7a)

Yellow solid, m.p. 182 ^{o}C. Anal.Calcd.for $C_{23}H_{27}N_5O_{10}S$: N, 12.38; S, 5.67. Found: N, 12.21; S, 5.47. $[\alpha]_D^{25}$ = +64 (c=0.2, chloroform).^{1}H NMR δ ppm (DMSO-d_6): 10.05(s, 1H, NH), 9.95(s, 1H, NH), 8.01(s, 1H, =CH), 6.78-7.67(m, 4H, Ar-H), 7.05(s, 1H, Ar-OH), 3.95-5.34(m, 7H, H_{1-7}), 1.97-2.03 (m, 12H, $COCH_3$). MS (m/z), 566.3 $(M+1)^+$.

2-Tetra-O-acetyl-β-D-glucopyranosylimino-5-(4-hydroxybenzylidinehydrazino)-1, 3, 4-thiadiazolidine (7b)

Yellow solid, m.p. 167^{o}C. Anal.Calcd.for $C_{23}H_{27}N_5O_{10}S$: N, 12.38; S, 5.67. Found: N, 12.29; S, 5.52. $[\alpha]_D^{25}$ = +56(c=0.2, chloroform).^{1}H NMR δ ppm (DMSO-d_6): 10.16(s, 1H, NH), 9.84(s, 1H, NH), 8.06(s, 1H, =CH), 6.82-7.44(m, 4H, Ar-H), 6.96(s, 1H, Ar-OH), 3.95-5.34(m, 7H, H_{1-7}), 1.98-2.02 (m, 12H, $COCH_3$). MS (m/z), 566.3 $(M+1)^+$.

2-Tetra-O-acetyl-β-D-glucopyranosylimino-5-(benzylidinehydrazino)-1,3,4-thiadiazolidine(7c)

Off white solid, m.p. 132 ^{o}C. Anal.Calcd.for $C_{23}H_{27}N_5O_9S$: N, 12.74; S, 5.83. Found: N, 12.48; S, 5.52. $[\alpha]_D^{25}$ = +26(c=0.2, chloroform).^{1}H NMR δ ppm ($CDCl_3$): 7.95(s, 1H, =CH), 6.48-7.61(m, 5H, Ar-H), 3.89-5.32(m, 7H, H_{1-7}), 1.94-2.00 (m, 12H, $COCH_3$). MS (m/z), 549.15 $(M)^+$.

2-Tetra-O-acetyl-β-D-glucopyranosylimino-5-(2-methylbenzylidinehydrazino)-1, 3, 4-thiadiazolidine (7d)

Yellow solid, m.p. 146^{o}C. Anal.Calcd.for $C_{24}H_{29}N5O_9S$: C, 51.15; H, 5.19; N, 12.43; S, 5.69. Found: C, 51.39; H, 4.97; N, 12.14; S, 5.55.$[\alpha]_D^{25}$ = +42 (c=0.2, chloroform).^{1}H NMR δ ppm (DMSO-d_6): 9.93 (s, 1H, NH), 9.87 (s, 1H, NH), 7.95 (s, 1H, =CH), 6.58-7.60 (m, 4H, Ar-H), 3.95-5.34(m, 7H, H_{1-7}), 2.21 (s, 3H, CH_3)1.97-2.03 (m, 12H, $COCH_3$). MS (m/z), 563.6 $(M+1)^+$.

2-Tetra-O-acetyl-β-D-glucopyranosylimino-5-(4-chlorobenzylidinehydrazino)-1, 3, 4-thiadiazolidine (7e)

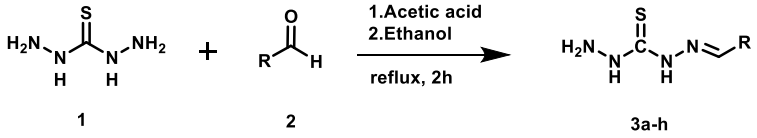
Brown solid, m.p. 157^{o}C. Anal.Calcd. for $C_{23}H_{26}ClN_5O_9S$: N, 11.99; S, 5.49. Found: N, 11.77; S, 5.59. $[\alpha]_D^{25}$ = +18(c=0.2, chloroform). ^{1}H NMR δ ppm (DMSO): 10.12 (s, 1H, NH), 9.98 (s, 1H, NH), 8.10 (s, 1H, =CH), 6.87-7.74 (m, 4H, Ar-H), 3.90-5.36 (m, 7H, H_{1-7}), 1.97-2.03 (m, 12H, $COCH_3$).

2-Tetra-O-acetyl-β-D-glucopyranosylimino-5-(4-methylbenzylidinehydrazino)-1,3,4-thiadiazolidine (7f)

Yellow solid, m.p. 137°C. Anal.Calcd.for $C_{24}H_{29}N5O_9S$: N, 12.43; S, 5.69. Found: N, 12.58; S, 5.73.$[\alpha]_D^{25}$ = +33(c=0.2, chloroform).^{1}H NMR δ ppm (DMSO-d_6): 9.98 (s, 1H, NH), 9.84 (s, 1H, NH), 7.85 (s, 1H, =CH), 6.50-7.71 (m, 4H, Ar-H), 3.92-5.34(m, 7H, H_{1-7}), 2.19 (s, 1H, CH_3)1.92-2.01 (m, 12H, $COCH_3$). MS (m/z), 563.6 $(M+1)^+$.

RESULTS AND DISCUSSION

We synthesized various substituted *N*-arylidine thiocarbohydrazides by the interaction of thicarbohydrazide and aryl aldehydes using traditional method. The synthesis of 2, 3, 4, 6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate has been carried in line of the previous method. The synthesis of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate and its dichloro derivative i.e. *N*-tetra-*O*-acetyl-β-D-glucopyranosyl isocyanodichloride was carried out by an extension of previously known methods in scheme 1, which has been successfully used for the synthesis of 2-tetra-*O*-acetyl-β-D-glucopyranosylimino-5-(arylidinehydrazino)-1,3,4-thiadiazolidines.



Scheme 1. Synthesis of N-arylidine thiocarbohydrazides

The yield of 2-tetra-*O*-acetyl-β-D-glucopyranosylimino-5-(arylidinehydrazino)-1,3,4-thiadiazolidines was 48% in chloroform. The above results showed that chloroform is comparatively a better solvent for these reactions. The synthesized compounds did not respond to hot alkaline lead plumbite solution indicating the absence of >C= S grouping.

The ^{1}H NMR spectra of thiadiazolidine showed all glucosyl aliphatic protons resonated as multiplets within δ 3.9-5.4 ppm region. The structure of compound were further confirmed by electron spray (ES) - mass spectra.

CONCLUSION

In the present study, novel 2-tetra-*O*-acetyl-β-D-glucopyranosylimino-5-(arylidinehydrazino)-1,3,4-thiadiazolidines derivatives were designed and synthesized in good yields. All the synthesized compounds were characterized by using elemental analysis, ^{1}H NMR. The thiadiazole rings was prepared by interaction of *N*-arylidine thiocarbohydrazide with newly synthesized *N*-tetra-*O*-acetyl-β-D-glucopyranosyl isocyanodichloride. The present method is found to be expedient and elegant. Further studies towards broadening the scope to include related heterocycles and applications are underway.

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