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Synthesis of Some Novel Substituted Benzaldehyde (Hepta-O-acetyl-β-maltosyl)thiosemicarbazones

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(Hepta-O-acetyl-β-maltosyl)thiosemicarbazide was synthesized from peracetated β-maltosyl isothiocyanate by reaction with hydrazine hydrate. A series of substituted benzaldehyde (hepta-O-acetyl-β-maltosyl)thiosemicarbazones were synthesized by condensation reactions of (hepta-O-acetyl-β-maltosyl)thiosemicarbazide with corresponding substituted benzaldehydes using microwave-assisted method.

Key Words: β-Maltosyl thiosemicarbazide, Thiosemicarbazones, Microwave-assisted method, Benzaldehyde.

INTRODUCTION

Azomethines constitute a densely populated class of compounds readily available by condensation of a carbonyl compound with an ammonia derivative[1]. Their widespread application in organic synthesis is based on the sensitivity of the C=N double bond towards attacks by nucleophiles and radicals and on additional various possibilities offered by substituents on the nitrogen especially when they are of heteroatomic nature[2]. Thiosemicarbazones are ones which contain the azomethine and thiourea bonds. Considerable attention has been focused on substituted thiosemicarbazone derivatives due to their interesting biological activity. Compounds with a thiosemicarbazone structure are known to possess tranquilizing, muscle relaxing, psychoanaleptic, hypnotic, ulcerogenic, antidepressant, antibacterial, antifungal, analgesic, anticonvulsant, antihypertensive, local anesthetic, anticancer, hypoglycemic, cytotoxic and antiinflammatory properties[3-7]. Such derivatives are well known among open chain carbohydrates as well and lend themselves to several ensuing transformations.

A number of glucosyl thiosemicarbazide derivatives showed significant *in vivo* antimicroorganisms and *in vitro* antioxidant activity, which could be used as leads for the development of effective antiatherosclerotic agents[8]. On the other hand, these molecules can also serve as phosphane-free multidentate ligands for transition-metal catalysis and they are efficient ligands for palladium-catalyzed coupling reactions in air[9]. In the past, some papers have been published for the synthesis of aldehyde/ketone (per-O-acetylated-β-D-glucopyranosyl)-thiosemicarbazones and their corresponding deacetylated analogues[10]. The main step for the synthesis of these molecules is being the reaction of a peracetylated glucosyl thiosemicarbazide with a carbonyl compound.

Continuing our studied on the synthesis and the reactivity of peracetated glycopyranosyl isothiocyanate and thiosemicarbazides[11], we report here a systematic study for the synthesis and spectral characterization of a series of benzaldehyde (hepta-O-acetyl-β-maltosyl)thiosemicarbazones using microwave-assisted method[12].

EXPERIMENTAL

Melting points were determined by open capillary method on STUART SMP3 instrument (BIBBY STERILIN, UK) and are uncorrected. IR spectra (KBr disc) were recorded on a Impact 410 FT-IR spectrometer (Nicolet, USA). ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance spectrometer AV500 (Bruker, Germany) at 500.13 and 125.77 MHz, respectively, using DMSO-d_6 as solvent and TMS as an internal standard. MS spectra were recorded on mass spectrometer AutoSpec Premier (WATERS, USA) using EI method and LTQ Orbitrap XL™ (ThermoScientific, USA) using ESI method. All the starting benzaldehydes were purchased from commercial suppliers (Merck, Germany) and used with no further purification. All other solvents and reagents were used as received or purified by standard protocols. Hepta-O-acetyl-β-maltosyl isothiocyanate and corresponding thiosemicarbazide were prepared by the reaction of per-O-acetylated-β-maltosyl bromide (prepared from β-maltose) with lead thiocyanate in dried toluene and then by the further reaction with hydrazine hydrate[10a].

General procedure for synthesis of substituted benzaldehyde 2,3,6,2',3',4',6'-hepta-O-acetyl-β-maltosyl thiosemicarbazones (**4a-k**). In a 10 mL one-necked round-bottomed flask was placed a suspension mixture hepta-O-acetyl-β-maltosyl thiosemicarbazide **1** (3.55 g, 5 mmol) and corresponding substituted benzaldehyde **2** (5 mmol) and glacial acetic acid (0.05 mL) in absolute ethanol (6-8 mL) (in case of **4d**, **4e** and **4g** acetic acid used as solvent instead). Reaction mixture was irradiated with reflux for 7-15 min in microwave oven. The suspension mixture became clear solution after irradiating in 4-5 min. After reaction the mixture was cooled to room temperature, the colourless crystals were filtered with suction. The crude product was recrystallized from ethanol or ethanol/toluene to yield corresponding substituted benzaldehyde (hepta-O-acetyl-β-maltosyl)thiosemicarbazones **4**.

4a: IR (KBr, ν_{max}, cm^{-1}): 3326, 3291, 3149, 1748, 1595, 1540, 1529, 1374, 1233, 1066, 1032; ^{1}H NMR (DMSO-d_6): δ 12.18 (s, 1H, NH), 8.92 (d, 1H, *J* = 9.0 Hz, NH), 8.25 (d, 2H, *J* = 9.0 Hz, H-2''' and H-6'''), 8.18 (s, 1H, CH=N), 8.11 (d, 2H, *J* = 9.0 Hz, H-3''' and H-5'''), 5.94 (t, 1H, *J* = 9.0 Hz, H-1'), 5.45 (t, 1H, *J* = 9.25 Hz, H-3'), 5.34 (d, 1H, *J* = 3.5 Hz, H-1''), 5.25 (t, 1H, *J* = 10.0 Hz, H-2'), 5.22 (t, 1H, *J* = 9.25 Hz, H-3''), 5.00 (t, 1H, *J* = 9.75 Hz, H-4''), 4.88 (dd, 1H, *J* = 10.5, 4.0 Hz, H-5''), 4.36 (dd, 1H, *J* = 12.0, 2.5 Hz, H-6''a), 4.21 (dd, 1H, *J* = 12.25, 4.75 Hz, H-6''b), 4.16 (dd, 1H, *J* = 12.0, 4.0 Hz, H-6'a), 4.06-3.97 (m, 2H, H-6'b and H-2''), 4.02 (d, 1H, *J* = 10.5 Hz, H-5'), 3.92 (t, 1H, *J* = 9.25 Hz, H-4'), 2.06-1.93 (7s, 21H, 7×$COCH_3$); ^{13}C NMR (DMSO-d_6): δ 179.7 (C=S), 171.0-169.1 (7C, 7×$COCH_3$), 148.8 (C-4'''), 142.1 (C-1'''), 141.1 (CH=N), 129.3 (C-2''' and C-6'''), 124.7 (C-3''' and C-5'''), 96.3 (C-1''), 82.1 (C-1'), 75.6 (C-3'), 74.7 (C-4'), 73.8 (C-5'), 72.3 (C-3''), 70.4 (C-5''), 69.8 (C-2'), 69.0 (C-2''), 68.7 (C-4''), 63.8 (C-6''), 62.3 (C-6'), 21.5-21.1 (7C, 7×$COCH_3$); HRMS (EI^+): $[M + H]^+$ = 843.9211, calcd. for $C_{34}H_{42}N_4O_{19}S$ 842.2164 Da, [M + H] = 843.2237 Da.

4b: IR (KBr, ν_{max}, cm^{-1}): 3322, 3136, 1744, 1600, 1550, 1528, 1373, 1232, 1043; ^{1}H NMR (DMSO-d_6): δ 12.10 (s, 1H, NH), 8.84 (d, 1H, *J* = 9.0 Hz, NH), 8.58 (t, 1H, *J* = 2.0 Hz, H-2'''), 8.31 (d, 1H, *J* = 7.5 Hz, H-6'''), 8.24 (ddd, 1H, *J* = 7.5, 2.0, 0.5 Hz, H-4'''), 8.21 (s, 1H, CH=N), 7.72 (t, 1H, *J* = 7.5 Hz, H-5'''), 5.92 (t, 1H, *J* = 9.0 Hz, H-1'), 5.45 (t, 1H, *J* = 9.25 Hz, H-3'), 5.34 (d, 1H, *J* = 4.0 Hz, H-1''), 5.24 (t, 1H, *J* = 10.0 Hz, H-2'), 5.19 (t, 1H, *J* = 9.5 Hz, H-3''), 4.99 (t, 1H, *J* = 9.75 Hz, H-4''), 4.86 (dd, 1H, *J* = 10.5, 3.5 Hz, H-5''), 4.36 (dd, 1H, *J* = 12.25, 2.25 Hz, H-6''a), 4.21 (dd, 1H, *J* = 12.5, 5.0 Hz, H-6''b), 4.16 (dd, 1H, *J* = 12.75, 4.75 Hz, H-6'a), 4.04-3.98 (m, 3H, H-6'b, H-2'' and H-5'), 3.94 (t, 1H, *J* = 9.25 Hz, H-4'), 2.06-1.91 (7s, 21H, 7×$COCH_3$); ^{13}C NMR (DMSO-d_6): δ 178.7 (C=S), 170.1-169.1 (7C, 7×$COCH_3$), 148.3 (C-3'''), 141.6 (CH=N), 135.7 (C-1'''), 133.4 (C-6'''), 130.1 (C-5'''), 124.4 (C-4'''), 121.9 (C-2'''), 95.4 (C-1''), 81.2 (C-1'), 74.6 (C-3'), 73.8 (C-4'), 73.0 (C-5'), 71.4 (C-3''), 69.5 (C-5''), 68.9 (C-2'), 68.0 (C-2''), 67.8 (C-4''), 62.9 (C-6''), 61.4 (C-6'), 20.6-20.2 (7C, 7×$COCH_3$). MS (ESI): $[M + Na]^+$ = 865.13, calcd. for $C_{34}H_{42}N_4O_{19}S$ 842.22 Da, [M + Na] = 865.21.

4c: IR (KBr, ν_{max}, cm^{-1}): 3326, 3145, 1747, 1625, 1369, 1228, 1054; ^{1}H NMR (DMSO-d_6): δ 11.95 (s, 1H, NH), 8.71 (d, 1H, *J* = 9.0 Hz, NH), 8.08 (s, 1H, CH=N), 7.85 (d, 2H, *J* = 8.5 Hz, H-2''' and H-6'''), 7.49 (d, 2H, *J* = 8.5 Hz, H-3''' and H-5'''), 5.91 (t, 1H, *J* = 9.25 Hz, H-1'), 5.44 (t, 1H, *J* = 9.0 Hz, H-3'), 5.33 (d, 1H, *J* = 3.5 Hz, H-1''), 5.24 (t, 1H, *J* = 10.0 Hz, H-2'), 5.19 (t, 1H, *J* = 9.25 Hz, H-3''), 4.99 (t, 1H, *J* = 9.75 Hz, H-4''), 4.87 (dd, 1H, *J* = 10.5, 4.0 Hz, H-5''), 4.36 (dd, 1H, *J* = 12.25, 2.25 Hz, H-6''a), 4.20 (dd, 1H, *J* = 12.5, 5.0 Hz, H-6''b), 4.16 (dd, 1H, *J* = 12.5, 4.75 Hz, H-6'a), 4.03-3.98 (m, 3H, H-6'b, H-2'' and H-5'), 3.92 (t, 1H, *J* = 9.25 Hz, H-4'), 2.02-1.90 (7s, 21H, 7×$COCH_3$); ^{13}C NMR (DMSO-d_6): δ 172.3 (C=S), 170.6-169.3 (7C, 7×$COCH_3$), 157.6 (CH=N), 136.1 (C-4'''), 133.3 (C-1'''), 130.4 (C-2''' and C-6'''), 129.5 (C-3''' and C-5'''), 95.9 (C-1''), 81.7 (C-1'), 80.8 (C-3'), 79.9 (C-4'), 75.2 (C-5'), 74.3 (C-3''), 71.9 (C-5''), 70.0 (C-2'), 69.0 (C-2''), 68.1 (C-4''), 67.6 (C-6''), 62.1 (C-6'), 21.1-20.7 (7C, 7×$COCH_3$). MS (ESI): $[M + Na]^+$ = 854.08/856.04, calcd. for $C_{34}H_{42}{}^{35}ClN_3O_{17}S/C_{34}H_{42}{}^{37}ClN_3O_{17}S$ = 831.19/833.19 Da, [M + Na] = 854.18/856.18.

4d: IR (KBr, ν_{max}, cm^{-1}): 3324, 3146, 1747, 1622, 1369, 1228, 1044; ^{1}H NMR (DMSO-d_6): δ 12.11 (s, 1H, NH), 8.85 (d, 1H, *J* = 9.0 Hz, NH), 8.46 (s, 1H, CH=N), 8.31 (d, 1H, *J* = 8.5 Hz, H-6'''), 7.67 (d, 1H, *J* = 2.0 Hz, H-3'''), 7.48 (dd, 1H, *J* = 8.5, 2.0 Hz, H-5'''), 5.92 (t, 1H, *J* = 9.25 Hz, H-1'), 5.44 (t, 1H, *J* = 9.25 Hz, H-3'), 5.33 (d, 1H, *J* = 3.5 Hz, H-1''), 5.24 (t, 1H, *J* = 10.0 Hz, H-2'), 5.19 (t, 1H, *J* = 9.25 Hz, H-3''), 5.00 (t, 1H, *J* = 9.75 Hz, H-4''), 4.87 (dd, 1H, *J* = 10.5, 4.0 Hz, H-5''), 4.36 (dd, 1H, *J* = 12.0, 2.0 Hz, H-6''a), 4.20 (dd, 1H, *J* = 12.75, 4.75 Hz, H-6''b), 4.16 (dd, 1H, *J* = 12.0, 4.5 Hz, H-6'a), 4.05-3.97 (m, 3H, H-6'b, H-2'' and H-5'), 3.91 (t, 1H, *J* = 9.5 Hz, H-4'), 2.05-1.90 (7s, 21H, 7 × $COCH_3$); ^{13}C NMR (DMSO-d_6): d 178.6 (C=S), 170.1-169.1 (7C, 7×$COCH_3$), 138.7 (CH=N), 135.2 (C-1'''), 134.1 (C-2'''), 130.2 (C-3'''), 129.3 (C-6'''), 128.7 (C-4'''), 127.6 (C-5'''), 95.3 (C-1''), 81.2 (C-1'), 74.7 (C-3'), 73.8 (C-4'), 72.9 (C-5'), 71.4 (C-3''), 69.5 (C-5''), 68.9 (C-2'), 68.0 (C-2''), 67.8 (C-4''), 62.9 (C-6''), 61.4 (C-6'), 20.6-20.2 (7C, 7×$COCH_3$); MS (ESI): [M]/[M + 2] 865.74/869.78, calcd. for $C_{34}H_{41}{}^{35}Cl_2N_3O_{17}S/C_{34}H_{41}{}^{37}Cl_2N_3O_{17}S$ = 865.15/869.15 Da.

4e: IR (KBr, ν_{max}, cm^{-1}): 3324, 3145, 1746, 1595, 1368, 1226, 1054; ^{1}H NMR (DMSO-d_6): δ 11.96 (s, 1H, NH), 8.72 (d, 1H, *J* = 9.0 Hz, NH), 8.06 (s, 1H, CH=N), 7.78 (d, 2H, *J* = 8.5 Hz, H-2''' and H-6'''), 7.62 (d, 2H, *J* = 8.5 Hz, H-3''' and H-5'''), 5.91 (t, 1H, *J* = 9.25 Hz, H-1'), 5.44 (t, 1H, *J* = 9.0 Hz, H-3'), 5.33 (d, 1H, *J* = 3.5 Hz, H-1''), 5.24 (t, 1H, *J* = 10.0 Hz, H-2'), 5.19 (t, 1H, *J* = 9.25 Hz, H-3''), 4.99 (t, 1H, *J* = 10.0 Hz, H-4''), 4.87 (dd, 1H, *J* = 10.5, 4.0 Hz, H-5''), 4.35 (dd, 1H, *J* = 12.0, 2.5 Hz, H-6''a), 4.19 (dd, 1H, *J* = 12.25, 4.75 Hz, H-6''b), 4.16 (dd, 1H, *J* = 12.25, 4.25 Hz, H-6'a), 4.03-3.98 (m, 3H, H-6'b, H-2'' and H-5'), 3.92 (t, 1H, *J* = 9.5 Hz, H-4'), 2.05-1.96 (7s, 21H, 7×$COCH_3$); ^{13}C NMR (DMSO-d_6): δ 178.3 (C=S), 170.1-169.1 (7C, 7×$COCH_3$), 142.5 (CH=N), 133.0 (C-1'''), 131.6 (C-3''' and C-5'''), 129.4 (C-2''' and C-6'''), 123.5 (C-4'''), 95.3 (C-1''), 81.1 (C-1'), 74.7 (C-3'), 73.8 (C-4'), 72.9 (C-5'), 71.4 (C-3''), 69.5 (C-5''), 68.9 (C-2'), 68.0 (C-2''), 67.9 (C-4''), 62.9 (C-6''), 62.4 (C-6'), 20.6-20.2 (7C, 7×$COCH_3$). MS (ESI): $[M]/[M + 2]^+$ = 875.98/877.91, $[M + Na]/[M + 2 + Na]^+$ =897.93/899.93, calcd. for $C_{34}H_{42}{}^{79}BrN_3O_{17}S/C_{34}H_{42}{}^{81}BrN_3O_{17}S$ = 875.14/877.14 Da, [M + Na] = 898.13/900.13 Da.

4f: IR (KBr, ν_{max}, cm^{-1}): 3291, 3171, 1746, 1605, 1550, 1507, 1470, 1374, 1235, 1047; ^{1}H NMR (DMSO-d_6): δ 11.96 (s, 1H, NH), 8.69 (d, 1H, *J* = 9.0 Hz, NH), 8.09 (s, 1H, CH=N), 7.83-7.81 (m, 2H, H-3''' and H-5'''), 7.44-7.43 (m, 3H, H-2''', H-3''' and H-5'''), 5.91 (t, 1H, *J* = 9.25 Hz, H-1'), 5.45 (t, 1H, *J* = 9.25 Hz, H-3'), 5.33 (d, 1H, *J* = 3.5 Hz, H-1''), 5.24 (t, 1H, *J* = 10.0 Hz, H-2'), 5.21 (t, 1H, *J* = 9.25 Hz, H-3''), 5.00 (t, 1H, *J* = 9.75 Hz, H-4''), 4.87 (dd, 1H, *J* = 10.5, 3.5 Hz, H-5''), 4.35 (dd, 1H, *J* = 12.0, 2.0 Hz, H-6''a), 4.19 (dd, 1H, *J* = 12.25, 4.75 Hz, H-6''b), 4.16 (dd, 1H, *J* = 11.25, 2.75 Hz, H-6'a), 4.04-3.97 (m, 3H, H-6'b, H-2'' and H-5'), 3.92 (t, 1H, *J* = 9.25 Hz, H-4'), 2.06-1.91 (7s, 21H, 7×$COCH_3$); ^{13}C NMR (DMSO-d_6): δ 178.3 (C=S), 170.1-169.2 (7C, 7×$COCH_3$), 143.8 (CH=N), 133.7 (C-1'''), 130.3 (C-4'''), 128.7 (C-2''' and C-6'''), 127.6 (C-3''' and C-5'''), 95.4 (C-1''), 81.1 (C-1'), 74.7 (C-3'), 73.7 (C-4'), 72.8 (C-5'), 71.4 (C-3''), 69.5 (C-5''), 68.9 (C-2'), 68.0 (C-2''), 67.8 (C-4''), 62.9 (C-6''), 61.4 (C-6'), 20.7-20.3 (7C, 7×$COCH_3$). MS (ESI): $[M + Na]^+$ = 820.17, calcd. for $C_{34}H_{43}N_3O_{17}S$ = 797.23 Da, [M + Na] = 820.22 Da.

4g: IR (KBr, ν_{max}, cm^{-1}): 3331, 1751, 1611, 1536, 1470, 1373, 1233, 1051; ^{1}H NMR (DMSO-d_6): δ 11.88 (s, 1H, NH), 8.59 (d, 1H, *J* = 9.0 Hz, NH), 8.07 (s, 1H, CH=N), 7.71 (d, 2H, *J* = 8.0 Hz, H-2''' and H-6'''), 7.29 (d, 2H, *J* = 8.0 Hz, H-3''' and H-5'''), 5.88 (t, 1H, *J* = 9.25 Hz, H-1'), 5.44 (t, 1H, *J* = 9.0 Hz, H-3'), 5.32 (d, 1H, *J* = 3.5 Hz, H-1''), 5.24 (t, 1H, *J* = 10.0 Hz, H-2'), 5.18 (t, 1H, *J* = 9.25 Hz, H-3''), 4.99 (t, 1H, *J* = 9.75 Hz, H-4''), 4.87 (dd, 1H, *J* = 10.5, 3.5 Hz, H-5''), 4.34 (d, 1H, *J* = 10.5 Hz, H-6''a), 4.21-4.14 (m, 2H, H-6'a Hz, H-6''b), 4.02-3.98 (m, 3H, H-6'b, H-2'' and H-5'), 3.93 (t, 1H, *J* = 9.25 Hz, H-4'), 2.91 [t, 1H, *J* = 7.0 Hz, $CH(CH_3)_2$], 2.05-1.90 (7s, 21H, 7×$COCH_3$), (d, 6H, *J* = 7.0 Hz, $CH(CH_3)_2$]; ^{13}C NMR (DMSO-d_6): δ 178.2 (C=S), 170.1-169.3 (7C, 7×$COCH_3$), 151.1 (C-4'''), 144.0 (CH=N), 131.4 (C-1'''), 127.7 (C-2''' and C-6'''), 126.7 (C-3''' and C-5'''), 95.4 (C-1''), 81.1 (C-1'), 74.7 (C-3'), 73.9 (C-4'), 72.9 (C-5'), 71.4 (C-3''), 69.6 (C-5''), 69.0 (C-2'), 68.1 (C-2''), 67.9 (C-4''), 63.0 (C-6''), 61.5 (C-6'), 33.4 [$CH(CH_3)_2$], 20.7-20.3 (7C, 7×$COCH_3$), 23.7 [$CH(CH_3)_2$]; MS (ESI): $[M + Na]^+$ = 862.17, calcd. for $C_{37}H_{49}N_3O_{17}S$ = 839.28 Da, [M + Na] = 862.27 Da.

4h: IR (KBr, ν_{max}, cm^{-1}): 3324, 1749, 1590, 1534, 1470, 1372, 1233, 1032; ^{1}H NMR (DMSO-d_6): δ 11.95 (s, 1H, NH-1), 8.64 (d, 1H, *J* = 9.5 Hz, NH-3), 8.06 (s, 1H, CH=N), 7.43 (s, 1H, H-2'''), 7.34 (t, 1H, *J* = 7.75 Hz, H-5'''), 7.31 (t, 1H, *J* = 7.25 Hz, H-6'''), 7.00 (dt, 1H, *J* = 8.0, 1.5 Hz, H-4'''), 5.84 (t, 1H, *J* = 9.25 Hz, H-1'), 5.45 (t, 1H, *J* = 9.25 Hz, H-3'), 5.32 (d, 1H, *J* = 3.5 Hz, H-1''), 5.24 (t, 1H, *J* = 10.0 Hz, H-2'), 5.18 (t, 1H, *J* = 9.25 Hz, H-3''), 4.99 (t, 1H, *J* = 9.75 Hz, H-4''), 4.87 (dd, 1H, *J* = 10.5, 3.5 Hz, H-5''), 4.35 (d, 1H, *J* = 10.0 Hz, H-6''a), 4.20 (dd, 1H, *J* = 12.5, 5.0 Hz, H-6''b), 4.16 (dd, 1H, *J* = 12.5, 4.5 Hz, H-6'a), 4.02-3.98 (m, 3H, H-6'b, H-2'' and H-5'), 3.93 (t, 1H, *J* = 9.25 Hz, H-4'), 3.81 (s, 3H, 3'''-OCH_3), 2.05-1.91 (7s, 21H, 7×$COCH_3$); ^{13}C NMR (DMSO-d_6): δ 178.5 (C=S), 170.2-169.2 (7C, 7×$COCH_3$), 159.6 (C-3'''), 143.7 (CH=N), 135.1 (C-1'''), 129.9 (C-5'''), 120.8 (C-6'''), 116.5 (C-4'''), 111.6 (C-2'''), 95.4 (C-1''), 81.1 (C-1'), 74.6 (C-4'), 73.9 (C-5'), 72.9 (C-3'), 71.3 (C-2'), 69.6 (C-3''), 69.0 (C-5''), 68.0 (C-2''), 67.9 (C-4''), 62.9 (C-6'), 61.5 (C-6''), 55.3 (3'''-OCH_3), 20.6-20.3 (7C, 7×$COCH_3$); MS (ESI): $[M]^+$ = 827.87, calcd. for $C_{35}H_{45}N_3O_{18}S$ = 827.24 Da.

4i: IR (KBr, ν_{max}, cm^{-1}): 3451, 3338, 1750, 1599, 1550, 1511, 1370, 1229, 1039; ^{1}H NMR (DMSO-d_6): δ 11.81 (s, 1H, NH-1), 9.45 (s, 1H, 4'''-OH), 8.48 (d, 1H, *J* = 9.0 Hz, NH-3), 7.98 (s, 1H, CH=N), 7.39 (d, 1H, *J* = 1.5 Hz, H-2'''), 7.12 (dd, 1H, *J* = 8.75, 1.75 Hz, H-6'''), 6.83 (d, 1H, *J* = 8.0 Hz, H-5'''), 5.81 (t, 1H, *J* = 9.25 Hz, H-1'), 5.46 (t, 1H, *J* = 9.25 Hz, H-3'), 5.32 (d, 1H, *J* = 3.5 Hz, H-1''), 5.25 (t, 1H, *J* = 10.0 Hz, H-2'), 5.14 (t, 1H, *J* = 9.25 Hz, H-3''), 4.99 (t, 1H, *J* = 9.75 Hz, H-4''), 4.87 (dd, 1H, *J* = 10.5, 4.0 Hz, H-5''), 4.35 (dd, 1H, *J* = 12.5, 2.0 Hz, H-6''a), 4.21 (dd, 1H, *J* = 12.5, 4.5 Hz, H-6''b), 4.18 (dd, 1H, *J* = 10.0, 4.5 Hz, H-6'a), 4.16-3.98 (m, 5H, H-6'b, H-2'', H-5' and 3'''-OCH_2CH_3), 3.94 (t, 1H, *J* = 9.25 Hz, H-4'), 2.06-1.91 (7s, 21H, 7×$COCH_3$), 1.35 (t, 3H, *J* = 7.0 Hz, 3'''-OCH_2CH_3); ^{13}C NMR (DMSO-d_6): δ 177.8 (C=S), 170.1-169.2 (7C, 7×$COCH_3$), 149.6 (C-4'''), 147.1 (C-3'''), 144.3 (CH=N), 125.0 (C-1'''), 122.4 (C-6'''), 115.5 (C-5'''), 111.3 (C-2'''), 95.3 (C-1''), 81.0 (C-1'), 74.4 (C-4'), 73.8 (C-5'), 72.8 (C-3'), 71.1 (C-2'), 69.5 (C-3''), 68.9 (C-5''), 68.0 (C-2''), 67.8 (C-4''), 63.9 (C-6'), 62.8 (C-6''), 61.4 (3'''-OCH_2CH_3), 20.6-20.2 (7C, 7×$COCH_3$), 14.7 (3'''-OCH_2CH_3); MS (ESI): $[M]^+$ = 880.09, calcd. for $C_{36}H_{47}N_3O_{19}S$ = 880.24 Da.

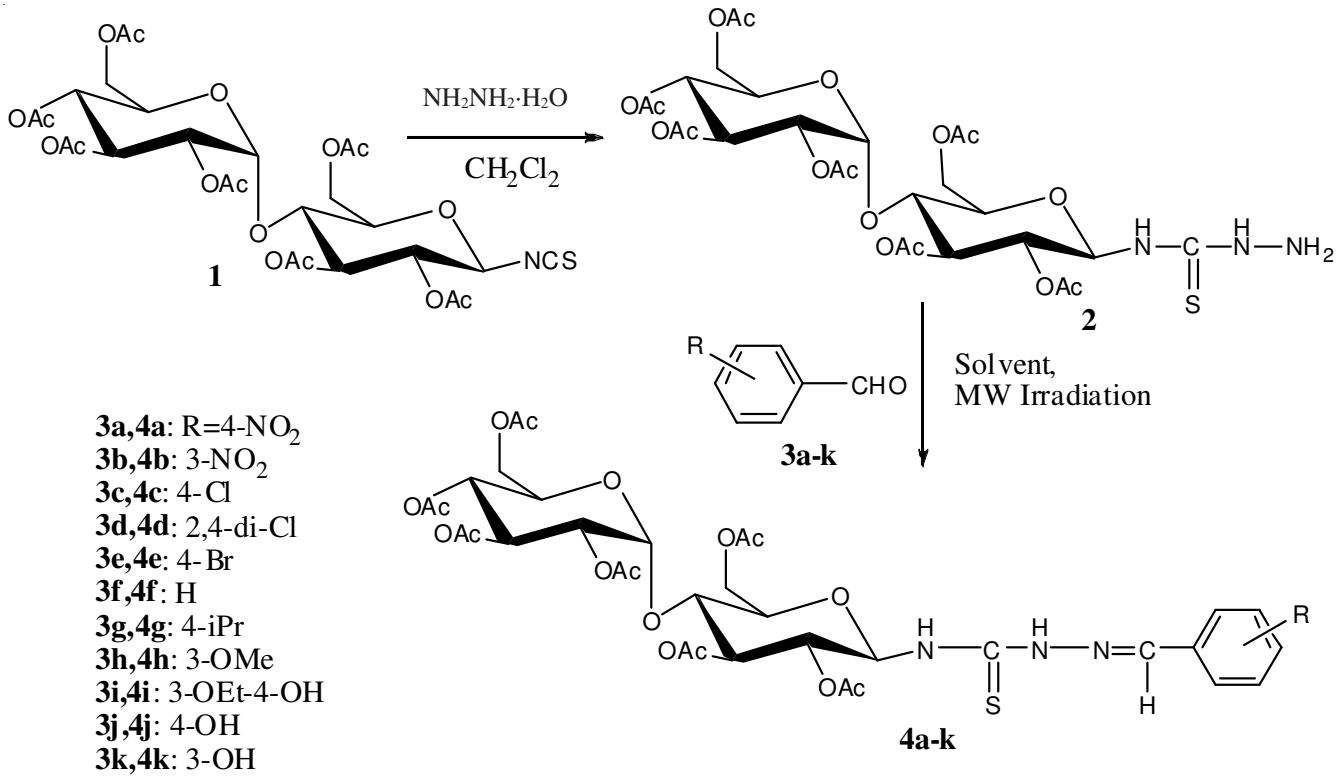
4j: IR (KBr, ν_{max}, cm^{-1}): 3338, 1747, 1612, 1368, 1244, 1044; ^{1}H NMR (DMSO-d_6): δ 11.74 (s, 1H, NH), 10.02 (s, 1H, 4'''-OH), 8.51 (d, 1H, *J* = 9.0 Hz, NH), 7.99 (s, 1H, CH=N), 7.63 (d, 2H, 8.75 Hz, H-2''' and H-6'''), 6.81 (d, 2H, 8.75 Hz, H-3''' and H-5'''), 5.87 (t, 1H, *J* = 9.25 Hz, H-1'), 5.42 (t, 1H, *J* = 9.0 Hz, H-3'), 5.32 (d, 1H, *J* = 3.5 Hz, H-1''), 5.23 (t, 1H, *J* = 10.0 Hz, H-2'), 5.17 (t, 1H, *J* = 9.25 Hz, H-3''), 4.99 (t, 1H, *J* = 9.75 Hz, H-4''), 4.87 (dd, 1H, *J* = 10.5, 3.5 Hz, H-5''), 4.34 (dd, 1H, *J* = 12.25, 2.25 Hz, H-6''a), 4.21 (dd, 1H, *J* = 12.25, 4.5 Hz, H-6''b), 4.02-3.98 (m, 4H, H-6'a, H-6'b, H-2'' and H-5'), 3.91 (t, 1H, *J* = 9.0 Hz, H-4'), 2.04-1.91 (7s, 21H, 7×$COCH_3$); ^{13}C NMR (DMSO-d_6): δ 177.8 (C=S), 170.2-169.2 (7C, 7×$COCH_3$), 159.7 (C-4'''), 144.3 (CH=N), 129.4 (C-2''' and C-6'''), 124.7 (C-1'''), 115.7 (C-3''' and C-5'''), 95.4 (C-1''), 81.1 (C-1'), 74.7 (C-3'), 73.9 (C-4'), 72.9 (C-5'), 71.4 (C-3''), 69.6 (C-5''), 69.0 (C-2'), 68.0 (C-2''), 67.9 (C-4''), 63.0(C-6''), 61.5 (C-6'), 20.7-20.3 (7C, 7×$COCH_3$); MS (ESI): $[M]^+$ = 813.90, calcd. for $C_{34}H_{43}N_3O_{18}S$ = 813.23 Da.

4k: IR (KBr, ν_{max}, cm^{-1}): 3323, 3224, 1749, 1600, 1590, 1534, 1470, 1377, 1237, 1036; ^{1}H NMR (DMSO-d_6): δ 11.86 (s, 1H, NH-1), 9.61 (s, 1H, 3'''-OH), 8.60 (d, 1H, *J* = 9.5 Hz, NH-3), 8.01 (s, 1H, CH=N), 7.14 (s, 1H, H-2'''), 7.22-7.21 (m, 2H, H-5''', H-6'''), 6.84 (d, 1H, *J* = 4.0 Hz, H-4'''), 5.91 (t, 1H, *J* = 9.0 Hz, H-1'), 5.44 (t, 1H, *J* = 9.0 Hz, H-3'), 5.32 (d, 1H, *J* = 4.0 Hz, H-1''), 5.24 (t, 1H, *J* = 10.0 Hz, H-2'), 5.18 (t, 1H, *J* = 9.25 Hz, H-3''), 4.99 (t, 1H, *J* = 9.75 Hz, H-4''), 4.87 (dd, 1H, *J* = 10.5, 3.5 Hz, H-5''), 4.34 (d, 1H, *J* = 10.5 Hz, H-6''a), 4.19 (dd, 1H, *J* = 13.0, 5.0 Hz, H-6''b), 4.16 (dd, 1H, *J* = 13.0, 5.0 Hz, H-6'a), 4.02-3.99 (m, 3H, H-6'b, H-2'' and H-5'), 3.92 (t, 1H, *J* = 9.0 Hz, H-4'), 2.06-1.91 (7s, 21H, 7×$COCH_3$); ^{13}C NMR (DMSO-d_6): δ 178.2 (C=S), 170.1-169.2 (7C, 7×$COCH_3$), 157.6 (C-3'''), 144.2 (CH=N), 134.9 (C-1'''), 129.7 (C-5'''), 118.7 (C-6'''), 117.5 (C-4'''), 113.9 (C-2'''), 95.3 (C-1''), 81.1 (C-1'), 74.6 (C-4'), 73.7 (C-5'), 72.9 (C-3'), 71.4 (C-2'), 69.5 (C-3''), 68.9 (C-5''), 68.0 (C-2''), 67.8 (C-4''), 62.9 (C-6'), 61.4 (C-6''), 20.6-20.2 (7C, 7×$COCH_3$); MS (ESI): $[M + Na]^+$ = 835.96, calcd. for $C_{34}H_{43}N_3O_{18}S$ = 813.23 Da, [M + Na] = 836.21 Da.

RESULTS AND DISCUSSION

The synthesis of the thiosemicarbazones is outlined in **Scheme-I**. Substituted benzaldehyde (hepta-O-acetyl-β-maltosyl)thiosemicarbazones **4** have been synthesized by condensation reaction of hepta-O-acetyl-β-maltosyl thiosemicarbazide **1** with a number of corresponding substituted benzaldehyde **3**. These syntheses were performed using minimum amount of absolute ethanol solvent (3-5 mL). In some cases, such as **4d**, **4e** and **4g**, acetic acid was used as solvent instead of absolute ethanol. The time interval of irradiation was 4-9 min (Table-1). The solid thiosemicarbazones **4** were filtered by suction and recrystallized from ethanol or ethanol/toluene (1:1 in volume). These compounds could be soluble in ethanol, toluene, chloroform, DMF and had high melting points. All the products were characterized by IR, ^{1}H and ^{13}C NMR and mass spectra.

The IR spectra of compounds **4** showed characteristic absorptions in the ranges of 3386-3376 and 3338-3304 cm^{-1} (N-H bond), 1758-1744, 1234-1223 cm^{-1} and 1045-1023 cm^{-1} (ester), 1377-1369 cm^{-1} (C=S) and 1622-1602 cm^{-1} (C=N bond). In the ^{1}H NMR spectra of **4**, the anomeric proton H-1 is represented as a triplet at the range 5.90-5.95 ppm due to the coupling with the N(4")-H and the H-2. The coupling constant, $J_{H\text{-}1,H\text{-}2}$ = 9.0-9.5 Hz, is an evidence which confirms the β configuration in compounds **4**[10,11]. The NH proton of the thioamide functionality of compounds **4** appeared at 10.71-10.98 ppm (singlet) for N(2")H and 8.77-8.58 ppm (doublet, $J_{NH,H\text{-}1}$ = 9.0-9.5 Hz) for N(4")H. The ^{13}C NMR spectra showed the thiocarbonyl carbon atom with chemical shift at δ = 179.0-179.7 ppm[10,11].



Scheme-I

TABLE-1
SUBSTITUTED BENZALDEHYDE (HEPTA-O-ACETYL-β-MALTOSYL)THIOSEMICARBAZONES **4a-k**

Entry	R	Microwave irradiation time (min)	Reaction solvent	m.p. (ºC)	Yield (%)
4a	4-NO_2	9	Ethanol	150-151	53
4b	3-NO_2	5	Ethanol	210-211	81
4c	4-Cl	9	Ethanol	197-198	59
4d	2,4-di-Cl	6	Acetic acid	118-119	86
4e	4-Br	4	Acetic acid	204-205	85
4f	H	5	Ethanol	165-166	51
4g	4-iPr	7	Acetic acid	127-128	53
4h	3-OMe	7	Ethanol	184-185	54
4i	3-OEt-4-OH	7	Ethanol	191-192	69
4j	4-OH	5	Ethanol	117-118	55
4k	3-OH	5	Ethanol	178-179	70

Conclusion

A highly efficient method for the synthesis of 2,3,6,2',3',4',6'-hepta-O-acetyl-β-maltosyl thiosemicarbazones of substituted benzaldehydes under microwave-assisted heating conditions is developed.

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