Asian Journal of Chemistry Vol. 21, No. 9 (2009), 6661-6666

Schiff Base Derivatives of 2-Amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose

ATUL N. BEDEKAR*, ADESH N. NAIK and ABHINAY C. PISE
B.N. Bandodkar College of Science, Chendani, Thane(W)-400 601, India
Tel: (91)(22)25824472; E-mail: atulbedekar@gmail.com

The present work deals with the synthesis of different Schiff bases of derivative of glucosamine. Schiff bases of glucosamine with salicylaldehyde or anisaldehyde could be easily synthesized. However Schiff bases of benzaldehyde and some other aldehydes could not be synthesized from glucosamine. Therefore glucosamine was converted to tetraacetyl derivative for synthesis of Schiff base. The amino group was protected during acetylation by converting it into Schiff base. The tetra-acetyl derivatives were also used to synthesize Schiff bases of benzaldehyde, 5-bromo-salicyaldehyde, vanillin and veratraldehyde. The product characterization was done with spectral analysis.

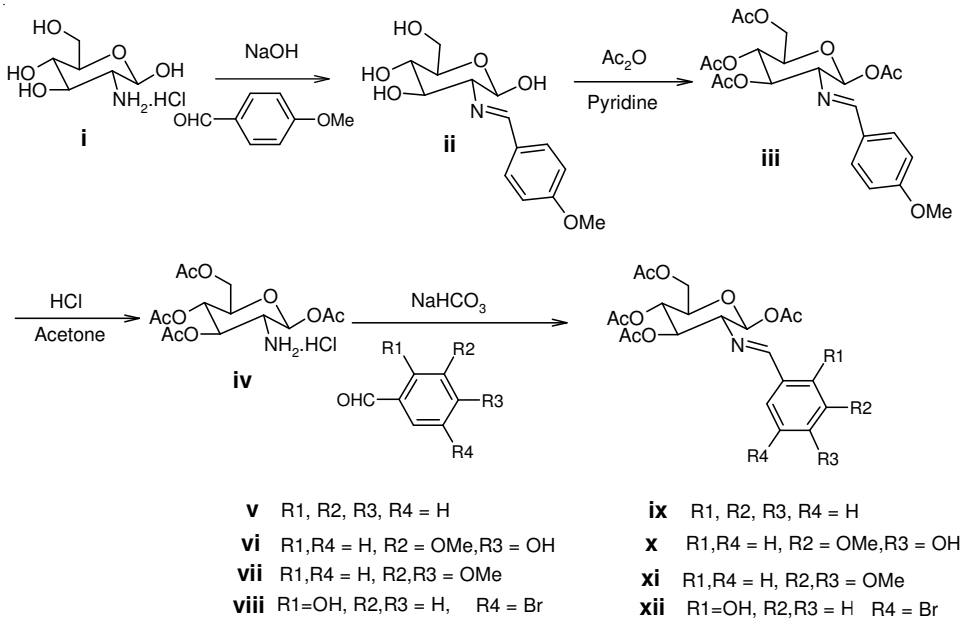
Key Words: Glucosamine, Schiff base, Tetraacetyl glucosamine, Aromatic aldehydes.

INTRODUCTION

Amino sugars, as the free base, readily form Schiff base derivatives with aromatic aldehydes, which are of value as characterizing derivatives and sometimes for isolation of an amino sugar from a reaction mixture[1]. They are also useful as removable N-blocking groups in synthesis[2]. The use of Schiff bases as ligand in formation of transition metal complexes has been extensively studied[3].

2-Amino-2-deoxy-β-D-glucopyranose (glucosamine) is an amino sugar endowed with 4 chiral centers and is prepared from chitin. Chitin is a natural biopolymer isolated from crustacean shell waste. Irvin and Earl first reported that Schiff base of glucosamine could be formed with salicylaldehyde[4]. Bergmann and Zervas described the corresponding anisaldehyde derivative[5]. The Schiff bases are stable in aqueous media at neutral or weakly basic pH, but are readily cleaved to the amine salts by brief treatment with dilute aqueous mineral acid, under conditions in which O-acetyl groups are stable. The attempts to prepare Schiff bases of glucosamine with benzaldehyde and veratraldehyde failed and also preparation of Schiff bases of glucosamine with vanillin and 5-bromosalicylaldehyde is difficult. Therefore, the present work was focused on preparing tetraacetyl derivative of glucosamine so that this substrate could be used for satisfactory formation of Schiff bases with the above-mentioned aldehydes. In order to prepare acetylated glucosamine, amino group of glucosamine was protected by preparing its Schiff base with

anisaldehyde, which was then acetylated to obtain 2-amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose(tetraacetylglucosamine). Deprotection of amino group was carried out by using HCl[2].



Reaction scheme

Present work is aimed at preparing tetraacetyl glucosamine hydrochloride and its Schiff bases with various aromatic aldehydes. Tetraacetyl glucosamine was condensed with aldehydes like benzaldehyde (**v**), vanillin (**vi**), veratraldehyde (**vii**) and 5-bromo-salicylaldehyde (**viii**), to produce the corresponding Schiff bases (**ix**, **x**, **xi**, **xii**). These Schiff bases were characterized on the basis of spectral data.

EXPERIMENTAL

Benzaldehyde, veratraldehyde, vanillin and acetic anhydride of LR grade were used. 5-Bromo salicylaldehyde was prepared by bromination of salicylaldehyde. ^{1}H NMR and ^{13}C NMR were recorded on 300 and 400 MHz Brooker instrument, respectively. FTIR was recorded on Perkin-Elmer. Thin layer chromatography (TLC) was performed on silica gel plates and visualized under UV for Schiff bases.

2-Amino-2-deoxy-β-D-glucopyranose hydrochloride (i) (glucosamine hydrochloride): Glucosamine was prepared in our laboratory from chitin by hydrolysis using concentrated HCl at 70-80 ºC for 2 h. The reaction mass was cooled and filtered to get crude (**i**) which was crystallized from water to get pure (**i**). m.p. 182 ºC.

2-(4-Methoxybenzylidene)imino-2-deoxy-β-D-glucopyranose (ii): Anisaldehyde (6.3 g, 0.0464 mol) was added to a stirred mixture of D-glucosamine hydrochloride (10 g, 0.0464 mol) in 50 mL of 1 N aqueous NaOH solution. This reaction mixture

was stirred vigorously for 2 h. The solid formed was isolated by filtration and washed with cold water followed by 1:1 mixture of cold ethyl ether and methanol. The wet cake was air dried to get 13.2 g (85 %) of (**ii**) as a white solid. m.p. 166 ºC[2] (decomp.).

2-(4-Methoxybenzylidene)imino-2-deoxy-1, 3,4,6-tetra-O-acetyl-β-D-glucopyranose (iii): To a stirred suspension of **ii** (10 g, 0.336 mol) and pyridine (54 mL), at 0 ºC, cold acetic anhydride (30 mL) was added drop wise over a period of 0.5 h maintaining temperature between 0-5 ºC. The resulting mixture was stirred at 0 ºC till a clear solution is obtained (1-2 h). It was then stirred at room temperature for 12 h. The reaction was quenched in 400 mL of ice water and stirred at 0-5 ºC for 1 h. The resulting precipitate was isolated by filtration and washed with water. Product was dried at 60 ºC to get crude **iii**. Recrystallization from ethanol yielded 10.5 g (65 %) of **iii** as crystals melts at 186 ºC[2].

^{1}H NMR (DMSO, 300 MHz) δ (ppm): 1.8 (s, 3H of acetyl), 2.01 (s, 9H of acetyl), 4.2 (q, 2H of sugar C-6), 4.92 (t, 1H of sugar C-4), 4.014 (q, 1H of sugar C-5), 3.402 (q, 1H of sugar C-2), 3.776 (s, 3H of -OCH_3), 5.403 (t, 1H of sugar C-3), 6.1 (d, 1H of sugar C-1), 8.2 (s, 1H of CH=N), 6.961-7.51, (m, 4H of aryl), IR (KBr, ν_{max}, cm^{-1}): 3460 (OH), 1753 (C=O), 1638 (C=N), 1605 (C=C aromatic), 1513, 1165 (C-O-C pyranose), 1077 (C-O pyranose).

2-Amino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl hydrochloride (iv): A stirred solution of (**iii**) (10 g, 0.215 mol) in 80 mL of acetone was heated to reflux and 6 N HCl solution (7 mL) was added. The product precipitated instantly. Then the reaction mixture was stirred at reflux for 0.5 h. It was then cooled to 15-20 ºC and stirred for 1 h. The product was isolated by filtration, washed with acetone (25 mL) and dried at 60 ºC to yield 10.6 g of (**iv**), (76 % by theory) as white solid melting at 199 ºC[2].

^{1}H NMR (DMSO, 300 MHz) δ (ppm): 2.035 (s, 3H of acetyl), 2.08-2.176 (s, 9H of acetyl), 4.294 (q, 2H of sugar C-1), 4.1 (q, 1H of sugar C-4), 3.8 (q, 1H of sugar C-5), 3.0 (q, 1H of sugar C-2), 5.474 (t, 1H of sugar C-3), 4.989 (q, 1H of sugar C-6), IR (KBr ν_{max}, cm^{-1}): 1760 (C=O), 1513, 1140 (C-O-C pyranose), 1084 (C-O pyranose).

General procedure for tetraacetyl Schiff base with aromatic aldehydes (ix, x, xi and xii): 0.68 g of sodium bicarbonate was dissolved in 25 mL of water and 2.5 g of (**iv**) (6.5 mmol) was added under stirring at room temperature. To the clear solution formed added solution of aromatic aldehydes (**v**, **vi**, **vii**, **viii**) (6.5 mmol) in 5 mL of methanol. The reaction mass was stirred for 1 h when precipitation was observed. Continued stirring for 2 h. The product was isolated by filtration, washed with acetone (10 mL) and dried at 60 ºC. Products were recrystallized using hot ethanol to yield Schiff bases of corresponding aldehydes (**ix**, **x**, **xi** and **xii**) in the yield range of 70-80 %.

2-(4-Benzylidene)imino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (ix): Yield 1.7 g (60 %), m.p. 166 ºC, R_f 0.6 (8:2 $CHCl_3$: EtOAc), ^{1}H NMR (DMSO,

300 MHz) δ (ppm): 1.8 (s, 3H of acetyl), 2.01 (s, 9H of acetyl), 4.28 (q, 2H of sugar C-6), 4.9 (t, 1H of sugar C-4), 4.02 (q, 1H of sugar C-5), 3.528 (q, 1H of sugar C-2), 5.49 (t, 1H of sugar C-3), 6.09 (d, 1H of sugar C-1), 8.355 (s, 1H of CH=N), 7.69-7.42 (m, 5H of aryl). ^{13}C NMR (DMSO, 400 MHz) δ (ppm): 169.94, 169.360, 168.923 and 168.479 (4 C=O of acetyl), 165.308 (C=N), 135.412, 131.353, 128.72, 128.72, 128.12 and 128.12 (6 C's of aryl), 92.44 (sugar C-1), 72.245 (sugar C-5), 72.245 (sugar C-3), 71.584 (sugar C-4), 67.86 (sugar C-6) and 61.665 (sugar C-2), 20.458, 20.38, 20.37, 20.122 (4 -CH_3 of acetyl), IR (KBr ν_{max}, cm^{-1}): 2880 (C-H), 1751 (C=O), 1646 (C=N), 1580 (C=C), 1133 (C-O-C pyranose), 1082 (C-O pyranose).

2-(4-Hydroxy-3-methoxy benzylidene)imino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (x): Yield 2.0 g (64 %), m.p. 145-147 ºC. R_f 0.226 (9:1 ethylene dichloride:acetone), ^{1}H NMR (DMSO, 300 MHz) δ (ppm) 1.82 (s, 3H of acetyl), 2.02 (s, 9H of acetyl), 4.26 (q, 2H of sugar C-6), 4.98 (t, 1H of sugar C-4), 4.01 (q, 1H of sugar C-5), 3.442 (q, 1H of sugar C-2), 5.47 (t, 1H of sugar C-3), 6.07 (d, 1H of sugar C-1), 8.11 (s, 1H of CH=N), 3.76 (q, 3H of -OCH_3), 7.01, 7.2, 6.8 (m, 3H of aryl), 9.61 (s, 1H of Ar-OH). ^{13}C NMR (DMSO, 400 MHz) δ (ppm): 170.0, 168.9, 168.5 and 169.4 (4 C=O of acetyl), 164.7 (C=N), 150.0, 147.8, 127.9, 123.0, 115.27 and 110.38 (6 C's of aryl), 92.5 (sugar C-1), 72.39 (sugar C-5), 72.2 (sugar C-3), 71.4 (sugar C-4), 67.0 (sugar C-6) and 61.6 (sugar C-2), 20.47, 20.43, 20.39, 20.17 (4-CH_3 of acetyl), 55.5 (C of -OCH_3). IR (KBr, ν_{max}, cm^{-1}): 3392 (-OH), 1748 (C=O), 1639 (C=N), 1602 (C=C aromatic), 1512, 1122 (C-O-C pyranose), 1084 (C-O pyranose).

2-(3,4-Dimethoxy benzylidene)imino-2-deoxy-1,3,4,6-tetra-O-acetyl-β-D-glucopyranose (xi): Yield 2.16 g (67 %), m.p. 156 ºC. R_f 0.40 (9:1 ethylene dichloride:acetone), ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 1.8 (s, 3H of acetyl), 2.01 (s, 9H of acetyl), 4.23 (q, 2H of sugar C-6), 4.98 (t, 1H of sugar C-4), 4.01 (q, 1H of sugar C-5), 3.47 (q, 1H of sugar C-2), 5.49 (t, 1H of sugar C-3), 6.09 (d, 1H of sugar C-1), 8.23 (s, 1H of CH=N), 3.79 (d, 6H of -OCH_3), 7.01-7.244 (m of 3H of aryl). ^{13}C NMR (DMSO, 400 MHz) δ (ppm): 169.9, 168.9, 168.5 and 169.4 (4 C=O of acetyl), 164.6 (C=N), 151.6, 148.8, 128.3, 122.8, 111.3 and 109.4 (6 C's of aryl), 92.4 (sugar C-1), 72.30, (sugar C-5), 72.28 (sugar C-3), 71.4 (sugar C-4), 67.8 (sugar C-6) and 61.6 (sugar C-2), 20.49, 20.43, 20.40, 20.17 (4 -CH_3 of acetyl), 55.5, 55.4 (2 C's of -OCH_3). IR (KBr, ν_{max}, cm^{-1}): 1752 (C=O), 1643 (C=N), 1583 (C=C aromatic), 1519, 1140 (C-O-C pyranose), 1084 (C-O pyranose).

2-(5-Bromo-2-hydroxy benzylidene)imino-2-deoxy-1, 3,4,6-tetra-O-acetyl-β-D-glucopyranose (xii): Yield 3.0 g (87 %), m.p. 165 ºC, R_f 0.6 (8:2 $CHCl_3$:EtOAc), ^{1}H NMR (DMSO, 300 MHz) δ (ppm): 1.8 (s, 3H of acetyl), 2.01 (s, 9H of acetyl), 4.24 (q, 2H of sugar C-6), 4.94 (t, 1H of sugar C-4), 4.01 (q, 1H of sugar C-5), 3.57 (q, 1H of sugar C-2), 5.5 (t, 1H of sugar C-3), 6.1 (d, 1H of sugar C-1), 8.5 (s, 1H of CH=N), 6.83-7.40 (m, 3H of Aryl), 12.25 (s, 1H of Ar-OH). ^{13}C NMR (DMSO, 400 MHz) δ (ppm): 169.92, 169.341, 169.174 and 167.296 (4 C=O of acetyl), 159.014 (C=N), 135.40, 133.47, 120.46, 118.97, 109.74 and 109.74 (6 C's of aryl), 92.038

(sugar C-1), 72.21 (sugar C-5), 71.559 (sugar C-3), 70.979 (sugar C-4), 67.68 (sugar C-6) and 61.607 (sugar C-2), 20.443, 20.345, 20.345, 20.138 (4-CH_3 of acetyl). IR (KBr ν_{max}, cm^{-1}): 3418 (OH), 1752 (C=O), 1637 (C=N), 1593 (C=C aromatic), 1519, 1160 (C-O-C pyranose), 1087 (C-O pyranose).

RESULTS AND DISCUSSION

The preparation of tetraacetyl glucosamine was carried out by protecting the amino group of glucosamine with anisaldehyde (Schiff base formation). Acetylation of (**ii**) was carried out using acetic anhydride. Anisaldehyde Schiff base was formed in almost quantitative yield but the acetylation using acetic anhydride resulted in 65 % yield. The acetylation reaction requires addition of acetic anhydride to be done at 0-5 ºC. Higher temperature during addition of acetic anhydride resulted in difficulty during isolation of product or lower yields.

Deprotection of amino group was carried out using 6 N HCl solution. Use of concentrated HCl was avoided due to the lump formation and therefore dilution of HCl to 6 N is recommended during hydrolysis. Further dilution of HCl results in lower yields of tetraacetyl glucosamine hydrochloride (**iv**).

In the spectral interpretation of (**iii**) three ^{1}H NMR protons of acetyl at 1.8 ppm and 9 protons of acetyl at 2.01 ppm confirms the presence of four acetyl groups. The presence of imine proton (CH=N) at 8.2 ppm indicates the intactness of Schiff base during acetylation. This is also supported by presence of a peak at 1638 cm^{-1} in IR specific for (-C=N). The deprotection of (**iii**) carried out by 6 N HCl gave (**iv**) which was confirmed by absence of signal for imine proton and aromatic protons in ^{1}H NMR. This is also supported by disappearance of C=N (1638 cm^{-1}) and (C=C) aromatic (1605 cm^{-1}) frequency in IR.

The condensation of aromatic aldehydes (**v**, **vi**, **vii**, **viii**) with tetraacetyl glucosamine (**iv**) yielded corresponding Schiff bases (**ix**, **x**, **xi** and **xii**). As these Schiff bases are not reported so far they were characterized by IR, NMR and physical constants. These Schiff bases were formed in good yields.

^{1}H NMR, ^{13}C NMR and IR spectra confirmed the formation of Schiff bases. The shifting of signal for imine proton in ^{1}H NMR is observed for **xii** at 8.5 ppm, which is most downfield compared to others due to presence of bromo group which is electron withdrawing group. The other Schiff bases (**ix**, **x** and **xi**) showed signals at 8.33, 8.11 and 8.23 ppm, respectively. Further in ^{13}C NMR, compounds (**ix**, **x** and **xi**) show imine carbon (C=N) signals at 165.3, 164.6 and 164.7 ppm, respectively, where as for **xii** signal is present at 159.01 ppm. In ^{1}H NMR signals for aromatic protons for compounds (**ix**, **x**, **xi** and **xii**) are present between 6.8 to 7.7 ppm. The aromatic carbon signals in ^{13}C NMR are present between 109 to 135 ppm.

The presence of imine is also supported by IR signals at 1646, 1639, 1583 and 1637 cm^{-1} for compounds (**ix**, **x**, **xi** and **xii**), respectively. The difficulties in preparation of Schiff bases of glucosamine with benzaldehyde, veratraldehyde, vanillin and 5-bromosalicylaldehyde were overcome by preparing tetraacetyl glucosamine, which gave encouraging results for synthesis of Schiff bases with satisfactory yields.

ACKNOWLEDGEMENT

The authors are thankful to B.N. Bandodkar College of Science, Thane for extending their support for conducting this work.

REFERENCES

1. Z.E. Jolles and W.T.J. Morgan, *Biochem. J.*, **34**, 1183 (1940).
2. A. Cunha, L. Pereira and V. Ferreira, *J. Chem. Educ.*, **76**, 79 (1999).
3. J. Costamagna, L. Lillo, B. Matsuhiro, M. Noseda and M. Villagran, *Carbohyd. Res.*, **338**, 1535 (2003).
4. J.C. Irvine and J.C. Earl, *J. Chem. Soc.*, **121**, 2376 (1922).
5. M. Bergmann and L. Zervas, *Chem. Ber.*, **64B**, 975 (1931).

(*Received*: 26 June 2008; *Accepted*: 8 July 2009) AJC-7674