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Schiff bases from D-glucosamine and aliphatic ketones

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ABSTRACT

Despite the comprehensive literature and enormous versatility of chiral imines derived from aminosugars and aldehydes, the corresponding counterparts generated from ketones remain an underestimated research subject. Filling in the gap, this manuscript sheds light on the synthetic and structural aspects of such substances and updates the few antecedents reported so far.

1. Introduction

Imines or Schiff bases, compounds dating back to the early days of synthetic organic chemistry, are easily generated by condensation of carbonyl groups and primary amines. The process takes place with the intermediacy of a carbinolamine that undergoes further dehydration to give a double carbon–nitrogen bond.[1] In carbohydrate chemistry, a large number of imines has been reported, both by reaction of sugar aldehydes with amines and by reaction of aminosugars with aldehydes. Such inherently chiral imines have been employed in asymmetric syntheses serving the carbohydrate fragment as a chiral inductor. Thus, Kunz et al.[2] have applied Schiff bases from O-protected glycosylamines to asymmetric versions of Strecker,[3] Ugi,[4] Mannich,[5] tandem Mannich-Michael,[6] hetero-Diels–Alder,[7] and organometallics addition reactions.[8] Likewise, Georg et al. have employed such sugar imines in the Staudinger reaction.[9] As mentioned above, these Schiff bases can easily be prepared by condensation of protected glycosylamines with the corresponding aldehyde.[4,10,11] Ugi and associates have also used a thiosugar-derived glycosylimine in the stereoselective synthesis of α-amino acids and peptides.[12] Finally, sugar imines have been postulated as intermediates in the formation of glycosylamines[13,14] and in their mutarotation reactions.[15]

The first imines derived from 2-amino-2-deoxyaldoses were described by Irvine and Hynd as early as 1913.[16] Since such transformations take place in high yield, produce insoluble products, and give the starting aminosugar back by reaction with dilute acids, these authors suggest the salicylidene derivative to be a suitable method for isolating D-glucosamine from a reaction mixture of synthetic or natural origin.[16a] Moreover, sugar imines have proven to be a convenient strategy for protecting free amino groups,[17–31] and in this context O-protected imines have been prepared by reacting aldehydes with O-protected aminosugars[32–38,10] or the corresponding phosphinimine.[39]

In stark contrast with the relatively abundant information on sugar imines derived from aldehydes, there are, to the best of our knowledge, only two examples of carbohydrate imines from ketones, without clear-cut structural evidences. In the mid-1950s, Micheel and Wulff report one of these ketone derivatives (**2**) by treating an unprotected glycosylazide (**1**) with acetone in acid medium.[36] Notably, these authors also reported the failure to obtain the per-O-acetylated imine **3** by conventional acetylation; instead 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-D-glucopyranosyl azide (**4**), a product lacking the isopropylidene moiety, was described (Scheme 1).

The second imine (**7**), equally derived from acetone, was prepared by Fodor and coworkers,[40] who described it as an oxazolidine derivative (**6**) resulting from the migration of a vicinal acetyl to the free amino group at C-2 of compound **5**. However, a further re-assessment by Capon and associates evidenced the structure of imine **7** (Scheme 2).[41]

2. Results and discussion

In order to explore the chemistry of sugar imines derived from aliphatic ketones still further, disclosing new structural data and potential applications, a series of such compounds has been prepared and fully characterized.

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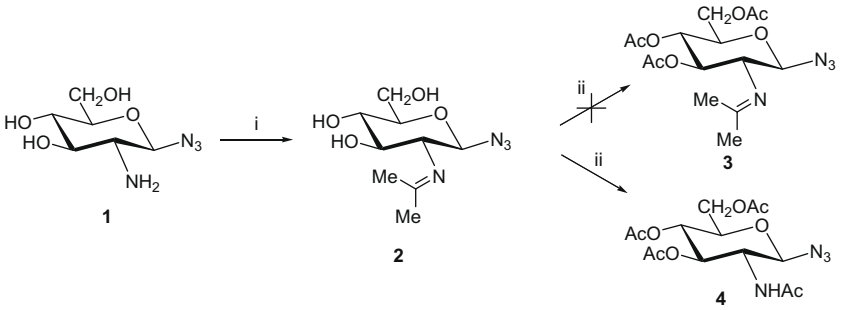
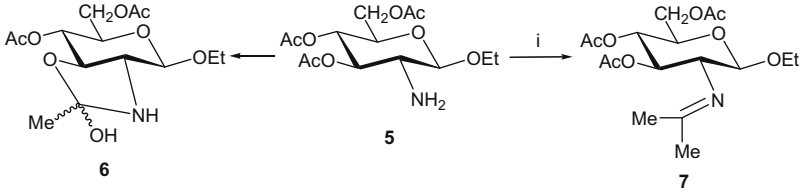


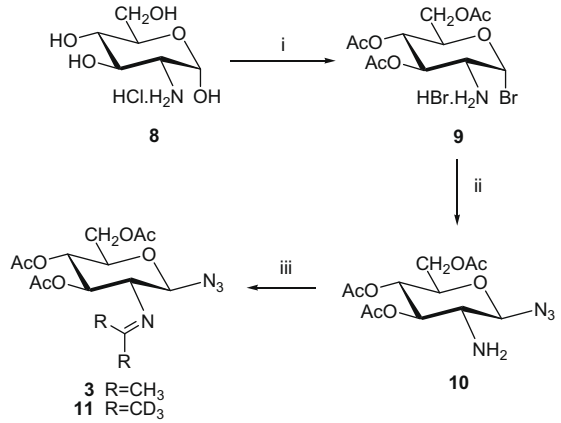
Scheme 1. Reagents: (i) CH_3COCH_3, HCl; (ii) Ac_2O, C_5H_5N.



Scheme 2. Reagents: (i) CH_3COCH_3.

Our starting point was the previous synthesis of Micheel and Wulff, who reported the facile synthesis of imine **2** by reaction of the unprotected azide **1** in acetone.[36] Extension of this protocol to D-glucosamine hydrochloride (**8**), deprotected as free base, was however unsuccessful. This fact points to a protection of the anomeric position, thus avoiding the formation of side products and diastereomeric mixtures. To this end, the synthesis of per-*O*-acetyl-D-glucopyranosyl azide (**10**) could easily be accomplished in a two-step protocol from **8**[35,42] (Scheme 3).

That imine formation occurs in the presence of aliphatic ketones could be sequentially determined by ^{1}H NMR monitoring of a solution of **10** in hexadeuterated acetone (Fig. 1). After three days at room temperature, the diagnostic proton signals of the starting material have almost disappeared, while a new signal set of equal multiplicity and coupling pattern, but markedly different chemical shifts, emerged, which should be attributed to the formation of compound **11**. The largest difference is observed for the H-2 proton, close to the nitrogen atom, which undergoes a strong deshielding ($\Delta\delta_{H\text{-}2}$ = 0.9 ppm). Similar effects, to a lesser extent in any case, are observed for the anomeric proton ($\Delta\delta_{H\text{-}1}$ = 0.3 ppm) and H-3 ($\Delta\delta_{H\text{-}3}$ = 0.2 ppm). Since the remaining signals undergo very small or negligible variations, one should reasonably conclude that the C=N bond has only appreciable effects on the vicinal atoms. The imine function can also be detected as a new carbon resonance at 172.48 ppm in the ^{13}C NMR spectrum (Table 1).



Scheme 3. Reagents: (i) CH_3COBr; (ii) AgN_3; (iii) CH_3COCH_3 or CD_3COCD_3.

The non-deuterated imine **3** could also be prepared by dissolving the starting azide (**10**) in acetone, evaporating the solvent after three days and crystallizing the residue from diethyl ether. Remarkably, this transformation can advantageously be monitored by polarimetry, on measuring the temporal variation of the optical rotation of compound **10** in acetone solution (Table 1, Fig. 2).

For comparative effects, we have also synthesized imines **12** and **13** (Scheme 4),[35] derived from anisaldehyde and salicylaldehyde, respectively, and evaluated their spectroscopic data.

The structures proposed for **3**, **12**, and **13** are supported by their elemental analysis and spectroscopic data. IR spectra of these compounds show the strong absorption for the azido group at ~2115 cm^{-1} along with a weaker band at ~1668 cm^{-1}, which is a characteristic of the imine functionality.

Both proton and carbon NMR spectra of **3** in $CDCl_3$ were almost coincidental with those recorded in acetone-d_6. The methyl groups of acetone show distinctive chemical shifts at 29.44 ppm and 19.44 ppm. Such a difference, similar to that observed for simple imines (e.g., Me_2C=NMe: 29.1 and 18.0 ppm),[43] also evidences the iminic structure attributed to **3**. The chemical shift for C-2 in **3** and **11** shows an appreciable deshielding ($\Delta\delta$ ~8 ppm) relative to the corresponding carbon atom in **10**, a fact supporting formation of the imino group. In addition, the high-resolution mass spectrum displays peaks corresponding to [M+Na^+] and [M+H^+] fragments (the latter with 100% intensity). Salient fragmentations also correspond to the loss of ketene and acetic acid, which are typical of monosaccharide acetyl derivatives.

In addition, the structure of **12**[44] was elucidated by single crystal X-ray diffraction analysis. The solid-state structure reveals an *E* configuration around the imine bond (Fig. 3).

As expected, the signal for the H-2 proton of **12** and **13** also undergoes a significant deshielding ($\Delta\delta_{H\text{-}2}$ = 0.43 ppm), although to a lesser extent than that of compounds **3** and **11**. In contrast, the deshielding for the C-2 atom of **12** and **13** is much larger ($\Delta\delta$ ~18 ppm) than that observed for **3** and **11**.

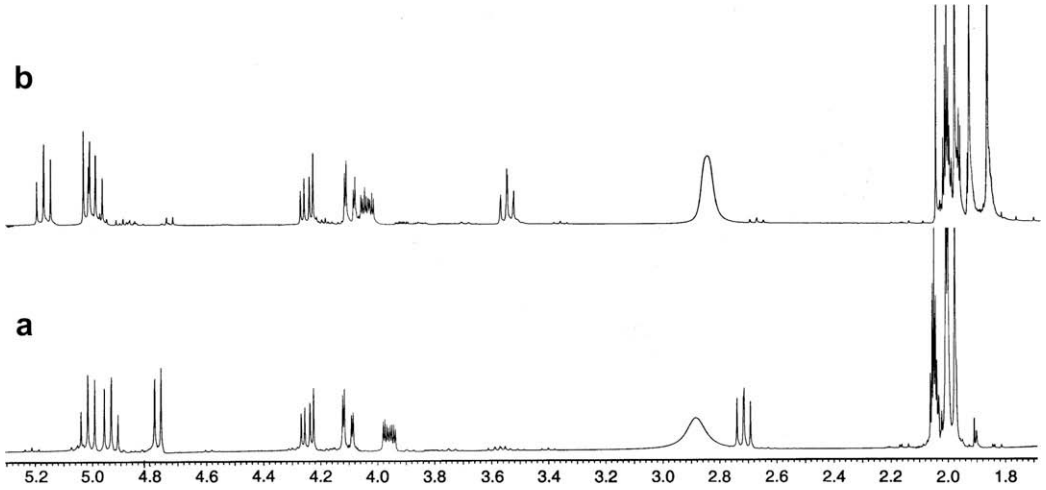


Figure 1. ^{1}H NMR spectra of compound **10** in acetone-d_6: (a) just dissolved, (b) after three days.

Table 1

t (h)	$[\alpha]_D$
5[a]	−14.8
2	−22.2
4.5	−34.8
6.5	−38.6
8.5	−40.4
23	−45.2
25	−46.0
26	−46.0
98	−51.2

[a] In min.

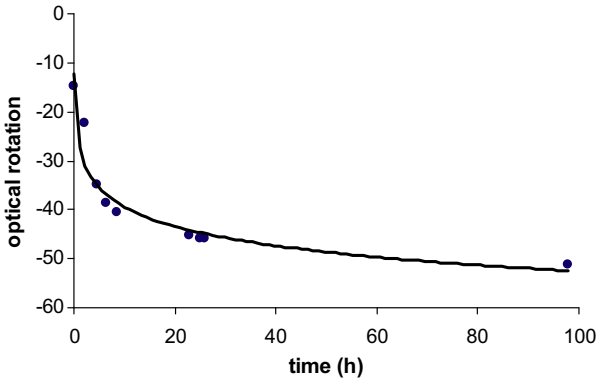
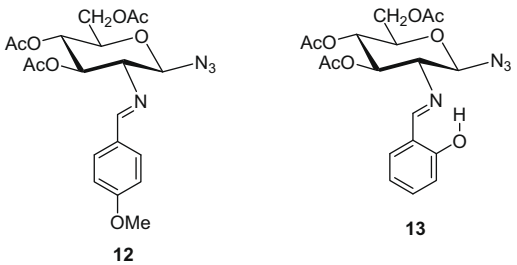


Figure 2. Plot of optical rotation (Table 1) versus time for the conversion of **10** to **3** in acetone.



Scheme 4.

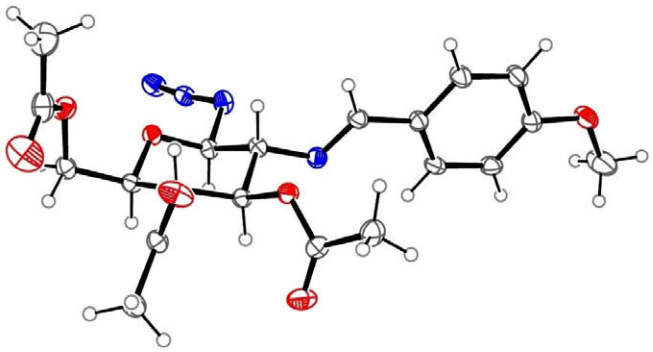


Figure 3. ORTEP diagram for **12**.

The hydroxy group of the phenolic moiety in **13** appears at 12.09 ppm, a deshielding pointing to a strong intramolecular hydrogen bond.

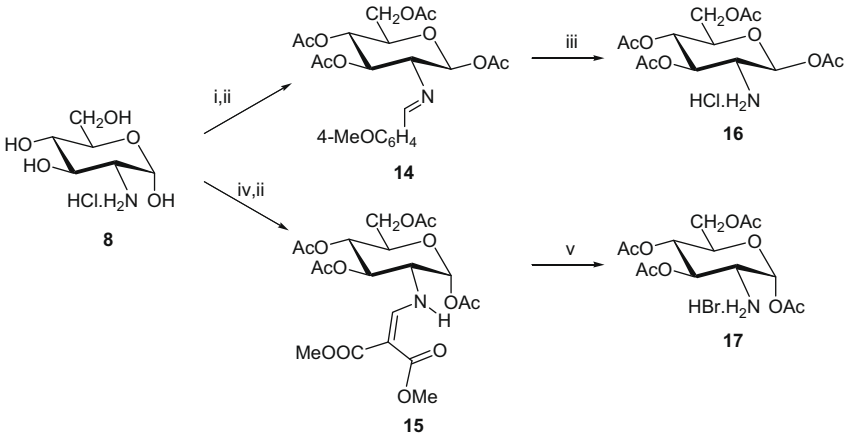
A similar study has been conducted for β and α 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-D-glucopyranoses (**18**[17] and **19**,[32,45] respectively), generated as free bases from their halohydrates **16**[17] and **17**,[32] which have also been obtained according to the well-established literature protocols (Scheme 5).

Similar results to those described for **10** can likewise be obtained in the case of imines **20** and **21**, whose formation has been gradually recorded by ^{1}H NMR in acetone-d_6. The non-deuterated imines **22** and **23** could also be isolated (Scheme 6).

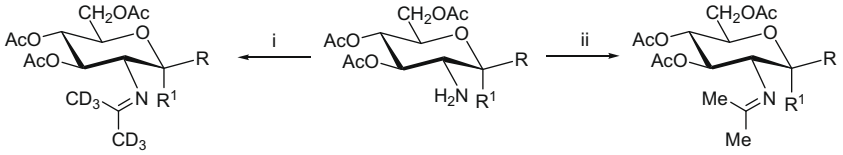
Within three to five days, the proton signals of the starting aminosugars have almost completely disappeared and replaced by those of the corresponding imines **20** and **21**. Likewise, the formation of imines **22** and **23** could also be monitored by polarimetry on measuring the temporal variation of the optical rotation of aminosugars **18** and **19** when dissolved in dry acetone.

Data collected in Table 2 reveal a series of significant variations in both proton and carbon resonances during imine formation. Thus, the H-2 proton undergoes a substantial change from ~3.0 ppm to ~3.9 ppm and C-2 from ~55 ppm to ~62 ppm. Again, the imino functionality (C=N bond) manifests itself as a typical carbon resonance at ~172 ppm in the ^{13}C NMR spectrum, as well as by its IR absorption at ~1650 cm^{-1} (stretching band). Consistent with the previous data, the methyl groups linked to the iminic carbon resonate at markedly different frequencies (corresponding to ~30 ppm and ~20 ppm).

For comparative purposes we were interested in assessing imines having β configuration (i.e., **14**) and α anomers (such as **24**). How-



Scheme 5. Reagents: (i) 4-MeOC$_6$H$_4$CHO, NaOH; (ii) Ac$_2$O, C$_5$H$_5$N; (iii) HCl 5 M, CH$_3$COCH$_3$; (iv) EtOCH=C(COOEt)$_2$, Et$_3$N, MeOH; (v) Br$_2$, H$_2$O, CHCl$_3$.



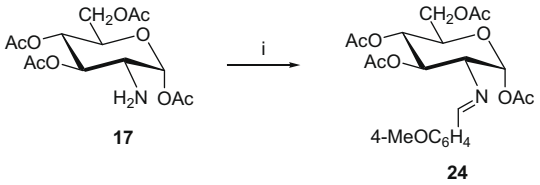
20 R=OAc, R^1=H
21 R=H, R^1=OAc
18 R=OAc, R^1=H
19 R=H, R^1=OAc
22 R=OAc, R^1=H
23 R=H, R^1=OAc

Scheme 6. Reagents: (i) CD$_3$COCD$_3$, (ii) CH$_3$COCH$_3$.

Table 2
NMR data (δ, ppm; J, Hz) of representative compounds

Compd	H-1	H-2	H-3	$J_{1,2}$	C=N	C-1	C-2	C-3
10[a]	4.77 d	2.71 t	5.02 t	8.8	—	92.44	56.95	74.82
10[b]	4.54 d	2.82 t	5.03 t	8.8	—	91.89	55.82	75.17
11[a]	5.06 d	3.59 t	5.21 t	8.6	172.48	90.80	65.05	74.54
3[b]	4.93 d	3.57 t	5.26 t	8.4	172.87	90.22	64.12	73.91
12[b]	5.04 d	3.25 t	5.38 t	8.3	164.80	89.56	73.94	73.12
13[b]	5.00 d	3.26 t	5.42 t	8.4	169.41	89.12	74.00	72.48
18[a]	5.59 d	2.90 t	5.10 t	8.4	—	95.23	55.50	72.28
18[b]	5.47 d	3.04 t	5.04 t	8.4	—	95.20	55.06	72.71
20[a]	5.81 d	3.77 t	5.30 t	8.4	171.28	93.76	63.55	73.77
22[b]	5.79 d	3.77 t	5.31 t	8.4	172.22	93.91	63.42	74.17
19[a]	6.07 d	3.04 dd	4.99 t	3.6	—	92.88	53.73	69.68
19[b]	6.20 d	3.13 dd	5.01 t	3.6	—	92.90	53.44	69.69
21[a]	6.01 d	3.98 dd	5.47 t	3.6	171.72	91.07	61.49	71.83
23[a]	6.07 d	3.89 dd	5.54 t	3.6	172.11	91.32	61.03	71.25
14[b]	5.95 d	3.45 t	5.43 t	8.3	164.29	93.14	73.23	72.73
24[b]	6.22 d	3.66 dd	5.60 t	3.6	164.28	91.80	71.14	70.05
28[b]	5.03 d	3.40 t	5.32 t	8.8	187.44	89.99	68.84	73.94
29[b]	4.93 d	3.60 t	5.27 t	8.4	176.91	90.27	64.23	73.97
30[b]	5.23 d	3.61 t	4.96 t	8.4	179.13	89.57	64.25	73.49

[a] In acetone-d_6 at 400 MHz.
[b] In CDCl$_3$ at 400 MHz.



Scheme 7. Reagents: (i) 4-MeOC$_6$H$_4$CHO.

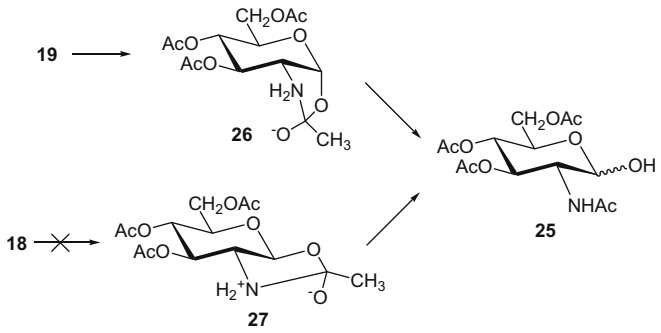
ever, compound **24** cannot be obtained by the procedure employed for the preparation of **14**. Alternatively, compound **24** can easily be generated by reaction of **17** with anisaldehyde (Scheme 7).

Elemental analyses of **22** and **24** as well as the high-resolution mass spectrum of **22** ([M+Na$^+$] and [M+H$^+$] peaks) fully agree with their structures. Again, the most relevant fragmentations correspond to sequential losses of acetic acid. An inspection of the coupling pattern in compounds **3**, **10**, **12**, and **13** evidences the same conformation ($^4C_1$) of the glucopyranose ring, as it occurs for **18**, **22**, and **24** as well as for **14**, **19**, and **23**.

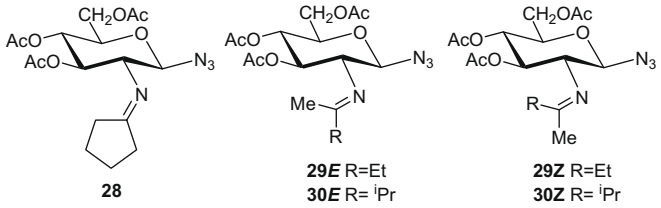
It is worthy to point out that both preparation and reactions of **19** (including work-up protocols) should be performed at 0 °C to avoid unwanted side products. This aminosugar underwent O→N acetyl migration leading to 2-acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-D-glucopyranose (**25**), which often contaminates the reaction mixture, thereby impeding to obtain the imine **23** as an analytically pure sample. In contrast, the opposite β anomer (**18**) does not experience this isomerization. Presumably, the *trans* relationship between the acetate at C-1 and the amino group at C-2 avoids the rearrangement as the intermediate adduct **27**, generated by intramolecular migration of the anomeric acetate, is considerably strained[46] and therefore less stable than **26** arising from the α anomer (Scheme 8).

These problems can be overcome by using compound **10** as the starting aminosugar for the preparation of other imines derived from aliphatic ketones. Thus, compound **28** (Scheme 9) could be isolated by reaction with clean cyclopentanone for three days at room temperature. Evaporation gave rise to an oily residue that crystallized on standing. Its IR spectrum showed the imine signal at ~1685 cm^{-1} and both proton and carbon shifts were similar to those encountered for compound **3**, although the proton H-2 undergoes a smaller variation (~0.6 ppm) when the imine **28** is generated than that observed for **11** (~0.9 ppm). The coupling pattern reveals no conformational change of the pyranose ring ($^4C_1$) with respect to the starting azide (**10**).

When the synthetic transformation was applied to 2-butanone and 3-methyl-2-butanone for six days at room temperature, the



Scheme 8.



Scheme 9.

corresponding imines (**29** and **30**) were obtained as mixtures of *E* and *Z* stereoisomers, in which the former is largely prevalent. Instead, 3,3-dimethyl-2-butanone led to a complex mixture, probably due to strong steric effects caused by the *tert*-butyl group.

The high-resolution mass spectrum of **30** shows the molecular peak [M+H$^+$] and fragmentations similar to those previously described. The imine function can equally be detected by the typical IR band of moderate intensity at ~1663 cm^{-1}. It is interesting to note that ^{1}H NMR monitoring of **29** reveals the facile decomposition of the imine derivative. Diagnostic signals of the imine can be inferred from its ^{1}H NMR spectrum such as the H-2 proton at 3.57 ppm, that is, a deshielding of ~0.8 ppm relative to that proton in azide **10**.

Although coupling constants are consistent with a $^4C_1$ conformation for the glucopyranose ring, the actual stereochemistry around the C=N bond for **29** and **30** cannot be unambiguously established. This should most likely correspond to an *E* geometry that minimizes the steric interactions among the different substituents. On the other hand, NOEs measured between the H-2 and imine protons in imines derived from aldehydes (**14** and **35**) are only compatible with an *E* configuration for the C=N bond (Fig. 4).

Additional information on the relative stability of both stereoisomers could be obtained from DFT calculations at the B3LYP/6-31G* level of theory[47,48] on **32**–**34**, the deacetylated analogs of **29**–**31**. Figure 6 shows the more stable conformations found for the *E* and *Z* isomers, the former being more stable (Table 3).

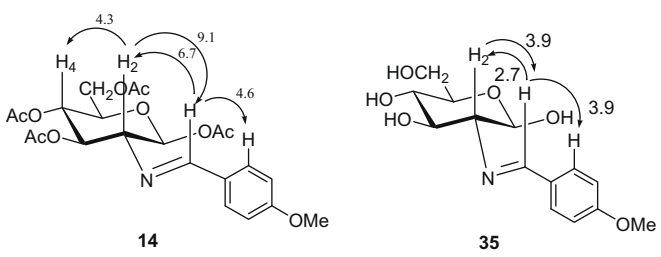


Figure 4. NOEs measured in compounds **14** and **35**.

The *E* stereochemistry certainly creates a allylic 1,3-strain between the H-2 proton and the methyl group of the imine (R = Me); however, the opposite *Z* geometry would give rise to a stronger 1,3-diaxial interaction between that proton and the ethyl, isopropyl or *tert*-butyl group (R = Et, ^{i}Pr, and ^{t}Bu). This interaction make them less stable and more susceptible to hydrolytic cleavage than their counterparts derived from aldehydes such as **12**–**14** and **24** (R = H, R^1 = Ar).

It is remarkable that in the geometries calculated above as well as in the solid-state structure elucidated for **12** (Fig. 3), the plane containing the imine functionality is roughly perpendicular to the mean plane of the pyranose ring. In other words, the imino group therefore adopts a preferential disposition relative to the pyranose ring in which the lone pair on the nitrogen atom is parallel to the axial substituents of the sugar skeleton (Fig. 6A). Moreover, the evaluation of NOE experiments likewise shows that imines derived from D-glucosamine adopt the same conformation in solution (Fig. 5), in both polar (DMSO-d_6, ε = 48.9, for **35**) and less polar solvents ($CDCl_3$, ε = 4.8, for **14**).

The conformational arrangement encountered in solution for imines derived from glycosylamines[4b] and aldehydes through NOE measurements[3,4b] (Fig. 6B) appears to be identical to that for imines derived from D-glucosamine. This particular conformation has been invoked to account for the stereoselectivity found in asymmetric reactions.[2–8] It has been argued that such a conformation arises from delocalization of the π electrons of the C=N bond into the σ^* orbital of the pyranose C–O-bond.[3,6] However, this delocalization cannot be attained in imines derived from D-glucosamine. In addition, *syn* arrangements of the $C_{amine}H$ and $C_{imine}H$ bonds are preferred for the lowest energy conformers of cyclohexane ring-substituted imines, according to both calculations (PM3 and DFT) and X-ray diffraction data.[49] Accordingly, the origin of these conformational features should largely be steric rather than stereoelectronic. In these conformations the C=N bond eclipses H-2 and, it is well established that eclipsed conformers of propene are more stable than gauche arrangements.[50,51] Furthermore, the eclipsed disposition is responsible to a significant extent of the strong deshielding that undergoes the H-2 proton in D-glucosamine imines. An analogous effect is provided by the carbonyl group in acyl derivatives (amides, ureas, and thioureas) of D-glucosamine in the *Z*-anti conformation, in which the plane containing the acyl moiety is approximately orthogonal to the mean plane of the pyranose ring.[52]

3. Conclusion

The present work constitutes the first detailed study on the Schiff bases formed by reaction of D-glucosamine with aliphatic ketones, a fact that contrasts with chiral imines derived from aminosugars and aldehydes which have been successfully employed in asymmetric transformations.

Previous syntheses of the title compounds, reported several decades ago, have been thoroughly reinvestigated, often with the help of the related model compounds. Formation of imines can be monitored by analytical and spectroscopic techniques. With non-symmetrical ketones, the formation of *E* and *Z* diastereomers is possible, although the former stereochemistry is prevalent. This observation is consistent with NOE experiments and DFT calculations of conformational stability.

Moreover, all data support a preferential disposition for the imino group in which the lone pair on the nitrogen atom is parallel to the axial substituents of the glucopyranose unit. Contrary to the previous arguments, the origin of this conformational feature lies in steric rather than stereoelectronic effects. Our rationale also supports the strong deshielding found experimentally for the H-2 resonance in D-glucosamine imines.

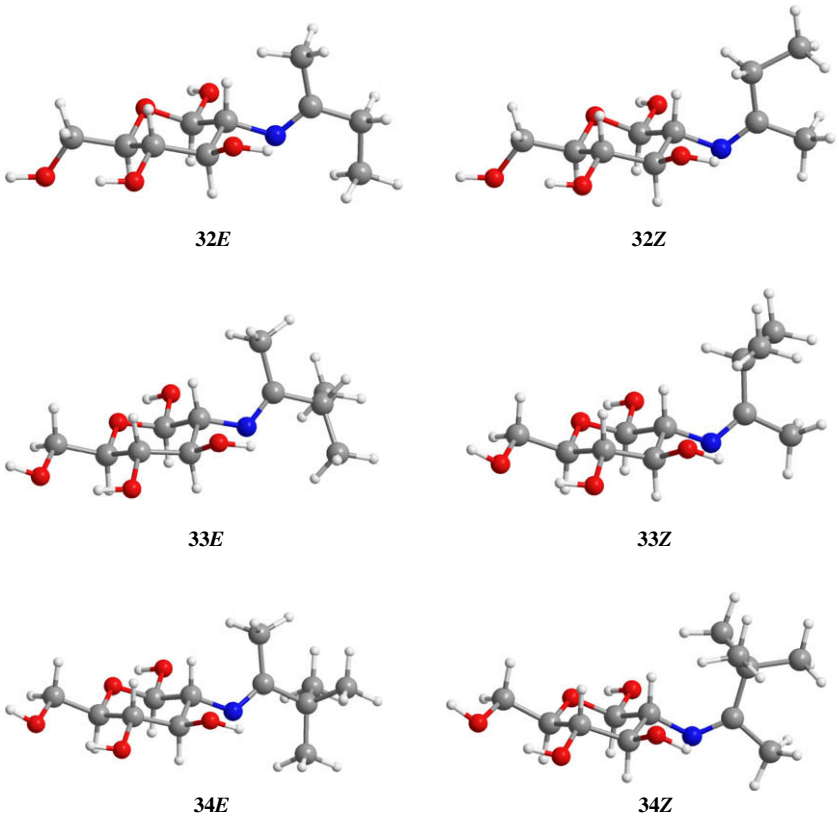


Figure 5. Stable conformations (at the B3LYP/6-31G* level) calculated for the *E* and *Z* isomers of **32**–**34**.

Table 3
Relative stability[a,b] for the *E* and *Z* isomers of **32**–**34**

Compound	E_E	E_Z	ΔE^c
32	−516640.292	−516638.006	2.29
33	−541309.267	−541308.174	1.09
34	−565970.720	−565977.493	6.77

[a] At B3LYP/6-31G*.
[b] In kcal mol^{-1}.
[c] $\Delta E = E_Z - E_E$.

4. Experimental

4.1. General methods

All solvents were purchased from commercial sources and were used as received unless otherwise stated. Melting points were determined with Gallenkamp and Electrothermal apparatus and are uncorrected. Optical rotations were measured at 20 ± 2 °C with a Perkin–Elmer 241 polarimeter. IR spectra were recorded in the range 4000–600 cm^{-1} with FT-IR THERMO spectrophotometer. Solid samples were recorded on KBr (Merck) pellets. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 instrument at 400 and 100 MHz, respectively, in different solvent systems. Assignments were confirmed by homo- and hetero-nuclear double-resonance and DEPT (distortionless enhancement by polarization transfer). TMS was used as the internal standard (δ = 0.00 ppm) and all *J* values are given in hertz. Microanalyses were determined with a Leco 932 analyser at the University of Extremadura (Spain). High-resolution mass spectra (chemical ionization) were recorded with a Micromass Autospec spectrometer by the 'Servicio de Espectrometría de Masas' of the University of Sevilla (Spain).

4.2. 3,4,6-Tri-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranosylazide (10)

To a suspension of AgN_3 in chloroform was added a solution of **9** (4.51 g, 10.90 mmol) in ethanol-free chloroform (40.0 mL). The mixture was refluxed under stirring at 60–70 °C. Then, it was filtered to eliminate the salts. Finally, it was evaporated to dryness and the obtained solid was recrystallized from EtOH (1.97 g, 55%); mp 124–126 °C (lit.[35] mp 123 °C); $[\alpha]_D^{25}$ −14.8; $[\alpha]_{578}^{25}$ −16.0 $[\alpha]_{546}^{25}$ −17.8; $[\alpha]_{436}^{25}$ −30.0 (*c* 0.5, dry acetone); $[\alpha]_{578}^{25}$ −18.8 $[\alpha]_{546}^{25}$ −19.0 (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 3375, 3326 (NH_2), 2964, 2855

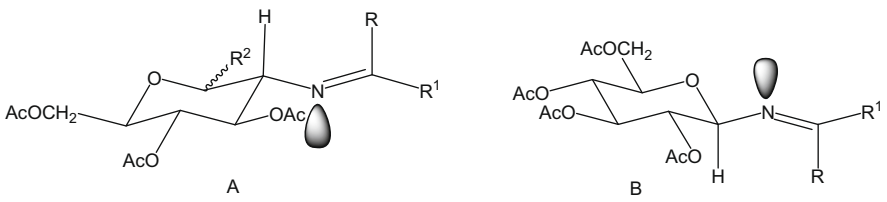


Figure 6. Preferential conformation of sugar imines derived from aldehydes (R = H) and ketones (R = R^1 = alkyl).

(CH_3), 2112 (N_3), 1758 (C=O), 1238 (C–O–C), 1104, 1058, 1041 (C–O) cm^{-1}; ^1H NMR (400 MHz, Me_2CO-d_6) δ 5.02 (t, 1H, $J_{3,4} = J_{2,3}$ 9.8 Hz, H-3), 4.93 (t, 1H, $J_{4,5} = J_{3,4}$ 9.6 Hz, H-4), 4.77 (d, 1H, $J_{1,2}$ 8.8 Hz, H-1), 4.25 (dd, 1H, $J_{5,6}$ 5.2 Hz, $J_{6,6'}$ 12.4 Hz, H-6), 4.10 (dd, 1H, $J_{5,6'}$ 2.2 Hz, $J_{6,6'}$ 12.2 Hz, H-6′), 3.96 (ddd, 1H, $J_{4,5}$ 10.0 Hz, $J_{5,6}$ 4.7 Hz, $J_{5,6'}$ 2.2 Hz, H-5), 2.71 (t, 1H, $J_{1,2} \approx J_{2,3}$ 9.4 Hz, H-2), 2.01, 2.00, 1.98 (s, 3 × 3H, CH_3); ^{13}C NMR (100 MHz, Me_2CO-d_6) δ 170.87, 170.26, 169.83 (4C=O), 92.44 (C-1), 56.95 (C-2), 75.82 (C-5), 74.54 (C-3), 65.05 (C-4), 62.87 (C-6), 20.80, 20.66, 20.55 (CH_3); ^1H NMR (400 MHz, $CDCl_3$) δ 5.03 (t, 1H, $J_{3,4} = J_{2,3}$ 9.4 Hz, H-3), 4.96 (t, 1H, $J_{4,5} = J_{3,4}$ 9.6 Hz, H-4), 4.54 (d, 1H, $J_{1,2}$ 8.8 Hz, H-1), 4.30 (dd, 1H, $J_{5,6}$ 4.8 Hz, $J_{6,6}$ 12.4 Hz, H-6), 4.14 (dd, 1H, $J_{5,6'}$ 2.4 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 3.78 (ddd, 1H, $J_{4,5}$ 9.6 Hz, $J_{5,6}$ 4.8 Hz, $J_{5,6'}$ 2.4 Hz, H-5), 2.82 (t, 1H, $J_{1,2} \approx J_{2,3}$ 9.4 Hz, H-2), 2.10, 2.08, 2.03 (s, 3 × 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 170.64, 169.62 (3C=O), 91.89 (C-1), 75.17 (C-5), 73.94 (C-3), 68.30 (C-4), 61.98 (C-6), 55.82 (C-2), 20.75, 20.73, 20.62 (CH_3).

4.3. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-isopropylidenamino-β-D-glucopyranosylazide (3)

A solution of **10** (0.50 g, 1.51 mmol) in dry acetone (25.0 mL) was kept for 40 h at room temperature. Then, the solvent was evaporated and the process was repeated, another solution in dry acetone (25.0 mL) was prepared and was kept for 40 h. After this, the solvent was evaporated and the residue was dried in vacuum (0.54 g, 97%); Mp 137–139 °C; $[\alpha]_D^{25}$ −51.2; $[\alpha]_{578}^{25}$ −66.6; $[\alpha]_{546}^{25}$ −63.2; $[\alpha]_{436}^{25}$ −47.8 (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 2114 (N_3, azide), 1747 (C=O, ester), 1668 (C=N), 1240 (C–O–C, ester), 1106, 1065, 1032 cm^{-1} (C–O); ^1H NMR (400 MHz, $CDCl_3$) δ 5.26 (t, 1H, $J_{3,4} = J_{2,3}$ 9.6 Hz, H-3), 5.11 (t, 1H, $J_{3,4} = J_{4,5}$ 9.8 Hz, H-4), 4.93 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 4.37 (dd, 1H, $J_{5,6}$ 4.8 Hz, $J_{6,6'}$ 12.4 Hz, H-6), 4.18 (dd, 1H, $J_{5,6'}$ 2.0 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 3.88 (ddd, 1H, $J_{4,5}$ 10.0 Hz, $J_{5,6}$ 4.8 Hz, $J_{5,6'}$ 2.0 Hz, H-5), 3.57 (t, 1H, $J_{1,2}$ 8.8 Hz, $J_{2,3}$ 9.6 Hz, H-2), 2.12, 2.05, 1.97, 1.94 (s, 5 × 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 172.87 (C=N), 170.87, 170.26, 169.83 (4C=O), 90.22 (C-1), 73.91 (C-3), 73.79 (C-5), 68.05 (C-4), 64.14 (C-2), 61.87 (C-6), 20.65, 20.53 (CH_3). Anal Calcd for $C_{15}H_{22}N_4O_7$: C, 48.64; H, 5.99; N, 15.13. Found: C, 48.33; H, 6.05; N, 15.01. HRMS-FAB calcd for $C_{15}H_{22}N_4O_7[M+Na]^+$: 393.1386; found: 393.1397.

4.4. Spectroscopic data of 3,4,6-tri-*O*-acetyl-2-deoxy-2-hexadeuterio-isopropyliden-amino-β-D-glucopyranosylazide (11)

^1H NMR (400 MHz, Me_2CO-d_6) δ 5.21 (t, 1H, $J_{3,4} = J_{2,3}$ 9.8 Hz, H-3), 5.03 (t, 1H, $J_{3,4} = J_{4,5}$ 8.6 Hz, H-4), 5.06 (d, 1H, $J_{1,2}$ 7.2 Hz, H-1), 4.29 (dd, 1H, $J_{5,6}$ 5.2 Hz, $J_{6,6'}$ 12.4 Hz, H-6), 4.14 (dd, 1H, $J_{5,6'}$ 2.4 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 4.08 (ddd, 1H, $J_{4,5}$ 10.0 Hz, $J_{5,6}$ 5.4 Hz, $J_{5,6'}$ 2.2 Hz, H-5), 3.59 (t, 1H, $J_{1,2}$ 8.6 Hz, $J_{2,3}$ 9.8 Hz, H-2), 2.02, 1.97, 1.91 (s, 5 × 3H, CH_3). ^{13}C NMR (100 MHz, Me_2CO-d_6): 172.48 (C=N), 170.80. 170.29, 169.83 (4C=O), 90.80 (C-1), 74.54 (C-3), 74.54 (C-5), 69.24 (C-4), 65.05 (C-2), 62.87 (C-6), 20.65, 20.53 (CH_3).

4.5. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(4-methoxybenzylidenamino)-β-D-glucopyranosyl-azide (12)

To a solution of **10** (0.033 g, 0.1 mmol) in MeOH (1 mL) was added a solution of 4-methoxybenzaldehyde (0.012 mL, 0.1 mmol) in MeOH (1 mL). The solution was stirred until a solid appeared, then was maintained in the refrigerator for a few hours. The solid was filtered, washed with a cold methanol and the product was recrystallized from MeOH (0.04 g, 90%). Mp 134–136 °C; [Lit.[35] mp 134 °C]; $[\alpha]_D^{23}$ +34.0; $[\alpha]_{578}^{23}$ +36.8; $[\alpha]_{546}^{23}$ +44.0; $[\alpha]_{436}^{23}$ +109.4 (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 2361 (N_3), 1749 (C=O), 1639 (C=N), 1604, 1513 (arom), 1240 (C–O–C, ester), 1037 cm^{-1} (C–O); ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H, N=CH), 7.67 (d, *J* 8.8 Hz, 2H, H-arom), 6.92 (d, 2H, *J* 8.8 Hz, H-arom), 5.38 (t, 1H, $J_{3,4} = J_{2,3}$ 9.6 Hz, H-3), 5.12 (t, 1H, $J_{3,4} = J_{4,5}$ 9.8 Hz, H-4), 5.04 (d, 1H, $J_{1,2}$ 8.3 Hz, H-1), 4.37 (dd, 1H, $J_{5,6}$ 5.0 Hz, $J_{6,6'}$ 12.4 Hz, H-6), 4.19 (dd, 1H, $J_{5,6'}$ 2.4 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 3.92 (ddd, 1H, $J_{4,5}$ 10.1 Hz, $J_{5,6}$ 4.8 Hz, $J_{5,6'}$ 2.4 Hz, H-5), 3.85 (s, 3H, OCH_3), 3.25 (t, 1H, $J_{1,2} \approx J_{2,3}$ 9.2 Hz, H-2), 2.13, 2.04, 1.88 (s, 3 × 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 170.65, 169.75, 169.53 (C=O), 164.80 (N=C), 162.29, 130.32, 128.07, 114.03 (C-arom), 89.56 (C-1), 73.94 (C-2), 73.69 (C-5), 73.12 (C-3), 67.96 (C-4), 61.96 (C-6), 55.38 (OCH_3), 20.74, 20.62, 20.47 (CH_3).

4.6. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2-hydroxybenzylidenamino)-β-D-glucopyranosylazide (13)

This compound was synthesized following the recipe for compound **12** (0.024 g, 56%); Mp 88–90 °C; [Lit.[35] mp 95 °C]; $[\alpha]_D^{24}$ −6.0; $[\alpha]_{578}^{24}$ −6.4; $[\alpha]_{546}^{24}$ −7.4; $[\alpha]_{436}^{24}$ −15.6 (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 2118 (N_3), 1753, 1742 (C=O), 1629 (C=N), 1578 (arom), 1279, 1239 (C–O–C, ester), 1040 cm^{-1} (C–O); ^1H NMR (400 MHz, $CDCl_3$) δ 12.09 (s, 1H, OH-arom), 8.33 (s, 1H, N=CH), 7.37 (t, 1H, H-arom), 7.31 (d, 1H, H-arom), 6.97 (t, 1H, H-arom), 6.92 (t, 1H, H-arom), 5.42 (t, 1H, $J_{3,4} = J_{2,3}$ 9.8 Hz, H-3), 5.13 (t, 1H, $J_{3,4} = J_{4,5}$ 9.8 Hz, H-4), 5.00 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 4.37 (dd, 1H, $J_{5,6}$ 4.8 Hz, $J_{6,6'}$ 12.4 Hz, H-6), 4.19 (dd, 1H, $J_{5,6'}$ 2.4 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 3.95 (ddd, 1H, $J_{4,5}$ 10.0 Hz, $J_{5,6}$ 4.8 Hz, $J_{5,6'}$ 1.6 Hz, H-5), 3.26 (t, 1H, $J_{1,2} \approx J_{2,3}$ 9.0 Hz, H-2), 2.12, 2.05, 1.92 (s, 3 × 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 170.72, 170.59, 169.68, 169.50 (C=O), 169.41 (N=C), 160.86, 133.50, 132.17, 119.04, 118.07, 117.28 (C-arom), 89.13 (C-1), 74.00 (C-2), 73.06 (C-5), 72.48 (C-3), 67.78 (C-4), 61.81 (C-6), 20.83, 20.71, 20.59, 20.44 (CH_3).

4.7. 1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose (18)

To compound **16** (1.0 g, 2.61 mmol) were added water (10 mL) and CH_2Cl_2 and the mixture was treated with $NaHCO_3$ (0.2 g). Then, the aqueous phase was extracted three times more with 10, 5, and 3 mL of CH_2Cl_2. Finally, it was dried ($MgSO_4$) and evaporated to dryness (0.6 g, 66%); mp 141 °C [Lit.[17] mp 143 °C, $[\alpha]_D$ +25.9° (chloroform)]; $[\alpha]_D^{25}$ +20.0; $[\alpha]_{578}^{25}$ +20.8; $[\alpha]_{546}^{25}$ +24.0; $[\alpha]_{436}^{25}$ +42.2 (*c* 0.5, dry acetone); IR (KBr) ν_{max} 3000–2597 NH_3^+, 2920 (OCH_3), 1755, 1738 (C=O), 1242, 1212 (C–O–C, ester), 1072, 1031, 1016 (C–O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.47 (d, 1H, $J_{1,2}$ 8,4 Hz, H-1), 5.04 (m, 2H, H-3 and H-4), 4.34 (dd, 1H, $J_{6,6'}$ 12.4 Hz, $J_{5,6}$ 4.4 Hz, H-6), 4.09 (dd, 1H, $J_{6,6'}$ 12.4 Hz, $J_{5,6'}$ 2.0 Hz, H-6′), 3.82 (ddd, 1H, $J_{4,5}$ 9.6 Hz, $J_{5,6}$ 4.4 Hz, $J_{5,6'}$ 2.5 Hz, H-5), 3.04 (t, 1H, $J_{1,2}$ 8,4 Hz, H-2), 2.19, 2.11, 2.09, 2.04 (4 × 3H, s, CH_3), 1.22 (2H, br s, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.66, 169.63, 169.69, 169.20 (4C=O), 95.26 (C-1), 75.11 (C-5), 72.71 (C-3), 68.22 (C-4), 61.77 (C-6), 55.06 (C-2), 20.97, 20.78, 20.65 (CH_3); ^1H NMR (400 MHz, Me_2CO-d_6) δ 5.59 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 5.10 (t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.96 (t, 1H, $J_{3,4} = J_{4,5}$ 9.6 Hz, H-4), 4.24 (dd, 1H, $J_{5,6}$ 4.8 Hz, $J_{6,6'}$ 12.4 Hz, H-6), 4.06 (dd, 1H, $J_{5,6}$ 2.4 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 3.97 (ddd, 1H, $J_{4,5}$ 10.0 Hz, $J_{5,6}$ 2.4 Hz, $J_{5,6'}$ 4.8 Hz, H-5), 2.90 (dd, 1H, $J_{1,2}$ 8.6 Hz, $J_{2,3}$ 10.4 Hz, H-2), 2.12, 2.02, 2.01, 1.99 (s, 4 × 3H, CH_3), 1.57 (br s, 1H, NH_2) ppm; ^{13}C NMR (100 MHz, Me_2CO-d_6): 169.87, 169.81, 169.27, 168.86 (4C=O), 95.23 (C-1), 74.86 (C-5), 72.28 (C-3), 68.59 (C-4), 61.88 (C-6), 55.50 (C-2), 19.95, 19.92, 19.80, 19.76 (CH_3).

4.8. 1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-α-D-glucopyranose (19)

To compound **17** (1.0 g, 2.34 mmol) was added water (10 mL) and CH_2Cl_2 (10 mL), the mixture was treated with $NaHCO_3$ (0.2 g). Then, the organic phase was separated and the aqueous

phase was extracted three times more with 10, 5, and 3 mL of CH_2Cl_2. Finally, it was dried and evaporated to dryness (0.7 g, 66%); Mp 119–121 °C; $[\alpha]_{578}^{24}$ +133.2; $[\alpha]_{546}^{24}$ +126.4; $[\alpha]_{436}^{24}$ +95.2 (*c* 0.5, $CHCl_3$); [Lit.[32] mp 118–9 °C; $[\alpha]_D$ +145.5° (*c* 1, $CHCl_3$)]; IR (KBr) ν_{max} 3380, 3293 (NH_2), 2992, 2910 (CH_3), 1753, 1736 (C=O), 1600 (NH_2), 1256, 1234 (C–O–C), 1110, 1074, 1040, 1020 (C–O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.20 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.16 (d, 1H, $J_{3,4} = J_{4,5}$ 10.0 Hz, H-4), 5.01 (dd, 1H, $J_{2,3} = J_{3,4}$ 9.7 Hz, H-3), 4.29 (dd, 1H, $J_{6,5}$ 3.8 Hz, $J_{6,6'}$ 12.2 Hz, H-6), 4.06 (m, 2H, H-5, H-6′), 3.13 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 10.4 Hz, H-2), 2.19 (s, 3H, OCH_3), 2.10, 2.08, 2.04 (m, 3 × 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.91, 170.58, 169.52, 169.02 (C=O, acetates), 92.90 (C-1), 73.99 (C-5), 69.69 (C-3), 68.17 (C-4), 61.72 (C-6), 53.44 (C-2), 20.86, 20.79, 20.65, 20.58 (OAc) ppm; ^1H NMR (400 MHz, acetone-d_6) δ 6.08 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.13 (d, 1H, $J_{3,4} = J_{4,5}$ 10.0 Hz, H-4), 5.00 (t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.21 (dd, 1H, $J_{6,5}$ 4.4 Hz, $J_{6,6'}$ 12.0 Hz, H-6), 4.11 (ddd, 1H, $J_{4,5}$ 10.0 Hz, $J_{5,6}$ 4.4 Hz, $J_{5,6'}$ 2.4 Hz, H-5), 4.01 (dd, 1H, $J_{5,6'}$ 2.4 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 3.06 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 10.4 Hz, H-2), 2.19, 2.07, 2.03, 2.00 (s, 4 × 3H, OCH_3) ppm; ^{13}C NMR (100 MHz, Me_2CO-d_6) δ 170.13, 169.80, 169.14, 169.00 (C=O, acetates), 92.88 (C-1), 73.71 (C-5), 69.68 (C-3), 68.47 (C-4), 61.82 (C-6), 53.73 (C-2), 19.95, 19.78, 19.74 (OAc) ppm.

4.9. 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-isopropylidenamino-β-D-glucopyranose (22)

Compound **18** (0.54 g, 1.55 mmol) was dissolved in dry Me_2CO (25.0 mL), and was kept at room temperature for 40 h. Then, it was evaporated to dryness and another 25.0 mL of dry Me_2CO was added. After 40 h the solvent was evaporated and the residue was dried in vacuum (0.42 g, 70%); mp 129–130 °C; $[\alpha]_D^{28}$ +7.2; $[\alpha]_{578}^{28}$ +7.4; $[\alpha]_{546}^{28}$ +8.8; $[\alpha]_{436}^{28}$ +17.6 (*c* 0.5, dry Me_2CO); $[\alpha]_D^{28}$ +11.6; $[\alpha]_{578}^{28}$ +13.0; $[\alpha]_{546}^{28}$ +14.2; $[\alpha]_{436}^{28}$ +28.0 (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 2952, 2907 (CH_3), 1756, 1732 (C=O), 1663 (C=N), 1242 (C–O–C, ester), 1100, 1077, 1046 (C–O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.78 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 5.31 (t, 1H, $J_{3,4} = J_{2,3}$ 9.4 Hz, H-3), 5.12 (t, 1H, $J_{3,4} = J_{4,5}$ 9.8 Hz, H-4), 4.37 (dd, 1H, $J_{5,6}$ 4.4 Hz, $J_{6,6'}$ 12.4 Hz, H-6), 4.10 (dd, 1H, $J_{5,6'}$ 2.2 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 3.92 (ddd, 1H, $J_{4,5}$ 10.2 Hz, $J_{5,6}$ 4.4 Hz, $J_{5,6'}$ 2.4 Hz, H-5), 3.78 (dd, 1H, $J_{1,2}$ 8.4 Hz, $J_{2,3}$ 9.8 Hz, H-2), 2.09, 2.06, 2.02, 1.99, 1.94, 1.92 (s, 6 × 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 172.22 (N=C), 170.68, 169.97, 169.44, 168.61 (C=O), 93.91 (C-1), 74.17 (C-3), 72.64 (C-5), 68.16 (C-4), 63.42 (C-2), 61.78 (C-6), 29.51 (2C, CH_3, isopropyl), 20.88, 20.78, 20.70, 20.61, 19.36 (5C, CH_3). Anal. Calcd for $C_{17}H_{25}NO_9$: C, 52.71; H, 6.50; N, 3.62. Found: C, 52.41; H, 6.30; N, 3.71. HRMS-FAB calcd for $C_{17}H_{25}N_4O_9[M+Na]^+$: 410.1419; found: 410.1427.

4.10. Spectroscopic data of 3,4,6-tri-*O*-acetyl-2-deoxy-2-*hexadeuterio*-isopropyliden-amino-β-D-glucopyranose (20)

^1H NMR (400 MHz, Me_2CO-d_6) δ 5.81 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 5.30 (t, 1H, $J_{3,4} = J_{2,3}$ 9.6 Hz, H-3), 5.03 (t, 1H, $J_{3,4} = J_{4,5}$ 9.6 Hz, H-4), 4.31 (dd, 1H, $J_{5,6}$ 5.0 Hz, $J_{6,6'}$ 13.0 Hz, H-6), 4.09 (d, 1H, $J_{6,6'}$ 10.8 Hz, H-6′), 4.08 (m, 1H, H-5), 3.77 (dd, 1H, $J_{1,2}$ 8.0 Hz, $J_{1,2}$ 9.6 Hz, H-2), 2.03, 2.02, 1.99, 1.96, 1.93, 1.92 (s, 6 × 3H, CH_3) ppm; ^{13}C NMR (100 MHz, Me_2CO-d_6): 171.28 (N=C), 169.80, 169.34, 168.84, 168.34 (C=O), 93.76 (C-1), 73.77 (C-3), 72.41 (C-5), 68.40 (C-4), 63.55 (C-2), 61.86 (C-6), 19.81, 19.71, 19.69, 18.28 (4C, CH_3).

4.11. 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-isopropylidenamino-α-D-glucopyranose (23)

Compound **19** (0.50 g, 1.44 mmol) was dissolved in dry Me_2CO (25.0 mL), and was kept for 40 h at room temperature. After this, the solvent was evaporated and another 25.0 mL of dry Me_2CO was added. After three days, the solvent was evaporated and the residue was dried in vacuum. $[\alpha]_D^{26}$ +80.2; $[\alpha]_{578}^{26}$ +84.4; $[\alpha]_{546}^{26}$ +95.1; $[\alpha]_{436}^{26}$ +157.3 (*c* 0.5, dry Me_2CO). IR (KBr) ν_{max} 2980, 2904 (CH_3), 1753 (C=O), 1663 (C=N), 1224 (C–O–C, ester), 1069, 1040 (C–O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.07 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.54 (t, 1H, $J_{3,4} = J_{2,3}$ 9.8 Hz, H-3), 5.15 (t, 1H, $J_{3,4} = J_{4,5}$ 10.2 Hz, H-4), 4.35 (dd, 1H, $J_{5,6}$ 3.8 Hz, $J_{6,6'}$ 12.2 Hz, H-6), 4.22 (m, 1H, H-5), 4.08 (m, 1H, H-6′), 3.89 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 10.0 Hz, H-2), 2.18, 2.09, 2.03, 2.00, 1.97, 1.95 (s, 6 × 3H, CH_3) ppm.

4.12. Spectroscopic data of 3,4,6-tri-*O*-acetyl-2-deoxy-2-*hexadeuterio*-isopropyliden-amino-α-D-glucopyranose (21)

^1H NMR (400 MHz, Me_2CO-d_6) δ 6.01 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.47 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.6 Hz, H-3), 5.12 (t, 1H, $J_{3,4} = J_{4,5}$ = 9.6 Hz, H-4), 4.24 (m, 1H, H-6, H-5), 4.05 (dd, 1H, $J_{6,6'}$ 12.0 Hz, $J_{5,6'}$ 1.2 Hz, H-6′), 3.98 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 10.0 Hz, H-2), 2.14, 2.07, 2.06, 2.05, 2.03, 1.92 (s, 6 × 3H, CH_3) ppm. ^{13}C NMR (100 MHz, Me_2CO-d_6): 171.72 (N=C), 169.78, 169.27, 169.06, 168.64 (C=O), 91.05 (C-1), 71.83 (C-3), 70.03 (C-5), 68.58 (C-4), 61.94 (C-6), 61.49 (C-2), 19.97, 19.79, 19.76 (4C, CH_3) ppm.

4.13. 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-(4-methoxybenzylidene)amino–D-glucopyranose (24)

To a suspension of **17** (1.4 g, 3.0 mmol) in EtOH 96% (14 mL) was added sodium acetate trihydrate (0.41 g, 3.0 mmol) dissolved in a mixture of water (2 mL) and pyridine (0.8 mL). Then, the 4-methoxybenzaldehyde was added (3.0 mmol) the mixture was heated for 2 min in a bath of boiling water. The solution was filtered to eliminate the impurities and kept to room temperature. When the solution was cooled the product crystallized. The solution was kept at room temperature for an hour and then maintained in the refrigerator. Finally, it was filtered, washed with a cooled mixture of EtOH–H_2O 50% and was dried in vacuum (0.44 g, 32%); Recrystallized from EtOH had mp 181–183 °C; $[\alpha]_D^{24}$ +104.2; $[\alpha]_{578}^{24}$ +108.8; $[\alpha]_{546}^{24}$ +126.0, $[\alpha]_{436}^{24}$ +240.6; $[\alpha]_{365}^{24}$ +474.2 (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 2857 (C–O, OCH_3), 1746 (C=O), 1643 (C=N), 1617, 1514 (arom), 1250 (C–O–C, ester), 1154, 1030 (C–O) and 841 cm^{-1} (arom); ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H, CH=), 7.62 (d, 2H, arom), 6.90 (d, 2H, arom), 6.22 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.60 (t, 1H, $J_{3,4} = J_{4,5}$ 9.8 Hz, H-4), 5.18 (t, 1H, $J_{2,3} = J_{3,4}$ 9.8 Hz, H-3), 4.35 (dd, 1H, $J_{5,6}$ 4.2 Hz, $J_{6,6}$12.3 Hz, H-6), 4.25 (ddd, 1H, $J_{4,5}$ 10.2 Hz, $J_{5,6}$ 4.0 Hz, $J_{5,6'}$ 2.1 Hz, H-5), 4.12 (dd, 1H, $J_{5,6'}$ 2.1 Hz, $J_{6,6'}$ 12.3 Hz, H-6′), 3.84 (s, 3H, OCH_3), 3.66 (dd, 1H,$J_{1,2}$ 3.6 Hz, $J_{2,3}$ 10.1 Hz, H-2), 2.21, 2.10, 2.05, 1.88 (s, 4 × 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): 170.64 (C=O), 169.81 (2C= O), 168.96 (C=O), 164.28 (CH=N), 162.23 (C-arom), 130.20 (2C-arom), 128.38 (C-arom), 113.97 (2C-arom), 91.80 (C-1), 71.14 (C-2), 70.87 (C-5), 70.05 (C-3), 68.30 (C-4), 61.90 (C-6), 55.34 (OCH_3), 21.00, 20.70, 20.65, 20.55 (CH_3). Anal. Calcd for $C_{22}H_{27}O_{10}N$: C, 56.77; H, 5.85; N, 3.01. Found: C, 56.42; H, 5.76; N, 3.13.

4.14. 3,4,6-Tri-*O*-acetyl-2-deoxy-2-cyclopentylidenamino-β-D-glucopyranosylazide (28)

A solution of **10** (0.15 g, 0.45 mmol) in cyclopentanone (10.0 mL) was kept for 3 days at room temperature. Then, the solvent was evaporated and a syrup was obtained (0.16 g, 27%); IR (KBr) ν_{max} 2964, 2920 (CH_3), 2117 (N_3), 1747 (C=O), 1685 (C=N), 1241 (C–O–C), 1065, 1038 (C–O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.32 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 5.09 (t, 1H, $J_{3,4} = J_{4,5}$ 9.6 Hz, H-4), 5.03 (d, 1H, $J_{1,2}$ 8.8 Hz, H-1), 4.35 (dd, 1H, $J_{5,6}$ 4.4 Hz, $J_{6,6'}$ 12.4 Hz, H-6), 4.16 (dd, 1H, $J_{5,6'}$ 2.0 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 3.90 (ddd, 1H, $J_{4,5}$ 10.0 Hz, $J_{5,6}$ 4.8 Hz, $J_{5,6'}$ 2.0 Hz, H-5), 3.40 (t, 1H, $J_{1,2} = J_{2,3}$ 9.6 Hz,

H-2), 2.45 (m, 2H, CH_2), 2.33 (m, 2H, CH_2), 1.95 (m, 2H, CH_2), 1.77 (m, 2H, CH_2), 2.11, 2.03, 1.96 (s, 3 × 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 187.44 (C=N), 170.69, 169.87, 169.38 (3C, C=O), 89.99 (C-1), 73.94 (C-3), 73.87 (C-5), 69.18 (C-4), 68.84 (C-2), 62.00 (C-6), 36.58 (CH_2), 30.40 (CH_2), 24.94 (CH_2), 24.17 (CH_2), 20.77, 20.68, 20.57 (3C, CH_3). HRMS-FAB calcd for $C_{17}H_{25}N_4O_9[M+H]^+$: 397.1723; found: 397.1728.

4.15. (*E*)- 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(1-methyl-1-propyliden)amino-β-D-glucopyranosylazide (29)

A solution of **10** (0.15 g, 0.45 mmol) in 2-butanone (10.0 mL) was kept for 4 days at room temperature. Then, the solvent was evaporated and a white solid was obtained (0.18 g, 98%); Mp 97–98 °C; $[\alpha]_D^{25}$ −20.2; $[\alpha]_{578}^{25}$ −22.8; $[\alpha]_{546}^{25}$ −38.0 (*c* 0.5, chloroform); IR (KBr) ν_{max} 2947 (CH_3), 2116 (N_3), 1747 (C=O), 1662 (C=N), 1241 (C–O–C), 1070, 1035 (C–O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.28 (t, 1H, $J_{2,3} = J_{3,4}$ 9.6 Hz, H-3), 5.11 (t, 1H, $J_{3,4} = J_{4,5}$ 9.8 Hz, H-4), 4.94 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 4.35 (dd, 1H, $J_{5,6}$ 4.8 Hz, $J_{6,6'}$ 12.4 Hz, H-6), 4.17 (dd, 1H, $J_{5,6'}$ 2.0 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 3.88 (ddd, 1H, $J_{4,5}$ 10.2 Hz, $J_{5,6}$ 4.8 Hz, $J_{5,6'}$ 2.0 H z, H-5), 3.58 (dd, 1H, $J_{1,2}$ 8.8 Hz, $J_{2,3}$ 9.2 Hz, H-2), 2.27 (q, 2H, $J_{CH2,CH3}$ 7.4 Hz, CH_2), 2.11, 2.04, 1.95, 1.92 (s, 4 × 3H, CH_3), 1.06 (t, $J_{CH2,CH3}$ 7.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 176.91 (C=N), 170.69, 168.88, 169.42 (3C, C=O), 90.46 (C-1), 73.97 (C-3), 73.93 (C-5), 68.11 (C-4), 64.23 (C-2), 62.02 (C-6), 35.92 (CH_2), 20.80, 20.71, 20.54 (3C, CH_3), 10.92 (CH_3).

4.16. (*E*)-3,4,6-Tri-*O*-acetyl-2-deoxy-2-(1,2-dimethyl-1-propyliden)amino-β-D-glucopyranosylazide (30)

A solution of **10** (0.15 g, 0.30 mmol) in 3-methyl-2-butanone (10.0 mL) was kept for 4 days at room temperature. Then, the solvent was evaporated and a white solid was obtained (0.28 g, 47%); Mp 65–68 °C; $[\alpha]_D^{24}$ −22.4; $[\alpha]_{578}^{24}$ −22.6; $[\alpha]_{546}^{24}$ −25.6; $[\alpha]_{436}^{24}$ −43.2 (*c* 0.5, $CHCl_3$); IR (KBr) ν_{max} 2963, 2932 (CH_3), 2118 (N_3), 1747 (C=O), 1660 (C=N), 1242 (C–O–C, ester), 1111, 1071, 1033 (C–O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.23 (d, 1H, $J_{1,2}$ 8.4 Hz, H-1), 5.21 (t, 1H, $J_{2,3} = J_{3,4}$ 10.0 Hz, H-4), 4.96 (t, 1H, $J_{3,4} = J_{4,5}$ 9.8 Hz, H-3), 4.20 (dd, 1H,, $J_{5,6}$ 4.8 Hz, $J_{6,6'}$ 12.0 Hz, H-6), 4.13 (m, 1H, $J_{4,5}$ 9.6 Hz, $J_{5,6'}$ 2.0 Hz, H-5), 4.06 (dd, 1H, $J_{5,6'}$ 2.0 Hz, $J_{6,6'}$ 12.0 Hz, H-6′), 3.61 (t, 1H, $J_{1,2} = J_{2,3}$ 9.0 Hz, H-2), 2.41 (m, 1H, $J_{CH,CH3}$ 6.8 Hz, CH), 2.04, 1.97, 1.90, 1.85 (s, 4 × 3H, CH_3), 0.96 (d, 3H, $J_{CH,CH3}$ 6.8 Hz, CH_3), 0.95 (d, 3H, $J_{CH,CH3}$ 6.8 Hz, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 179.13 (C=N), 170.53, 169.89, 169.41 (3C, C=O), 89.57 (C-1), 73.49 (C-3), 73.34 (C-5), 68.32 (C-4), 64.25 (C-2), 62.37 (C-6), 39.69 (CH), 21.04, 20.91, 20.69, 20.09, 19.91 (5C, CH_3), 16.57 (CH_3). HRMS-FAB calcd for $C_{17}H_{27}N_4O_7$ $[M+H]^+$: 399.1873; found: 399.1880.

5. Supplementary data

Complete crystallographic data for compound **12** have been deposited with the Cambrigde Crystallographic Data Centre (CCDC 728626). Copies of this information may be obtained free of charge from the Director, Cambrigde Crystallographic Data Centre, 12 Union Road, Cambridge CBL 1EZ, UK. (fax: +44 1223 336033, e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

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