Research Article

Reaction of *N*-alkylisatins with 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazide

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Some *N*-alkylisatins were converted to corresponding thiosemicarbazones by reaction with 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazide using microwave-assisted heating method. The structure of products have been confirmed by IR, NMR, and mass spectra.

1. Introduction

Isatin- β -thiosemicarbazone and *N*-methylisatin- β -thiosemicarbazone (methisazone, marboran) are extensively studied thiosemicarbazones that demonstrate an inhibitory effect against the replication of poxviruses [1]. Methisazone has also been used in the clinical treatment of smallpox [2]. This drug plays an important role as a smallpox chemoprophylactic agent. The spectrum of antiviral activity of this drug has been extended by additional *in vitro* studies to include other groups of viruses, such as adenovirus, herpesvirus, picornavirus, reovirus, arbovirus, myxo- and paramyxovirus, and retrovirus [3]. *N*-alkylation of isatin reduces the lability of the isatin nucleus towards bases, while maintaining its typical reactivity. Thus, *N*-substituted isatins have been frequently used as intermediates and synthetic precursors for the preparation of a wide variety of heterocyclic compounds [4, 5]. In addition, properly functionalized *N*-alkyl isatins present different biological activities [4], and in recent years compounds showing potent cytotoxicity *in vitro* [6], antiviral activity [7], and potent and selective caspase inhibition [8] have been reported, among others. Thiosemicarbazides exhibit various biological activities and are extensively applied in medicine, particularly in the treatment of tuberculosis [9, 10]. Numerous compounds with a thiosemicarbazone moiety also exhibit biological activity [11, 12]. Several peracetylated glucopyranosyl thiosemicarbazones were synthesized [13, 14].

Some tetra-*O*-acetyl- β -D-glucopyranosyl thiosemicarbazones containing isatin ring were synthesized in good yields by the reactions of substituted isatins with tetra-*O*-acetyl- β -D-glucopyranosyl thiosemicarbazide in our lab [15]. Continuing our works on glucopyranosyl thiosemicarbazones [16, 17], we report herein the synthesis of some *N*-alkylisatin 4-(tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazones.

2. Experimental

Melting points were measured on STUART SMP3 (BIBBY STERILIN-UK). The FTIS spectra were recorded on Impact 410 FT-IR Spectrometer (Nicolet, USA) in form of KBr. The ^1H NMR and ^{13}C NMR spectra were recorded on an Avance Spectrometer AV500 (Bruker, Germany) at 500.13 MHz and 125.77 MHz, respectively, using DMSO- d_6 as solvent and TMS as an internal reference. MS spectra were recorded on mass spectrometer AutoSpec Premier (Water, USA) using EI method. All other solvents and reagents were used as received or purified by standard protocols. 4-(Tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazide using our method [9].

General Procedure for Synthesis of *N*-alkylisatins 2a-h. To a solution of isatin **1** (0.03 mol) in DMF (7 mL) corresponding alkyl halide (0.03 mol) and K_2CO_3 (0.042 mol, 6.20 g) were added. Reaction mixture was irradiated for appropriate time and then cooled to room temperature and

mixed thoroughly with ice water. The product recrystallized from the suitable solvent. Reaction time, yield, melting point, and recrystallization solvents for these *N*-alkylisatins are following: *N*-methylisatin (**2a**), 2 min, 84%, 130–131°C (96% ethanol), [18, 19]: 130–133°C; *N*-ethylisatin (**2b**), 3 min, 71%, 86–87°C (96% ethanol), [18, 19]: 88–89°C; *N*-*n*-propylisatin (**2c**), 3 min, 75%, 196–197°C (96% ethanol), [18]: 198°C; *N*-*n*-butylisatin (**2d**), 4 min, 63%, 34–36°C (diethyl ether), [20]: 36°C; *N*-allylisatin (**2f**), 2 min, 72%, 90–91°C (96% ethanol), [18]: 88–89°C; *N*-benzylisatin (**2g**), 3 min, 88%, 129–130°C (96% ethanol), [18]: 131–132°C. Compounds **2e** and **2h** were prepared similarly and used for synthesis of corresponding thiosemicarbazones: *N*-isobutylisatin (**2e**), 5 min, 74%, 88–89°C (96% ethanol); *N*-phenethylisatin (**2h**), 4 min, 90%, 110–112°C (96% ethanol).

General Procedure for Synthesis of *N*-alkylisatin 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazones **3a–h.** To a solution of 4-(tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazide (1 mmol) in 99% ethanol (10 mL) *N*-alkylisatin **2** (1 mmol) was added. Glacial acetic acid (0.5 mL) as catalyst was added dropwise with stirring. The obtained mixture was then irradiated in microwave oven for 8–20 min; cooled to room temperature and the separated precipitate was filtered and recrystallized from 96% ethanol to yield the title compounds **3**.

***N*-Methylisatin 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazone (**3a**).** Yellow solid, mp 208–209°C (from 96% ethanol), yield 82%; IR (KBr) ν/cm^{-1} : 3320, 1755, 1610, 1228, 1040, 1370; ^1H NMR (DMSO- d_6) δ (ppm): 12.71 (s, 1H, NH-2), 9.61 (d, 1H, J = 9.0 Hz, NH-4), 7.75 (d, 1H, J = 8.0 Hz, H-7'), 7.48 (t, 1H, J = 7.75 Hz, H-5'), 7.19 (t, 1H, J = 7.5 Hz, H-6'), 7.16 (d, 1H, J = 7.5 Hz, H-4'), 6.01 (t, 1H, J = 9.0 Hz, H-1), 5.46 (t, 1H, J = 9.5 Hz, H-3), 5.34 (t, 1H, J = 9.0 Hz, H-2), 4.99 (t, 1H, J = 9.75 Hz, H-4), 4.24 (t, 1H, J = 12.5, 5.0 Hz, H-6a), 4.18 (m, 1H, H-5), 4.00 (dd, 1H, J = 11.0 Hz, H-6b), 3.21 (s, 3H, CH₃, *N*-methyl), 2.01–1.93 (s, 12H, 4 $\times$ CH₃CO); ^{13}C NMR (DMSO- d_6) δ (ppm): 179.0 (C=S), 169.3–169.9 (COCH₃), 160.7 (C=O isatin), 144.0 (C-3'), 132.5 (C-4'), 131.6 (C-4'a), 122.9 (C-5'), 121.0 (C-6'), 119.0 (C-7'), 109.9 (C-7'a), 81.9 (C-1), 70.9 (C-2), 72.7 (C-3), 67.7 (C-4), 72.4 (C-5), 61.7 (C-6), 25.7 (CH₃, *N*-methyl), 20.5–20.3 (4 $\times$ CH₃CO); EI-HRMS: C₂₄H₂₈N₄O₁₀S, calc. for $[M]^{++}$ = 564.1526 Da, found: m/z 564.1533.

***N*-Ethylisatin 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazone (**3b**).** Yellow solid, mp 152–153°C (from 96% ethanol), yield 81%; IR (KBr) ν/cm^{-1} : 3350, 1751, 1614, 1367, 1232, 1039; ^1H NMR (DMSO- d_6) δ (ppm): 12.72 (s, 1H, NH-2), 9.61 (d, 1H, J = 9.5 Hz, NH-4), 7.76 (d, 1H, J = 7.5 Hz, H-7'), 7.72 (d, 1H, J = 8.0 Hz, H-4'), 7.46 (t, 1H, J = 7.75 Hz, H-6'), 7.19 (t, 1H, J = 7.75 Hz, H-5'), 6.01 (t, 1H, J = 9.0 Hz, H-1), 5.46 (t, 1H, J = 9.5 Hz, H-3), 5.34 (t, 1H, J = 9.25 Hz, H-2), 4.98 (t, 1H, J = 9.75 Hz, H-4), 4.24 (dd, 1H, J = 12.5, 4.5 Hz, H-6a), 4.17 (ddd, 1H, J = 9.5, 4.5, 2.0 Hz, H-5), 4.00 (dd, 1H, J = 12.0, 1.5 Hz, H-6b), 3.77 (t, 2H, CH₂, *N*-ethyl); 2.01–1.93 (s, 12H, 4 $\times$ CH₃CO), 1.20 (t, 3H, CH₃, *N*-ethyl); ^{13}C NMR (DMSO- d_6) δ (ppm): 179.0 (C=S), 169.9–169.3 (4 $\times$ COCH₃), 160.3 (C=O isatin),

142.9 (C-3'), 132.6 (C-4'), 131.7 (C-4'a), 122.8 (C-5'), 121.3 (C-6'), 119.2 (C-7'), 110.0 (C-7'a), 81.9 (C-1), 70.9 (C-2), 72.7 (C-3), 67.7 (C-4), 72.4 (C-5), 61.7 (C-6), 34.1 (CH₂, *N*-ethyl), 20.5–18.5 (4 $\times$ CH₃CO), 12.5 (CH₃, *N*-ethyl); EI-HRMS: C₂₅H₃₀N₄O₁₀S, calc. for $[M]^{++}$ = 578.1682 Da, found: m/z 578.1692.

***N*-*n*-Propylisatin 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazone (**3c**).** Yellow solid, mp 187–189°C (from 96% ethanol), yield 93%; IR (KBr) ν/cm^{-1} : 3294, 1743, 1615, 1367, 1235, 1035; ^1H NMR (DMSO- d_6) δ (ppm): 12.73 (s, 1H, NH-2), 9.62 (d, 1H, J = 9.0 Hz, NH-4), 7.77 (d, 1H, J = 7.5 Hz, H-7'), 7.21 (t, 1H, J = 8.0 Hz, H-4'), 7.46 (t, 1H, J = 7.75 Hz, H-6'), 7.19 (t, 1H, J = 7.75 Hz, H-5'), 6.01 (t, 1H, J = 9.0 Hz, H-1), 5.46 (t, 1H, J = 9.5 Hz, H-3), 5.34 (t, 1H, J = 9.0 Hz, H-2), 4.98 (t, 1H, J = 9.75 Hz, H-4), 4.24 (dd, 1H, J = 12.25, 4.75 Hz, H-6a), 4.17 (ddd, 1H, J = 9.5, 4.5, 2.0 Hz, H-5), 4.00 (d, 1H, J = 12.0, H-6b), 3.71 (t, 2H, J = 7.25 Hz, NCH₂, *N*-propyl); 2.01–1.93 (4 $\times$ CH₃CO), 1.65 (sextet, 2H, J = 7.25 Hz, CH₂, *N*-propyl), 0.89 (t, 3H, J = 7.25 Hz, CH₃, *N*-propyl); EI-HRMS: C₂₆H₃₂N₄O₁₀S, calc. for $[M]^{++}$ = 592.1839 Da, found: m/z 592.1852.

***N*-*n*-Butylisatin 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazone (**3d**).** Yellow solid, mp 186–189°C (from 96% ethanol), yield 91%; IR (KBr) ν/cm^{-1} : 3346, 1749, 1612, 1376, 1227, 1043; ^1H NMR (DMSO- d_6) δ (ppm): 12.73 (s, 1H, NH-2), 9.61 (d, 1H, J = 9.0 Hz, NH-4), 7.77 (d, 1H, J = 7.5 Hz, H-7'), 7.46 (t, 1H, J = 7.5 Hz, H-6'), 7.20 (d, 1H, J = 7.5 Hz, H-4'), 7.19 (t, 1H, J = 7.75 Hz, H-5'), 6.01 (t, 1H, J = 9.25 Hz, H-1), 5.46 (t, 1H, J = 9.5 Hz, H-3), 5.34 (t, 1H, J = 9.25 Hz, H-2), 4.98 (t, 1H, J = 9.75 Hz, H-4), 4.24 (dd, 1H, J = 12.5, 4.5 Hz, H-6a), 4.17 (dt, 1H, J = 7.5, 2.0 Hz, H-5), 4.00 (d, 1H, J = 12.0 Hz, H-6b), 3.74 (t, 2H, J = 6.5 Hz, CH₂, *N*-butyl), 2.07 (m, 1H, CH, *N*-butyl); 2.01–1.93 (s, 12H, 4 $\times$ CH₃CO), 1.61 (m, 2H, CH₂, *N*-butyl), 1.61 (m, 2H, CH₂, *N*-butyl), 0.90 (t, 3H, J = 7.0 Hz, CH₃, *N*-butyl); EI-HRMS: C₂₇H₃₄N₄O₁₀S, calc. for $[M]^{++}$ = 606.1996 Da, found: m/z 606.2008.

***N*-Isobutylisatin 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazone (**3e**).** Yellow solid, mp 190–193°C (from 96% ethanol), yield 86%; IR (KBr) ν/cm^{-1} : 3287, 1747, 1617, 1370, 1230, 1040; ^1H NMR (DMSO- d_6) δ (ppm): 12.73 (s, 1H, NH-2), 9.63 (d, 1H, J = 9.0 Hz, NH-4), 7.77 (d, 1H, J = 7.5 Hz, H-7'), 7.45 (t, 1H, J = 7.75 Hz, H-6'), 7.20 (d, 1H, J = 7.5 Hz, H-4'), 7.19 (t, 1H, J = 7.75 Hz, H-5'), 6.01 (t, 1H, J = 9.0 Hz, H-1), 5.46 (t, 1H, J = 9.25 Hz, H-3), 5.34 (t, 1H, J = 9.25 Hz, H-2), 4.98 (t, 1H, J = 9.75 Hz, H-4), 4.24 (dd, 1H, J = 12.5, 4.5 Hz, H-6a), 4.17 (ddd, 1H, J = 10.0, 4.75, 2.0 Hz, H-5), 3.98 (dd, 1H, J = 11.25, 1.5 Hz, H-6b), 3.55 (d, 2H, CH₂, *N*-isobutyl), 2.07 (m, 1H, CH, *N*-isobutyl); 2.01–1.93 (s, 12H, 4 $\times$ CH₃CO), 0.91 [d, 6H, (CH₃)₂, *N*-isobutyl]; ^{13}C NMR (DMSO- d_6) δ (ppm): 179.0 (C=S), 170.0–169.3 (4 $\times$ COCH₃), 161.0 (C=O isatin), 143.6 (C-3'), 132.4 (C-4'), 131.6 (C-4'a), 122.8 (C-5'), 121.1 (C-6'), 119.0 (C-7'), 110.4 (C-7'a), 81.8 (C-1), 70.9 (C-2), 72.7 (C-3), 67.7 (C-4), 72.4 (C-5), 61.7 (C-6), 46.6 (CH₂, *N*-isobutyl), 26.8 (CH, *N*-isobutyl), 20.5–18.3 (4 $\times$ CH₃CO);

SCHEME 1: Synthetic path for *N*-alkylisatin 4-(tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazones.

19.9 [(CH₃)₂, *N*-isobutyl]; EI-HRMS: C₂₇H₃₄N₄O₁₀S, calc. for [M]⁺⁺ = 606.1996 Da, found: *m/z* 606.2011.

N-Allylisatin 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazone (**3f**). Yellow solid, mp 150–151 °C (from 96% ethanol), yield 88%; IR (KBr) ν /cm⁻¹: 3303, 1747, 1611, 1373, 1229, 1037; ¹H NMR (DMSO-*d*₆) δ (ppm): 12.68 (s, 1H, NH-2), 9.64 (d, 1H, *J* = 9.5 Hz, NH-4), 7.78 (d, 1H, *J* = 2.5 Hz, H-7'), 7.44 (t, 1H, *J* = 7.75 Hz, H-6'), 7.19 (t, 1H, *J* = 7.5 Hz, H-5'), 7.09 (d, 1H, *J* = 8.0 Hz, H-4'), 6.02 (t, 1H, *J* = 9.0; 9.0 Hz, H-1), 5.46 (t, 1H, *J* = 9.5 Hz, H-3), 5.35 (t, 1H, *J* = 9.25 Hz, H-2), 5.88 (m, 1H, N-CH₂-CH=CH₂), 5.21 (m, 2H, N-CH₂-CH=CH₂), 4.37 (m, 2H, N-CH₂-CH=CH₂), 4.99 (t, 1H, *J* = 9.75 Hz, H-4), 4.24 (dd, 1H, *J* = 12.5, 5.0 Hz, H-6a), 4.17 (ddd, 1H, *J* = 10.0, 4.5, 2.0 Hz, H-5), 4.00 (dd, 1H, *J* = 11.75, 1.5 Hz, H-6b), 2.01–1.93 (s, 12H, 4 $\times$ CH₃CO); ¹³C NMR (DMSO-*d*₆) δ (ppm): 179.00 (C=S), 169.3–167.0 (4 $\times$ COCH₃), 160.4 (C=O isatin), 143.0 (C-3'), 132.3 (C-4'), 131.5 (C-4'a), 131.3 (N-CH₂-CH=CH₂), 122.9 (C-5'), 121.2 (C-6'), 119.1 (C-7'), 110.4 (C-7'a), 117.4 (N-CH₂-CH=CH₂), 81.9 (C-1), 70.9 (C-2), 72.7 (C-3), 67.7 (C-4), 72.4 (C-5), 61.7 (C-6), 41.3 (N-CH₂-CH=CH₂), 20.5–20.3 (4 $\times$ CH₃CO); EI-HRMS: C₂₇H₃₄N₄O₁₀S, calc. for [M]⁺⁺ = 590.1683 Da, found: *m/z* 590.1692.

N-Benzylisatin 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazone (**3g**). Yellow solid, mp 195–196 °C (from 96% ethanol), yield 90%; IR (KBr) ν /cm⁻¹: 3341, 1750, 1608, 1370, 1229, 1064; ¹H NMR (DMSO-*d*₆) δ (ppm): 12.72 (s, 1H, NH-2), 9.67 (d, 1H, *J* = 9.5 Hz, NH-4), 7.79 (d, 1H, *J* = 7.5 Hz, H-7'), 7.33 (t, 1H, *J* = 7.25 Hz, H-6'), 7.39–7.32 (5H, C₆H₅, *N*-benzyl), 7.17 (t, 1H, *J* = 7.5 Hz, H-5'), 7.04 (d, 1H, *J* = 8.0 Hz, H-4'), 6.04 (t, 1H, *J* = 9.0 Hz, H-1), 5.47 (t, 1H, *J* = 9.5 Hz, H-3), 5.36 (t, 1H, *J* = 9.25 Hz, H-2), 5.00 (t, 1H, *J* = 9.75 Hz, H-4), 4.98 (s, 2H, CH₂, *N*-benzyl), 4.24 (dd,

1H, *J* = 12.5, 5.0 Hz, H-6a), 4.19 (ddd, 1H, *J* = 9.5, 4.75, 1.5 Hz, H-5), 4.01 (dd, 1H, *J* = 11.0 Hz, H-6b), 2.01–1.93 (s, 12H, 4 $\times$ CH₃CO); ¹³C NMR (DMSO-*d*₆) δ (ppm): 179.0 (C=S), 169.9–169.3 (4 $\times$ COCH₃), 160.7 (C=O (isatin), 142.9 (C-3'), 135.6 (C-1'), *N*-benzyl), 132.2 (C-4'), 131.5 (C-4', *N*-benzyl), 128.8 (C-4'a), 128.6 (C-3'' and C-5'', *N*-benzyl), 127.4 (C-2'' and C-6'', *N*-benzyl), 123.0 (C-5'), 121.2 (C-6'), 119.2 (C-7'), 110.4 (C-7'a), 81.9 (C-1), 70.9 (C-2), 72.7 (C-3), 67.7 (C-4), 72.4 (C-5), 61.7 (C-6), 42.6 (CH₂, *N*-benzyl), 20.5–20.3 (4 $\times$ CH₃CO); EI-HRMS: C₂₇H₃₂N₄O₁₀S, calc. for [M]⁺⁺ = 640.1839 Da, found: *m/z* 640.1850.

N-Phenethylisatin 4-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazone (**3h**). Yellow solid, mp 200–203 °C (from 96% ethanol), yield 73%; IR (KBr) ν /cm⁻¹: 3290, 1735, 1614, 1367, 1234, 1040; ¹H NMR (DMSO-*d*₆) δ (ppm): 12.66 (s, 1H, NH-2), 9.62 (d, 1H, *J* = 9.0 Hz, NH-4), 7.75 (d, 1H, *J* = 7.0 Hz, H-7'), 7.42 (t, 1H, *J* = 7.5 Hz, H-6'), 7.28–7.21 (5H, C₆H₅, *N*-phenethyl), 7.19–7.16 (m, 2H, H-4' and H-5'), 6.00 (t, 1H, *J* = 9.0 Hz, H-1), 5.46 (t, 1H, *J* = 9.5 Hz, H-3), 5.33 (t, 1H, *J* = 9.25 Hz, H-2), 4.98 (t, 1H, *J* = 9.75 Hz, H-4), 4.34 (t, 2H, *J* = 5.0 Hz, CH₂, *N*-phenethyl), 4.24 (dd, 1H, *J* = 12.25, 4.75 Hz, H-6a), 4.17 (ddd, 1H, *J* = 6.5, 4.5, 1.5 Hz, H-5), 4.02 (d, 1H, *J* = 9.0 Hz, H-6b), 3.46–3.41 (m, 2H, CH₂, *N*-phenethyl), 2.08–1.93 (s, 12H, 4 $\times$ CH₃CO); EI-HRMS: C₃₁H₃₄N₄O₁₀S, calc. for [M]⁺⁺ = 654.1996 Da, found: *m/z* 654.2007.

3. Results and Discussion

Alkylation reaction in isatin **1** using corresponding alkyl bromide in the presence of potassium carbonate as base in DMF under microwave-assisted heating method gave required *N*-alkylisatins **2a-h** [21]. Condensation of *N*-alkylisatins

2a-h with 4-(tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazide was carried out on refluxing in the presence of glacial acetic acid as catalyst. These reactions were executed under microwave-assisted heating method. Reaction products usually separated as color solid after cooling to room temperature. The products are soluble in common organic solvents, such as toluene, ethanol, methanol, DMF, acetone, and ethyl acetate (Scheme 1).

The structure of these thiosemicarbazones was first confirmed using IR spectroscopic method. IR spectra show the characteristic absorption bands at 3462–3313 and 3331–3212 cm^{-1} (ν_{NH}), 1752–1747 cm^{-1} ($\nu_{\text{C=O}}$ ester), 1697–1688 ($\nu_{\text{C=O}}$ lactam in isatin), 1618–1610 cm^{-1} ($\nu_{\text{C=N}}$), 1228–1218 and 1060–1049 cm^{-1} (ν_{COC} ester), and 1092–1090 cm^{-1} ($\nu_{\text{C=S}}$), some bands at 1597–1490 cm^{-1} ($\nu_{\text{C=C}}$ aromatic). The evidence that confirms the success of reactions is the absence of C=O band (that belong to isatin) in IR spectra at 1780–1745 cm^{-1} and chemical shifts of NH and NH_2 (in thiosemicarbazide) at δ = 9.32, 8.08, and 4.63 ppm, respectively, that belong to thiosemicarbazide link, NHCSNHNH_2 , of 4-(tetra-*O*-acetyl- β -D-glucopyranosyl) thiosemicarbazide (in ^1H NMR spectra). Other evidence is the appearance of C=S signals at δ = 179.6–177.5 ppm and of C=N signals at δ = 138.0–127.9 ppm.

The assignments of ^1H and ^{13}C were confirmed using HMBC and HSQC methods in case of compound **3a** ($\text{R}=\text{Me}$). The ^1H NMR spectra of the *N*-methylisatin 4-(tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazones (**3a-h**) showed resonance signals for proton NH-2 in range at δ = 12.75–12.67 ppm (singlet) and for proton NH-4 at δ = 9.71–9.62 ppm (doublet) with coupling constants 3J = 8.5–9.0 Hz. Protons in glucopyranose ring have resonance signals in range at δ = 5.97–4.07 ppm. Methyl groups in acetate ester have chemical shifts in range at δ = 2.17–1.95 ppm. The β anomeric configuration of **3a-h** was confirmed on the basis of the coupling constant $J_{1,2}$ = 8.5–9.0 Hz in agreement with the 1,2-*trans*-diaxial relationships between protons H-1 and H-2. The ^{13}C NMR spectrum of compound **3a-h** showed resonance signals at δ = 179.6–179.1 ppm (carbon atom in C=S group), δ = 170.5–169.3 ppm (carbon atoms in C=O bond of acetyl groups), and δ = 82.8–61.3 ppm (protons in glucopyranose ring).

Antibacterial activity was done by the paper-disc plate method. The nutrient agar medium (peptone, beef extract, NaCl, and agar-agar) and 5-mm diameter paper discs (Whatman No. 1) were used. The compounds were dissolved in DMSO in 50, 100, and 150 $\mu\text{g/mL}$ concentrations. The filterpaper discs were soaked in different solutions of the compounds, dried, and then placed in the petri dishes previously seeded with the test organisms (*Escherichia coli* and *Candida albicans*). The plates were incubated for 24 h at $28 \pm 2^\circ\text{C}$ and the inhibition zone around each disc was measured. All these thiosemicarbazones have antibacterial activities on *E. coli* and *C. albicans*. The diameter of inhibition zone is 15–21 mm and 10–30 mm for *E. coli* and *C. albicans*, respectively. The antibacterial activities on *C. albicans* are somewhat higher than on *E. coli*.

4. Conclusion

In summary, an efficient method for synthesis of *N*-alkylisatin 4-(tetra-*O*-acetyl- β -D-glucopyranosyl)thiosemicarbazones under microwave-assisted refluxing conditions has been performed. Reaction yields were 73–93%.

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