Allylic azide rearrangement in tandem with intramolecular Huisgen cycloaddition for iminosugar and glycomimetic synthesis. Functionalized piperidine, pyrrolidine and pyrrolotriazoles from D-mannose

Allylic azide rearrangement in tandem with intramolecular Huisgen cycloaddition for iminosugar and glycomimetic synthesis. Functionalized piperidine, pyrrolidine and pyrrolotriazoles from D-mannose

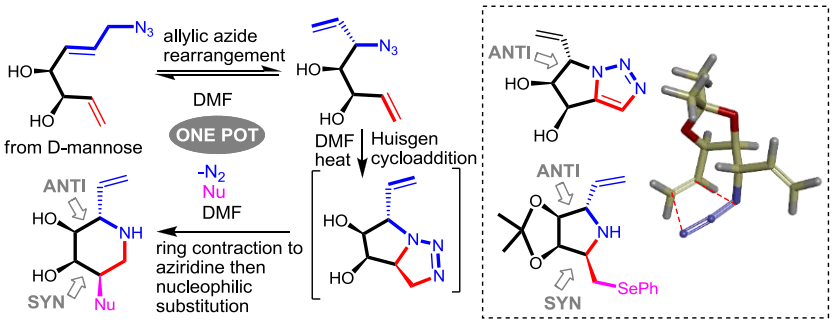
Rekha Chadda
Patrick McArdle
Paul V. Murphy*

School of Chemistry, National University of Ireland Galway, University Road, Galway, Ireland H91 TK33

* corresponding author.

paul.v.murphy@nuigalway.ie

Click here to insert a dedication.

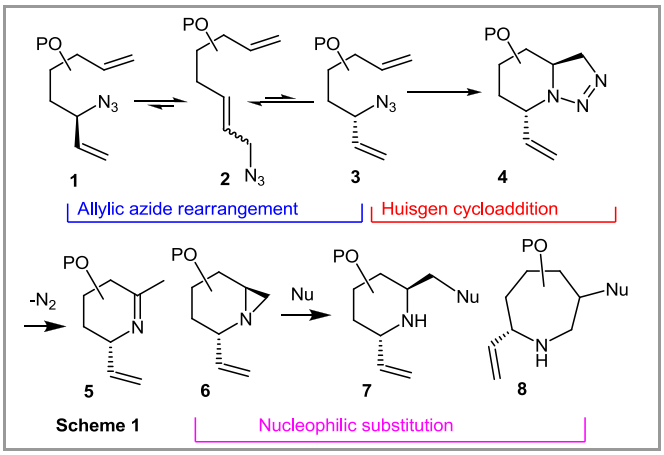


Received:
Accepted:
Published online:
DOI:

Abstract Intramolecular Huisgen azide-alkene cycloaddition reaction of 7-azido-hepta-1,5-diene-3,4-diols, prepared from methyl α-D-mannopyranoside, were carried out. Allylic azide rearrangement to secondary azides occurred in tandem with triazoline formation and this intermediate was then decomposed in the presence of nucleophilic reagents to give pyrrolidines, piperidines or azepanes depending on whether cyclic constraint was incorporated or not, on diol stereochemistry and on the nucleophile. The tandem reaction worked best when aziridine formation from the triazoline was efficient, and this efficiency improved on removal of cyclic constraint. Proposals to account for the observed diastereoselectivities are provided. The allylic azide rearrangement in tandem with the intramolecular Huisgen azide-alkyne cycloaddition was also investigated from azidoheptaenynediols and gave dihydropyrrolotriazoles. All reactions were diastereoselective, and this was high in some cases. Two X-ray crystal structural determinations, ^{13}C-NMR data and 1D and 2D NOESY experiments were used for stereochemical assignment.

Key words tandem reaction, allylic azide rearrangement, azide-alkene cycloaddition, stereoselective synthesis, iminosugar, glycomimetic

Organic azides[1] are 1,3-dipoles[2] in cycloaddition reactions (Huisgen cycloaddition[3]) and when reacted with an alkene dipolarophile give a triazoline that can subsequently produce an aziridine that can undergo further reactions. This sequence was initially used by us[4] in the synthesis of 1-deoxynojirmycin derivatives and has more recently been progressed to incorporate the allylic azide rearrangement[5] in tandem with triazoline formation and its subsequent decomposition to give 1-vinyl-1-deoxyiminosugars or C-iminoglycosyl compounds (Scheme 1).[6] This was, as far as we are aware, the first application of this tandem reaction in synthesis. In this sequence, the allylic azide **2** is in equilibrium with secondary azides **1** and **3**, either of which can undergo intramolecular cycloaddition to give the product. If one of the secondary azides reacts faster than the other (e.g. if **3** reacts faster than **1**) then a stereoselective reaction results.[7] Due to different conformers of the alkene dipolarophile being accessible then the possibility for a second stereocentre being generated results and this can also be achieved stereoselectively. Furthermore, the resulting triazoline formed may then lose nitrogen to form the imine **5** or the aziridine **6**, leading in the presence of a nucleophile to products such as **7** or **8**.[8]



Scheme 1

Herein we report the synthesis of new chiral building blocks from methyl α-D-mannopyranoside, suitable for the tandem reaction, and report on their conversion to N-heterocyclic products. An example of an azide-alkyne cycloaddition to give dihydropyrrolotriazoles, is also included.[9,10] In our previous paper we reported that cyclic conformational constraint using an isopropylidene protecting group on a diol was required for successful reaction. Here we extend the approach to preparation of pyrrolidines and identify a new route to piperidines. The

research work led to examples described herein which were successful without the requirement for cyclic conformational constraint.

The synthesis of allylic azides used in this study are shown in Scheme 2. In the original planning it was anticipated that their rearrangement-cycloaddition-decomposition in presence of nucleophiles would give pyrrolidines from the secondary azides. Alternatively, in the event of reaction from the primary allylic azide, azepanes were expected. Thus, methyl α-D-mannopyranoside was converted into the iodide **9** in three steps as previously described.[6] The preparation of dialkene **10** was next investigated. Initially, zinc reductive fragmentation,[11,12] from **9**, gave the expected aldehyde intermediate and this was followed by Wittig reaction to give **10** (~50 %, 2 steps). Alternatively, the one pot reductive fragmentation (Scheme 3) promoted by n-butylithium (nBuLi) followed by in-situ Wittig reaction was used and this provided **10** in higher yield (80 %). The latter reaction was adapted from a strategy reported by Davies and co-workers.[13] In this reaction lithium iodide exchange occurs, and the intermediate formed undergoes elimination and loss of methanol to provide desired the intermediate aldehyde. Careful reaction monitoring was very important as prolonged reaction time led to epimerisation at the carbon atom adjacent to the aldehyde group. Removal of the triethylsilyl protecting group was next carried out using TBAF to give **11**. While the removal of the fluorotriethylsilane (TESF) proceeded smoothly, the separation of the TESF from the alcohol product required investigation. Various work-up conditions (satd. $NaHCO_3$, $CaCO_3$ - DOWEX 50WX8,[14] 1M NaOH) were attempted in order to remove the TESF but, in the end, it was found that washing with 3M NaOH was most satisfactory. The alcohol **11** produced was then subjected to reaction with DIAD and DPPA to give the desired azide **12**. While four isomers were potentially observable due to allylic azide rearrangement, the trans-primary azide **12** was the isomer mainly observed according to NMR analysis. This observation is in agreement with the lesser substituted allylic azide being the preferred isomer.[9] Removal of the isopropylidene group gave **13**. Removal of the isopropylidene group from **11** followed by reaction of the triol intermediate with acetone under acidic conditions gave **14**. This acetonide was readily converted to **15** and **16** (Scheme 2). In the case of **15** the primary azide **15a** was the major component obtained, but a fraction containing a small amount of **15b** was observed by NMR.

With various azidoheptadienes in hand their tandem allylic azide rearrangement-Huisgen cycloaddition reactions were investigated. Both polar DMF and lower polarity toluene were investigated as solvents. The products from reactions of **12-13** are summarised in Table 1 and products from **15** are in Scheme 4. Hence, the azide **12** in DMF (or toluene) was typically heated at 90-100 °C for 1.5-3 h to first promote reaction. The reaction needs to be monitored carefully (e.g. by TLC) to ensure consumption of the azide, but should not be heated for a prolonged period. Once the azide was consumed then the nucleophile was promptly added and the reaction is heated for a further period which can vary from a few minutes to 36 h, with the reaction time varying for each specific reaction being studied. The formation and presence of triazolines at 90 °C from **12** was supported by NMR analysis of the reaction mixture via carrying out the reaction in deuterated DMF in an NMR tube. In the NMR experiment, all of azide **12** was consumed after 1.5 h at 90 °C and analysis of the mixture at this time indicated the presence of one major triazoline isomer as supported by signals for its ring CH_2 at δ 4.15 ppm (dd, J = 16.4, 10.1 Hz, 1H) and at δ 4.68 ppm (1H, dd, J = 16.3 Hz and 2.3 Hz). In addition, the presence of a second triazoline stereoisomer was indicated by a visible signal at δ 4.04 (dd, J = 16.2, 10.0 Hz) for one of its triazoline ring protons. The ratio of triazolines in the mixture was 5:2 based on integration of the aforementioned signals. There was also evidence for the formation of two isomeric imines, in the same 5:2 ratio by further prolonged heating of the triazolines, which was supported by the observation of two singlets at δ 2.06 (br s) and δ 2.03 (d, J = 2.3 Hz). There was no indication that aziridines were formed from this triazoline by NMR analysis. Further heating of the mixture at 90 °C without further addition of nucleophile showed that the triazoline was fully depleted after 3 h, with a concomitant increase in the intensity of the signals for the imines. This indicated that the addition of any nucleophile to react with the triazoline should be carried out before its decomposition occurs and explains why careful monitoring and prompt addition of nucleophile is important.

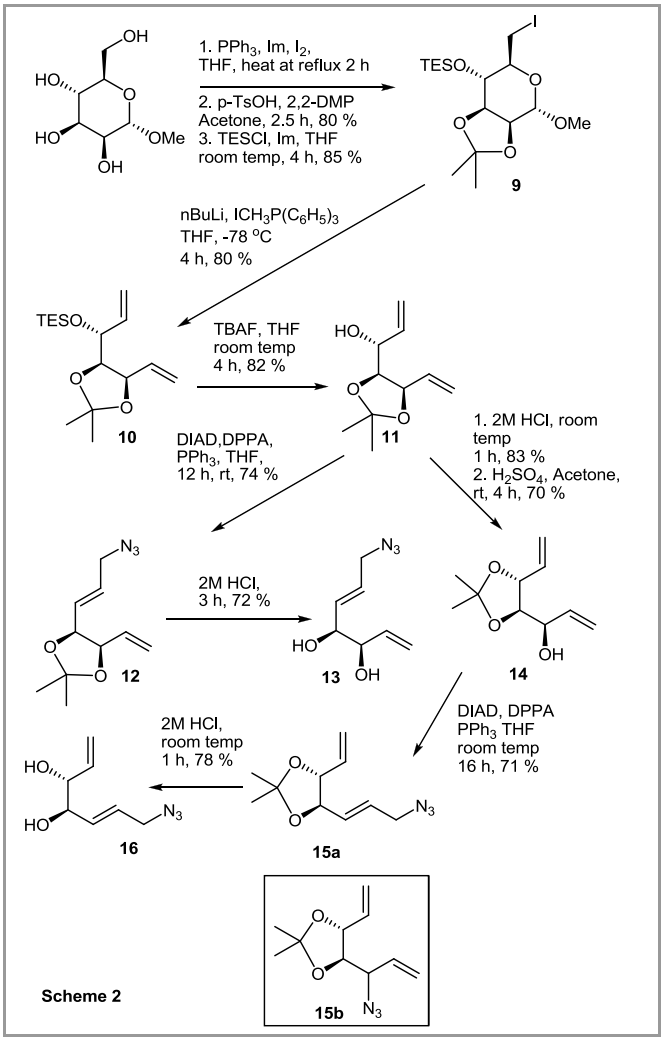
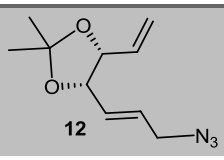
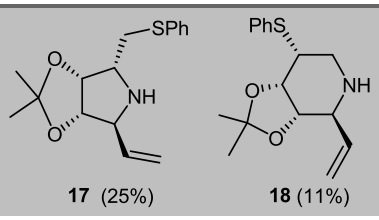
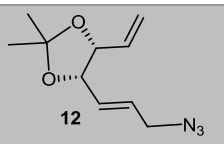
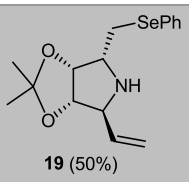
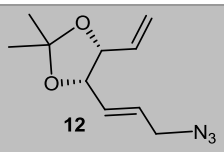
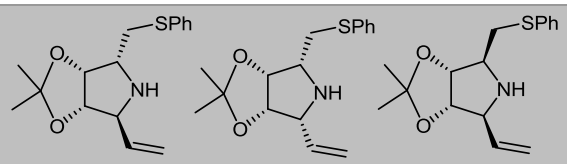
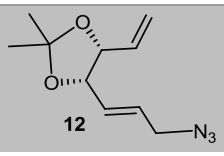
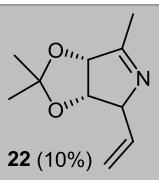
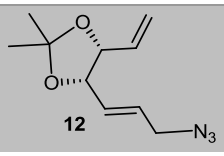
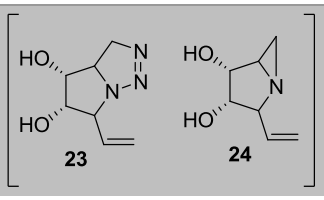
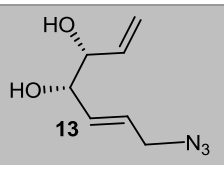
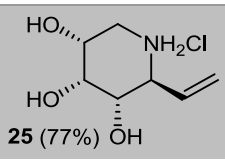
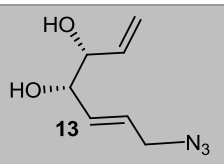
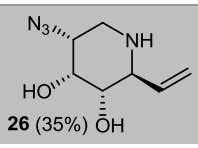
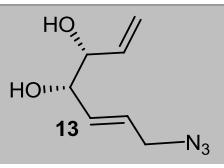
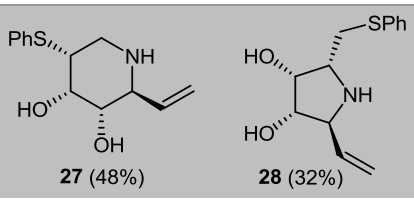
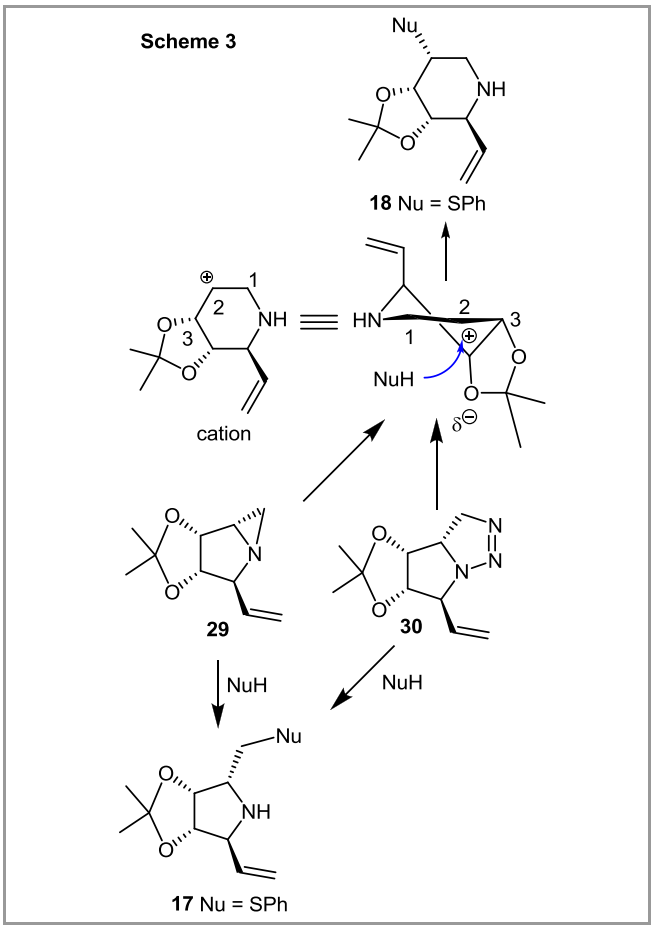


Table 1 Reactions of **12** and **13**

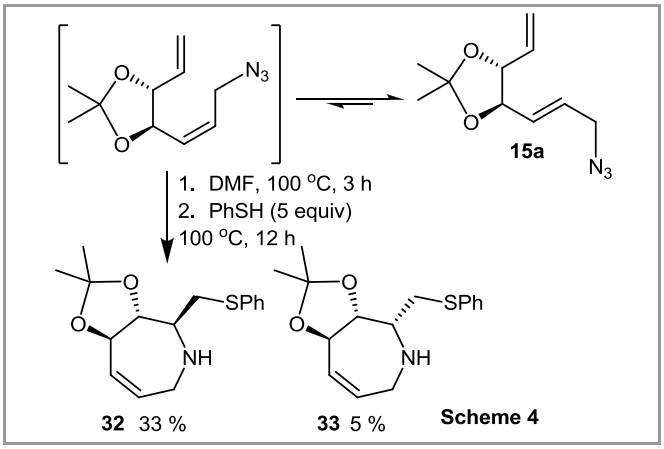
Entry	Reactant	Reaction Conditions	Isolated Products (Yields)
1	 **12**	1. DMF, 100 °C, 1.5-3 h 2. PhSH, DMF, 100 °C, 3 days	 **17** (25%) **18** (11%)
2	 **12**	1. DMF, 100 °C, 1.5-3 h 2. Ph_2Se_2, DMF 100 °C, 12 h	 **19** (50%)
3	 **12**	1. Tol, 100 °C, 3 h 2. PhSH, Tol, 100°C 16 h	 **17** (30%) **20** (10%) **21** (7%)
4	 **12**	Tol, 120 °C	 **22** (10%)
5	 **12**	DMF, 100 °C, 30 min	 **23** **24**
6	 **13**	1. DMF, 100 °C, 30 min 2. AcOH (5 equiv), rt, 10 min 3. 2M HCl, 12 h	 **25** (77%)
7	 **13**	1. DMF, 100 °C, 30 min 2. NaN_3 (5.0 equiv), AcOH (1.5 equiv), rt, 10 min	 **26** (35%)
8	 **13**	1. DMF, 100 °C, 30 min 2. PhSH (5 equiv), rt, 10 min	 **27** (48%) **28** (32%)

The efficient breakdown of the triazoline generated from **12** was not trivial as indicated by unproductive reactions with various nucleophiles including CsOAc, NaN_3, AcOH, NaOAc, TBAI and diethylmalonate. Improvements occurred when S and Se based reagents were instead investigated (Table 1). Thus, for the reaction of **12** with thiophenol as nucleophile (Table 1, entry 1) both the pyrrolidine **17** (25%) and the piperidine **18** (11%) were isolated. Formation of these products possibly result from the aziridine **29** or via triazoline **30** (Scheme 3), with the possibility that **30** reacts directly with the nucleophile, rather than **29**, not being ruled out given that the triazolines from **12** decompose to imines rather than aziridines as indicated by NMR. In the case of **29/30**, they may react directly with the nucleophile by S_N2 reaction, which would give the pyrrolidine, but, there may be cation formation which would give the piperidine (Scheme 3). In the second case the cation (Scheme 3), proposed to be stabilized by electrostatic interaction with nearby axial oxygen, may react to give the syn product because reaction from this conformer gives a chair-like transition state, as opposed to reaction giving the anti-product which would proceed via a higher energy twist boat transition structure.

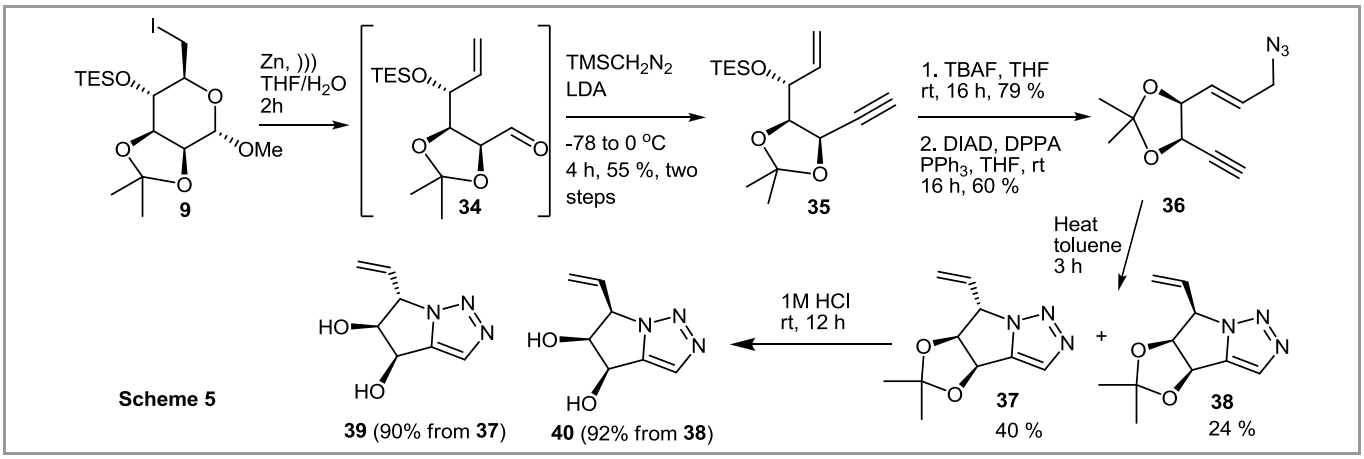


The heating of **12** in DMF in the presence of the diphenyl diselenide (PhSeSePh) resulted in isolation of only the pyrrolidine **19** in 50% yield (entry 2, Table 1). This could be due to the diselenide being more nucleophilic than thiophenol which would enhance the importance of the S_N2 reaction pathway. When the triazoline was generated in-situ in toluene and then reacted with thiophenol then a mixture of stereoisomeric pyrrolidines (**17**, **20**, **21**) were observed (entry 3). The absence of piperidines in this case is consistent with use of lower polarity solvent which would enhance the importance of the S_N2 reaction. Excessive heating of azide **12** in the absence of any nucleophile in toluene led to isolation of the imine **22** in low yield (10%), as the only identifiable product. The low yield of **22** could be a result of the rapid decomposition of this relatively unstable ketimine during the isolation procedure.

Notably, the reaction of unprotected **13** in the absence of any nucleophile gave the triazoline **23** in only 15 min, much more rapidly and cleanly than corresponding triazoline formation occurred in the reaction of **12**. The formation of the triazoline **23** in the mixture was supported by ^{1}H-NMR, ^{13}C-NMR and HSQC experiments (see Figure 1). Hence, there were signals in the range δ 4.20-4.80 ppm characteristic for the triazoline CH_2, as seen for **30**. Further heating of this mixture led to a reduction in quantity of triazoline present and in contrast with the reaction from **12**, there was evidence for conversion of the triazoline **23** to aziridine **24**. The NMR spectroscopic analysis of the reaction mixture obtained by heating in deuterated DMF indicated more efficient formation of **24** by the presence of ^{1}H-NMR signals at δ 2.40 (td, J = 5.5, 3.3 Hz, 1H), 2.16 (d, J = 3.3 Hz, 1H) and 1.60 (d, J = 5.5 Hz, 1H). In addition, the presence of imines (not shown) to a minor degree were suggested by presence of signals for methyl groups observed at δ 2.01 ppm (br s) and δ 1.96 ppm (d, J = 2 Hz). The heating of triazoline **23** in the presence of acetic acid as nucleophile was productive, as its reaction in situ for 10 mins followed by deacetylation and salt formation using aq HCl gave piperidine **25** in good yield from **13**. It appears that carbocation formation from the aziridine in the presence of acetic acid is favoured and that syn addition (to the adjacent OH group) of the acetate is occurring for reasons depicted earlier (Scheme 3). Similarly, the reaction of **13** via **23** gave azide **26**, but in significantly lower yield. Reaction of **13** with thiophenol as nucleophile gave the piperidine **27** as the major product, but pyrrolidine **28** was also formed in this case, possibly because the thiol nucleophilicity led to increased competition by the contending S_N2 pathway.



The reaction of **15** led to the formation of azepanes **32/33** (Scheme 4) rather than pyrrolidines or piperidines. This is possibly due to increased strain in the annulation due to the trans-acetonide in the transition structure and the cycloaddition proceeded instead from the cis primary allylic azide, generated via rearrangements from **15,** giving the 7-membered products.



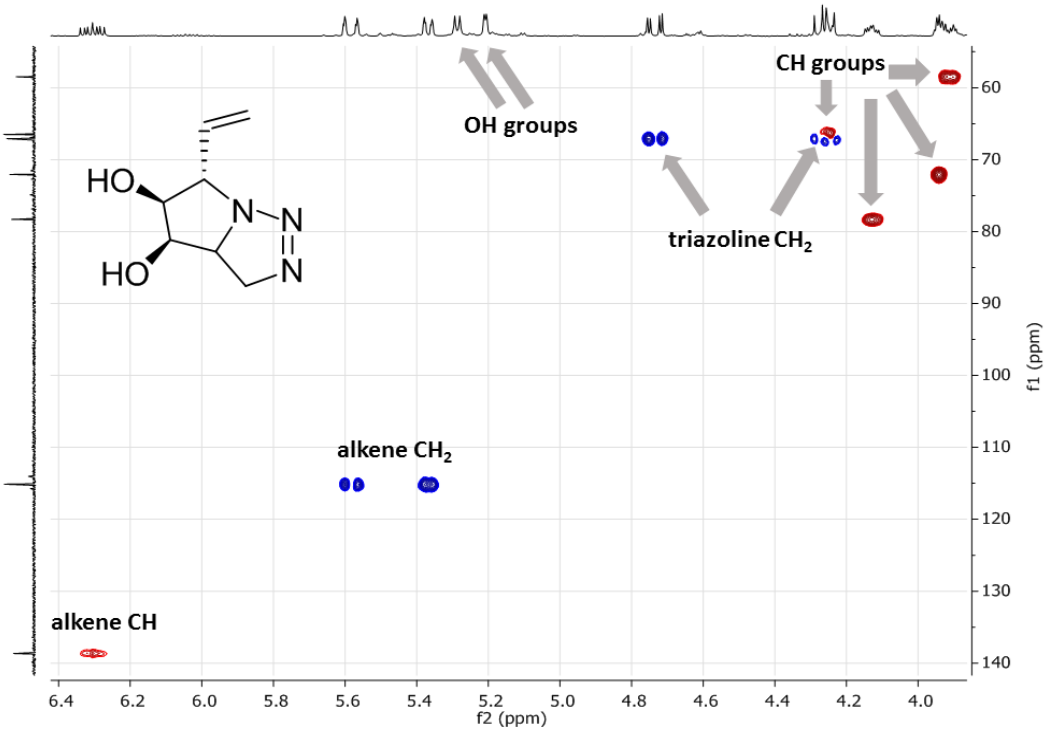


Figure 1: The HSQC spectrum of **23** generated in deuterated DMF

The treatment of **16** with thiophenol led to the formation of numerous inseparable products and no useful product could be isolated from the reaction. Attempts to form other azepane derivatives from unprotected azide **16** were also investigated with nucleophiles (AcOH, NaN_3) for a variety of reaction times and solvents (toluene and DMF). However, in contrast with **12/13**, only intractable product mixtures were obtained.

Next, the formation of pyrrolidines fused to triazoles was investigated by intramolecular azide-alkyne cycloadditions.[15] Firstly, the zinc mediated reductive fragmentation was carried out as it converts **9** to an open chain aldehyde intermediate **34**. Then different reaction conditions, such as using the Ohira-Bestmann and the Corey-Fuchs alkyne forming reactions were investigated for the synthesis of alkyne **35**, but these were unsuccessful. However, the Colvin-Hamill procedure[16] yielded **35**. Removal of the TES group using TBAF and subsequent reaction with DIAD-DPPA gave azide **36**. Azide **36** was then subsequently heated in toluene to give a 5:3 mixture of diastereoisomeric pyrrolotriazoles[17] with **37** and **38** (66%). Removal of the isopropylidene groups from **37** and **38** gave **39** and **40**, respec-tively.

Finally, the protecting groups on a number of derivatives were removed and/or HCl salts were generated to give **41-45** (Fig. 2) with a view to giving stable iminosugar derivatives for storage to enable biological testing in the future. It was found that free amines generated were generally susceptible to decomposition on storage and salt formation is recommended.

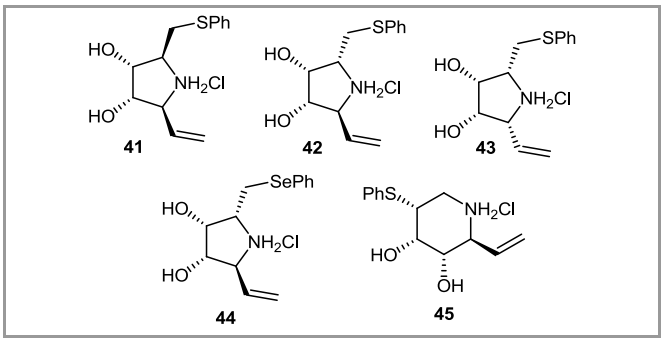


Figure 2. Structures of **41-45**

During this research work, the stereochemical assignment at C-1 in **38** was confirmed by X-ray crystal structure determination (Figure 3), which enabled assignment of **37** and **39-40**. In addition, the X-ray crystal structure of **42** was determined and confirmed its stereochemical assignment and therefore also that of its precursor **19**.

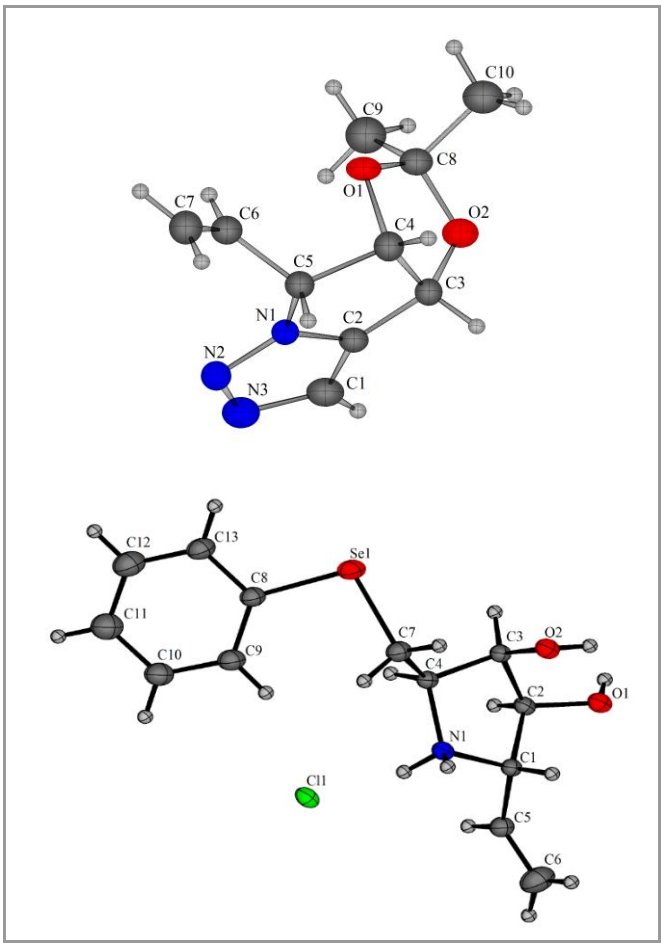


Figure 3. X-Ray crystal structures of **38** (top) and **42** (bottom)

The comparison of ^{13}C-NMR data for ring carbon atoms of **42** (δ = 63.2, 75.4, 70.6, 59.5 ppm) and **44** (δ = 63.3, 75.5, 70.6, 60.5 ppm) strongly supported the proposal that these rings had the same relative stereochemical arrangement[18] and consequently this also enabled stereochemical assignment to **17**. The stereochemical assignments given to **20** and **21** were based on comparisons of ^{13}C signals for the ring carbons and CH_2SPh of these compounds with **17**. For example, the ^{13}C signal for the methylene in **20** was found at δ 32.1 ppm, which agrees well with the corresponding methylene signal in **17** at δ 32.5 ppm whereas this methylene carbon in **21** occurred at δ 38.0 ppm. In addition NOESY experiments (Fig. 3) for **20** (enhancements observed between H-a and H-d but not between the vinyl CH and H-b) and **21** (enhancements observed between H-a and H-d and between the vinyl CH and H-b) supported the proposed structures. The NOESY of **17** could not be studied due to signal overlap but no crosspeak was observed between H-a and H-d for the corresponding protons in its deprotected free amine form **28** whereas there was an enhancement between the vinyl CH and H-b. (Figure 3). With regard to piperidines, compound **25** was prepared previously by an alternative route[19] and the ^{13}C-NMR data we obtained for the salt was in agreement with previously reported data, although there was less good agreement with the ^{1}H-NMR data reported. The coupling constants observed in the ^{1}H-NMR spectrum for its analogue **45**, indicated that it, and **25/26**, adopt a chair conformer as shown in Fig. 4 and that both its vinyl and thiophenyl groups are equatorial. The observation of NOESY crosspeaks between H-b and H-d for **45** as well as between H-b and the vinyl CH were also consistent with the stereochemical assignment and conformation of **45**. The use of NOESY experiments also supported the assignments made to azepanes **32** and **33**. Whereas strong NOE enhancements were observed between H-d and H-f in **32**, there are no such enhancements observed in **33**. In contrast a strong NOE enhancement is observed between H-d and one of the methylene protons (H-g) adjacent to the sulfur atom in **33** with the corresponding correlation being absent for **32** (Figure 4).

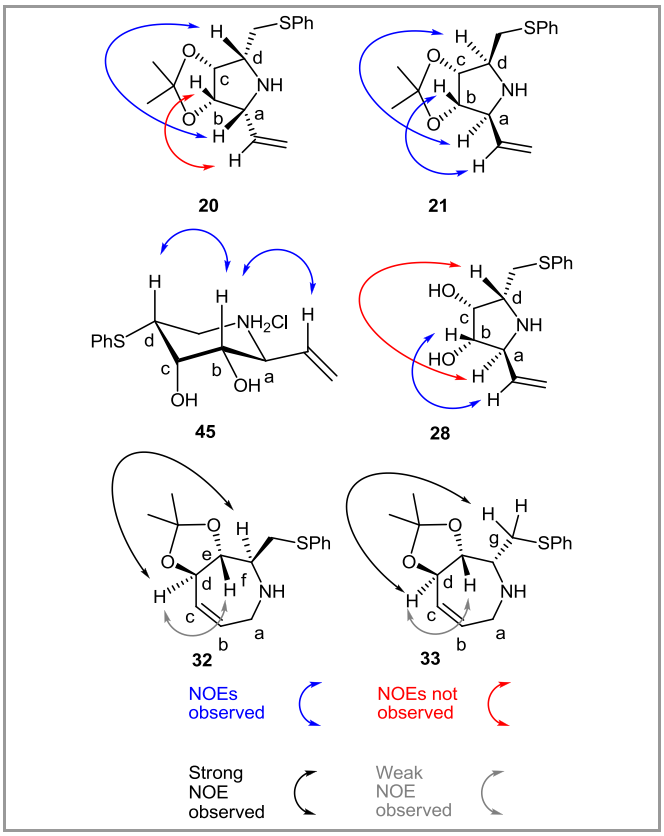


Figure 4. NOESY Experiments

In our earlier work, we found that there was a preference for reaction of one conformation of alkene dipolarophile in the cycloaddition. In **17** and **20**, the major products isolated in their reactions, the CH_2SPh group is syn to the adjacent OR group; this was unexpected on the basis of previous observations and was typical for the pyrrolidine forming reactions reported here. Allylic strain is recognised as a controlling element in intramolecular cycloaddition reactions[20] and in earlier work[6] we used it rationalize the preferred formation of anti-products, which was based on the preferential reaction of the lowest energy conformer of the allyl group. In the allyl group's lowest energy conformer the C=C-C-H dihedral angle is approximately 0° with the C=C and C-H bonds being eclipsed. However, it is clear that the reaction of the alkene dipolarophile giving rise to the major pyrrolidine observed cannot involve this conformer and instead involves that where the C=C-C-H dihedral angle is approximately -120° with instead the C-O and C=C bonds being eclipsed. A model **46** of this latter conformer was built and minimised, with constraints applied so that atoms involved in the cycloaddition are planar,[21] and this may be thus considered as a precursor to an early cycloaddition transition state structure. An alternative conformer **47** was also similarly built and minimised and, in turn, it may be considered to be the precursor to the early cycloaddition transition state that would give the anti-product; in this latter case the C=C-C-H dihedral angle was distorted by ~30° from the strictly eclipsed arrangement. Aside from the allyl group's torsion, the other torsion of most relevance to the stereochemical outcome is defined by the H-C-N-N atoms, which defines the azide group orientation in the cycloaddition and this was different in both **46** and **47**. Energy calculations performed using Macromodel (OPLS-AA force field) did indicated that **46** was lower in energy than **47** and reaction from **46** would account for the stereochemical preference exhibited. The selectivity at the second stereocentre generated, that where the vinyl group is located in the product, can be explained where the faster reacting secondary azide stereoisomer gives rise to less steric interactions in the transition state.[6]

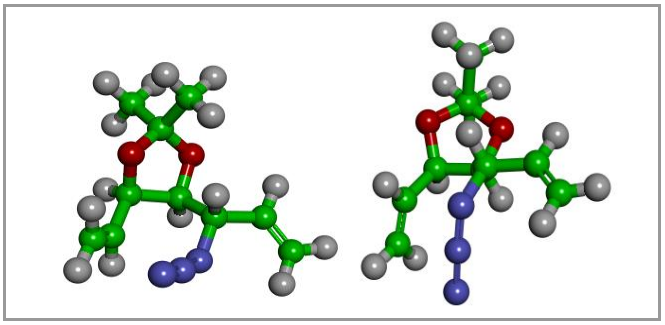


Figure 5. Conformers **46** (left) and **47** (right)

To conclude, we have concisely prepared a number of allylic azide derivatives incorporating an alkene dipolarophile. We have studied their rearrangement leading to Huisgen cycloaddition reactions to give triazolines and the subsequent decomposition reactions of these triazoline intermediates give functionalised pyrrolidines, piperidines and azepanes in a diastereoselective manner. The efficient decomposition of the triazoline with a suitable nucleophile, or efficient ring contraction to its aziridine and subsequent reaction with nucleophile is required for the generation of iminosugars or other glycomimetics. Previous work has shown that additional cyclic constraint in the precursor was important for achieving the intramolecular cycloaddition, but here we provide examples that gave successful outcomes when constraint was not employed that led to higher yields and stereoselectivity, albeit giving different heterocyclic frameworks. Interestingly, the breakdown to aziridine from triazoline was more efficient in absence of the fused ring system, which may suggest it could be worth to remove the cyclic protecting groups, where these are required, before triazoline decomposition in future work. We also provide an example of azide-alkyne cycloaddition that gives dihydropyrrolotriazoles, producing an additional scaffold. Iminosugars, which include piperidines or pyrrolidines[22] with a number of hydroxyl groups are of considerable synthetic,[23] biological and medical interest and a number have already been approved as drugs for use in the clinic.[24] Iminosugars and glycomimetics continue to be investigated for various applications,[25] which include glycosidase inhibition,[26] as pharmacological chaperones[27] or as scaffolds for peptidomimetic design.[28] Taken all together, the further study of the potential of the approach reported herein to generate compounds of biological and medicinal interest is warranted.

The experimental section has no title; please leave this line here.

General experimental

NMR spectra were recorded using a 500 or 600 MHz spectrometer. Chemical shifts are reported relative to internal Me_4Si in $CDCl_3$ (δ 0.0), HOD for D_2O (δ 4.65) and CD_2HOD (δ 3.31) for ^1H and $CDCl_3$ (δ 77.16) and CD_3OD (δ 49.0) for ^{13}C. ^1H-NMR signals were assigned with the aid of COSY. ^{13}C signals were assigned with the aid of HSQC and HMBC. Coupling constants (*J*) are reported in Hertz and are reported uncorrected. High resolution mass spectra were measured in positive and/or negative mode as indicated using MeCN, H_2O and/or MeOH as solvents using a Waters LCT Mass Spectrometry instrument. FT-IR spectra were recorded using a polarized UATR (Universal Attenuated Total Reflectance) Accessory. Optical rotations were determined at the sodium D line at 23 °C with a Schmidt & Haensch Unipol L 1000 polarimeter using $CHCl_3$, MeOH or D_2O as indicated. TLC was performed on aluminium sheets pre-coated with Silica Gel 60 (HF254, E. Merck) and spots visualized by UV and charring with cerium (IV) molybdate solution or ninhydrin solutions. Flash column chromatography was generally employed and was carried out using silica gel 60 (0.040-0.630 mm) using a stepwise solvent polarity gradient correlated with TLC mobility. Chromatography solvents used were petroleum ether, EtOAc, CH_2Cl_2, MeOH (Fischer Scientific and Sigma Aldrich) and H_2O (distilled). THF, toluene, CH_2Cl_2, Et_2O, DMF and methanol were used as obtained from a Pure-Solv™ solvent purification system. CAS registry numbers for known compounds are: **9** 1837795-79-5, **11** 503302-88-3 and NMR data for **9** and **11** were in agreement with those data reported previously.

(((R)-1-((4R,5R)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)allyl)oxy)triethylsilane 10

Compound **9** (2.5 g, 5.45 mmol) was dissolved in THF and cooled to -78 °C. nBuLi (1.1 mL, 2.5 M in hexanes) was added and solution stirred until full conversion to the aldehyde was complete as observed by TLC. In a separate vessel methyltriphenylphosphonium iodide (4.43 g, 10.9 mmol) was suspended in THF (26 mL) and cooled to -78 °C and to this nBuLi (2.7 mL, 2.5 M in hexanes) was slowly added and solution stirred at -78 °C for a further 15 min. The solution containing the in-situ generated aldehyde was transferred to the second vessel and reaction allowed to attain room temp over 2 h. Satd. NH_4Cl solution was added and the mixture then extracted with EtOAc, dried over Na_2SO_4 and the solvent was removed under reduced pressure. Flash chromatography (1:40 EtOAc-hexane) gave **10** (1.62 g, 80 %) as a clear oil.

R_f = 0.48 (EtOAc-hexane, 1:20)

FTIR: 2986, 2954, 2877, 1458, 1415, 1379, 1369, 1238, 1216, 1146, 1123, 1092, 1036, 1003, 973, 927, 869, 844, 778 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 5.96 (ddd, *J* = 17.8, 10.3, 8.2 Hz, 1H), 5.87 (ddd, *J* = 16.6, 10.5, 5.6 Hz, 1H), 5.36 – 5.27 (m, 2H, overlapping signals), 5.23 (dd, *J* = 10.3, 1.5 Hz, 1H), 5.15 (dt, *J* = 10.5, 1.8 Hz, 1H), 4.45 (dd, *J* = 8.2, 6.9 Hz, 1H), 4.16 (t, *J* = 6.3 Hz, 1H), 3.98 (t, *J* = 6.5 Hz, 1H), 1.50 (s, 3H, -C(CH_3)$_2$), 1.35 (s, 3H, -C(CH_3)$_2$), 0.96 (t, *J* = 8.0 Hz, 9H, -Si(CH_2CH_3)$_3$), 0.61 (m, *J* = 7.9, 3.0 Hz, 6H, -Si(CH_2CH_3)$_3$)

^{13}C NMR (126 MHz, $CDCl_3$): δ 136.9, 134.5, 118.6, 116.5 (alkene CH/CH_2), 108.6 (-*C*(CH_3)$_2$), 81.7 (CH-O), 79.0 (CH-O) 72.4 (CH-O), 27.7 (-C(*C*H_3)$_2$), 25.5 (-C(*C*H_3)$_2$), 6.7 (-Si(CH_2*C*H_3)$_3$), 5.0 (-Si(*C*H_2CH_3)$_3$)

HRMS (ESI): *m/z* calc for $C_{16}H_{31}O_3Si$: 299.2042, found: 299.2034 $[M+H]^+$;

(R)-1-((4S,5R)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl)prop-2-en-1-ol 11

Compound **10** (3.80 g, 12.7 mmol) was dissolved in anhydrous THF (100 mL). TBAF (38 mL, 1 M in THF) was charged slowly and solution stirred at room temp overnight. Reaction mixture was then quenched with 3M NaOH (50 mL) and stirred for 15 min. The organic layer was separated and aqueous layer extracted with EtOAc. Combined organic layers were washed with 3M NaOH, H_2O, dried over Na_2SO_4, filtered and solvent removed under reduced pressure. Flash chromatography (1:4 EtOAc-hexane) gave alkene **11** (1.92 g, 82 %) as a clear oil. The NMR spectroscopic data (400 MHz, 100 MHz) published previously[29] showed agreement with those data (500 MHz, 126 MHz) obtained for **11** prepared here.

R_f = 0.56 (EtOAc-hexane, 1:4)

FTIR 3482, 2987, 2936, 1644, 1457, 1428, 1380, 1214, 1165, 1146, 1110, 992, 925, 869, 804, 690, 662 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$) δ 6.02 (ddd, *J* = 17.7, 10.3, 7.8 Hz, 1H), 5.85 (ddd, *J* = 16.6, 10.5, 5.4 Hz, 1H), 5.43 – 5.34 (2H, overlapping signals), 5.30 (d, *J* = 10.2 Hz, 1H), 5.23 (d, *J* = 10.5 Hz, 1H), 4.61 (t, *J* = 7.3 Hz, 1H), 4.17 – 4.05 (2H, overlapping signals), 2.30 (d, *J* = 5.3 Hz, 1H, OH), 1.54 (s, 3H, C(CH_3)$_2$), 1.40 (s, 3H, -C(CH_3)$_2$)

^{13}C NMR (126 MHz, $CDCl_3$): δ 136.7, 133.9, 119.4, 117.0 (alkene CH&CH_2), 108.7 (-*C*(CH_3)$_2$), 80.6, 78.9, 70.5 (each OCH), 27.3 (-C(*C*H_3)$_2$), 24.9 (-C(*C*H_3)$_2$)

HRMS (ESI): *m/z* calc for $C_{10}H_{17}O_3$:185.1178, found: 185.1186 $[M+H]^+$

(4S,5R)-4-((E)-3-azidoprop-1-en-1-yl)-2,2-dimethyl-5-vinyl-1,3-dioxolane 12

Compound **11** (0.4 g, 2.17 mmol) was dissolved in anhydrous THF (13 mL) and then PPh_3 (0.97 g, 3.69 mmol) was added and solution cooled to 0°C. DIAD (0.73 mL, 3.69 mmol) and DPPA (0.8 mL, 3.69 mmol) were charged slowly and solution allowed to adjust to room temp overnight. The solvent was removed under reduced pressure. Flash chromatography (hexane-EtOAc, 40:1) gave azide **12** (0.34 g, 74 %) as a clear oil.

R_f = 0.31 (EtOAc-hexane, 1:20)

FTIR 2987, 2936, 2097, 1455, 1380, 1371, 1245, 1214, 1163, 1114, 1043, 1018, 972, 929, 871, 792, 663 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$) δ 5.86 – 5.63 (m, 3H, overlapping signals), 5.33 (d, *J* = 17.3 Hz, 1H), 5.25 (d, *J* = 10.4 Hz, 1H), 4.67 (t, *J* = 6.8 Hz, 1H), 4.63 (t, *J* = 7.0 Hz, 1H), 3.82-3.74 (m, 2H), 1.54 (s, 3H, -C(CH_3)$_2$), 1.41 (s, 3H, -C(CH_3)$_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 133.9, 131.2, 126.7, 118.5 (alkene CH&CH_2), 109.9 (-*C*(CH_3)$_2$), 79.7, 78.5 (each CH), 52.0 (CH_2N_3), 27.9 (-C(*C*H_3)$_2$), 25.4 (-C(*C*H_3)$_2$)

HRMS (ESI): m/z calc for $C_{10}H_{16}N_3O_2$: 210.1243, found: 210.1245 $[M+H]^+$

(3R,4S,E)-7-azidohepta-1,5-diene-3,4-diol 13

Compound **12** (0.1, 0.48 mmol**)** was dissolved in dil. HCl (2 mL) and the mixture was stirred at room temp for 30 min. The solution was extracted with EtOAc, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Flash chromatography (hexane-EtOAc, 1:1) gave **13** (58 mg, 72 %) as a pale yellow oil

R_f = 0.29 (hexane-EtOAc, 1:1)

^1H NMR (500 MHz, $CDCl_3$) δ 6.21 – 5.70 (3H, overlapping signals), 5.39 (d, *J* = 16.2 Hz, 1H), 5.30 (d, *J* = 10.6 Hz, 1H), 4.27 (t, *J* = 4.5 Hz, 1H), 4.23 (t, *J* = 5.0 Hz, 1H), 3.82 (d, *J* = 5.0 Hz, 2H), 2.26 (s, 1H, -OH), 2.17 (s, 1H, -OH)

^{13}C NMR (126 MHz, $CDCl_3$): δ 135.6, 132.8, 126.2, 117.9 (alkene CH/CH_2), 75.4 (CH-O), 74.1 (CH-O), 52.1 (CH_2N_3)

HRMS (ESI): *m/z* calc for $C_7H_{11}N_3O_2Cl$: 204.0540, found: 204.0544 $[M+Cl]^-$

(R)-1-((4R,5R)-2,2-dimethyl-5-vinyl-1,3-dioxolan-4-yl)prop-2-en-1-ol 14

Compound **13** (1 g, 5.43 mmol) was dissolved in 2M HCl and MeOH (10:1, 10 mL) and the mixture stirred at room temp for 1 h. The solution was then extracted with EtOAc, dried over Na_2SO_4, filtered and the solvent was removed under diminished pressure. Flash chromatography (7:3 EtOAc-petroleum ether bp 40-60 °C) gave the intermediate diol (0.65 g, 83 %) as a clear oil (R_f 0.3, 7:3 EtOAc-hexane). This intermediate (0.5 g, 3.47 mmol) was dissolved in CH_2Cl_2 (10 mL) and cooled to 0 ˚C. *p*-TsOH (0.12 g, 0.69 mmol) was added and the mixture was stirred for a further 10 min. Then 2,2-DMP (0.85 mL, 6.94 mmol) was added & reaction mixture stirred at room temp for 15 min. Triethylamine (0.48 mL, 3.47 mmol) was added and the solvent was then removed under reduced pressure. Flash chromatography (7:3 hexane-EtOAc) gave **14** (0.5 g, 70 %) as a clear oil

R_f = 0.54 (hexane-EtOAc, 7:3)

FTIR 3460, 2987, 2882, 1646, 1427, 1371, 1214, 1168, 1122, 1052, 987, 923, 873, 812, 744 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 5.90-5.78 (m, 2H), 5.44 – 5.33 (m, 2H), 5.27 – 5.21 (m, 2H), 4.45 – 4.34 (m, 2H), 3.82 (dd, J = 8.2, 3.8 Hz, 1H), 2.18 (d, J = 3.1 Hz, 1H, OH), 1.45 (s, 3H, (-C(CH_3)$_2$), 1.43 (s, 3H, (-C(CH_3)$_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 136.0, 135.2, 118.3), 117.1 (alkene CH&CH_2), 109.1 (-*C*(CH_3)$_2$), 82.7, 77.4, 71.5 (each O-CH), 26.8 (-C(*C*H_3)$_2$), 26.8 (-C(*C*H_3)$_2$)

HRMS (ESI): *m/z* calc for $C_{10}H_{16}NaO_3$: 207.0997, found: 207.0990 $[M+Na]^+$

(4R,5R)-4-((E)-3-azidoprop-1-en-1-yl)-2,2-dimethyl-5-vinyl-1,3-dioxolane 15a

Compound **14** (0.28 g, 1.52 mmol) was dissolved in anhydrous THF (10 mL) and PPh_3 (0.71 g, 2.58 mmol) was added and solution cooled to 0°C. DIAD (0.4 mL, 2.58 mmol) and DPPA (0.66 mL, 2.58 mmol) were charged slowly and solution allowed to adjust to room temp overnight. The reaction mixture was concentrated and then flash chromatography (hexane-EtOAc, 40:1) gave **15a** (0.179 g, 56 %) and a 31:69 mixture of **15a** and **15b** (48 mg, 15%) as clear oils.

Data for **15a:**

R_f = 0.15 (EtOAc-hexane, 1:80)

^1H NMR (500 MHz, $CDCl_3$) δ 5.87 – 5.75 (m, 3H), 5.39 (d, J = 17.1 Hz, 1H), 5.29 (d, J = 10.0 Hz, 1H), 4.18 – 4.04 (m, 2H), 3.81 (t, J = 5.5 Hz, 2H), 1.46 (s, 3H, -C(CH_3)$_2$), 1.46 (s, 3H, -C(CH_3)$_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 133.7, 130.9, 127.3, 119.3 (alkene CH/CH_2), 109.4 (-*C*(CH_3)$_2$), 82.5 (CH-O), 80.9 (CH-O), 51.9 (CH_2N_3), 26.9 (-C(*C*H_3)$_2$), 26.9 (-C(*C*H_3)$_2$);

HRMS (ESI): m/z calc for $C_{10}H_{16}N_3O_2$: 210.1243, found: 210.1237 $[M+H]^+$

(3R,4R,E)-7-Azidohepta-1,5-diene-3,4-diol 16

Compound **15a** (0.3 g, 1.43 mmol) was suspended in 2M HCl for 1 h and the mixture was then extracted with EtOAc, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Flash chromatography (3:2 hexane-EtOAc) gave **16** (0.24 g, 78 %) as a clear oil

R_f = 0.27 (hexane-EtOAc, 7:3)

^1H NMR (500 MHz, $CDCl_3$) δ 5.98 – 5.81 (m, 3H), 5.40 (d, J = 17.3 Hz, 1H), 5.30 (d, J = 10.7 Hz, 1H), 4.09 (t, J = 5.9 Hz, 1H), 4.04 (t, J = 6.2 Hz, 1H), 3.82 (d, J = 5.8 Hz, 2H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 136.3, 133.4, 126.1, 117.9 (alkene CH/CH_2), 75.8 (CH-O), 74.5 (CH-O), 52.1 (CHN_3)

HRMS (ESI): *m/z* calc for $C_7H_{11}N_3O_2Cl$: 204.0540, found: 204.0549 $[M+Cl]^-$

(3aR,4R,6S,6aS)-2,2-Dimethyl-4-((phenylthio)methyl)-6-vinyltetrahydro-4H-[1,3]dioxolo[4,5-c]pyrrole 17 and (3aS,4S,7R,7aS)-2,2-dimethyl-7-(phenylthio)-4-vinylhexahydro-[1,3]dioxolo[4,5-c]pyridine 18

Azide **12** (0.075 g, 0.36 mmol) was dissolved in DMF (30 mL) and the solution was heated to 100 °C and stirred until TLC analysis showed the azide was consumed (1-3 h). Then PhSH (0.18 mL, 1.79 mmol) was added and solution allowed to attain room temp and left overnight. The reaction mixture was then diluted with Et_2O and washed with aqueous satd. NH_4Cl, dried over Na_2SO_4 and the solvent was removed under reduced pressure. Flash chromatography (7:3, hexane-EtOAc) gave **17** (26 mg, 25 %) and **18** (12 mg, 11 %), both as clear oils

Data for **17**

R_f = 0.34 (EtOAc-hexane, 2:3)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.4 Hz, 2H, aromatic H), 7.31 – 7.24 (m, 2H, aromatic H), 7.18 (t, *J* = 7.3 Hz, 1H, aromatic H), 5.72 (ddd, *J* = 17.4, 10.6, 5.0 Hz, 1H), 5.24 (dt, *J* = 17.0, 1.6 Hz, 1H), 5.11 (dt, *J* = 10.6, 1.7 Hz, 1H), 4.63 – 4.53 (m, 2H), 3.74 (dd, *J* = 4.9, 2.3 Hz, 1H), 3.23 – 3.11 (m, 3H), 1.50 (s, 3H, -C(CH_3)$_2$), 1.32 (s, 3H, -C(CH_3)$_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 136.4 (aromatic C), 136.0 (alkene CH), 129.1 (2 aromatic CH), 128.8 (2 aromatic CH), 126.0 (aromatic CH), 115.9 (alkene CH_2), 111.2(-*C*(CH_3)$_2$), 85.8 (CH-O), 81.2 (CH-O), 65.0 (CH-N), 60.0 (CH-N), 32.7 (CH_2S), 26.0 (C(*C*H_3)$_2$), 24.1 (C(*C*H_3)$_2$)

HRMS (ESI): m/z calc for $C_{16}H_{22}NSO_2$: 292.1371, found: 292.1365 $[M+H]^+$

Data for **18**

R_f = 0.22 (EtOAc-hexane, 2:3)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 2H, aromatic H), 7.32 – 7.21 (m, 3H, aromatic H), 5.85 (ddd, *J* = 17.1, 10.5, 6.5 Hz, 1H), 5.27 (d, *J* = 17.2 Hz, 1H), 5.20 (d, *J* = 10.5 Hz, 1H), 4.46 (t, *J* = 4.1 Hz, 1H), 3.80 (dd, *J* = 8.9, 4.5 Hz, 1H), 3.53 (dt, *J* = 9.4, 4.5 Hz, 1H), 3.19 (dd, *J* = 9.0, 6.6 Hz, 1H), 3.07 (dd, *J* = 12.0, 5.2 Hz, 1H), 2.96 (t, *J* = 11.8 Hz, 1H)

^{13}C NMR (126 MHz, $CDCl_3$) δ 137.0 (alkene CH) 134.1 (aromatic C), 131.7 (2 aromatic CH), 129.0 (2 aromatic CH), 127.3 (aromatic CH), 117.1 (alkene CH_2), 109.6 (*C*(CH_3)$_2$), 77.4 (CH-O), 74.7 (CH-O), 60.8 (CHN), 46.5 (CH_2N), 45.6 (CH-S), 28.3 (-C(*C*H_3)$_2$), 26.3 (-C(*C*H_3)$_2$)

HRMS (ESI): m/z calc for $C_{16}H_{22}NSO_2$: 292.1371, found: 292.1363 $[M+H]^+$

(3aR,4R,6S,6aS)-2,2-Dimethyl-4-((phenylselanyl)methyl)-6-vinyltetrahydro-4H-[1,3]dioxolo[4,5-c]pyrrole 19

Diphenyl diselenide (0.373 g, 1.195 mmol) was dissolved in degassed DMF (15 mL) and heated to 60 °C. $NaBH_4$ (0.045 g, 1.195 mmol) was added and solution stirred at 60 °C for 30 mins. This reaction mixture was subsequently heated to 110 °C for 1 h. In a separate vessel the azide **12** (0.050 g, 0.239 mmol) was dissolved in degassed DMF (5 mL) and heated to 100 °C until TLC analysis showed consumption of the azide **12** (1-3 h). Under inert conditions, the contents of the latter vessel were then transferred to the mixture containing in situ generated sodium phenylselenolate. The mixture was allowed to attain room temp and stirred for 12 h. This mixture was diluted with Et_2O and washed with aqueous satd. NH_4Cl solution, dried over Na_2SO_4, filtered and solvent removed under reduced pressure. Flash chromatography (7:3 hexane-EtOAc) gave **19** (40 mg, 50 %)

R_f = 0.35 (EtOAc-hexane, 3:7)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (d, *J* = 7.0 Hz, 2H, aromatic H), 7.29 – 7.18 (m, 3H, aromatic H), 5.72 (ddd, *J* = 16.4, 10.6, 5.0 Hz, 1H), 5.23 (d, *J* = 17.2 Hz, 1H), 5.11 (d, *J* = 10.6 Hz, 1H), 4.59 (s, 2H), 3.75 (d, *J* = 4.9 Hz, 1H), 3.24 – 3.14 (m, 2H), 3.11 (dd, *J* = 11.9, 7.0 Hz, 1H), 1.50 (s, 3H, -C(CH_3)$_2$), 1.31 (s, 3H, -C(CH_3)$_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 136.13 (alkene CH), 132.51 (2 aromatic CH), 130.68 (aromatic C), 129.01(2 aromatic CH), 126.84 (aromatic CH), 115.90 (alkene CH_2), 111.19 (*C*(CH_3)$_2$), 86.07 (CH-O), 81.61 (CH-O), 65.07 (CH-N), 60.70 (CH-N), 26.52 (CH_2Se), 26.00 (C(*C*H_3)$_2$), 24.11 (C(*C*H_3)$_2$)

HRMS (ESI): m/z calc for $C_{16}H_{22}NO_2Se$: 340.0816, found: 340.0822 $[M+H]^+$

(3aR,4R,6R,6aS)-2,2-Dimethyl-4-((phenylthio)methyl)-6-vinyltetrahydro-4H-[1,3]dioxolo[4,5-c]pyrrole 20 and (3aR,4S,6S,6aS)-2,2-dimethyl-4-((phenylthio)methyl)-6-vinyltetrahydro-4H-[1,3]dioxolo[4,5-c]pyrrole 21

Compound **12** (0.075 g, 0.36 mmol) was dissolved in toluene (30 mL) and the mixture was heated to 100 °C and then stirred for 1 h. Thiophenol (0.18 mL, 1.79 mmol) was subsequently added and solution allowed to attain room temp and left overnight. The solvent was removed under reduced pressure and flash chromatography (3:2 hexane-EtOAc) gave **17** (27 mg, 30 %), **21** (7 mg, 7 %) & **20** (10 mg, 10 %), all as clear oils.

Data for **20**

R_f = 0.43 (EtOAc-hexane, 1:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.7 Hz, 2H, aromatic H), 7.31 – 7.25 (m, 2H, aromatic H), 7.18 (t, *J* = 7.4 Hz, 1H, aromatic H), 5.93 (ddd, *J* = 17.4, 10.5, 6.8 Hz, 1H), 5.29 (d, *J* = 17.3 Hz, 1H), 5.23 (d, *J* = 10.4 Hz, 1H), 4.65 (t, *J* = 4.9 Hz, 1H), 4.58 (t, *J* = 4.9 Hz, 1H), 3.34 – 3.30 (m, 1H), 3.25 – 3.12 (m, 2H), 3.00 (td, *J* = 6.9, 3.9 Hz, 1H), 1.48 (s, 3H, C(CH_3)$_2$), 1.32 (s, 3H, C(CH_3)$_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 136.30 (aromatic C), 133.72 (C-6), 129.08 (2 aromatic CH), 128.91 (2 aromatic CH), 126.01 (aromatic CH), 117.68 (alkene CH_2), 111.24 (-*C*(CH_3)$_2$), 83.08 (CH-O), 81.30 (CH-O), 64.89 (CH-N), 61.36 (CH-N), 32.18 (CH_2S), 25.68 (-C(*C*H_3)$_2$), 24.21 (-C(*C*H_3)$_2$)

HRMS (ESI): m/z calc for $C_{16}H_{22}NSO_2$: 292.1371, found: 292.1382 $[M+H]^+$

Data for **21**

R_f = 0.64 (EtOAc-hexane, 1:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.7 Hz, 2H, aromatic H), 7.28 (dd, *J* = 13.9, 6.3 Hz, 2H, aromatic H), 7.19 (t, *J* = 7.3 Hz, 1H, aromatic H), 5.88 (ddd, *J* = 17.0, 10.2, 6.3 Hz, 1H), 5.30 (d, *J* = 17.5 Hz, 1H), 5.14 (d, *J* = 10.3 Hz, 1H), 4.46-4.34 (m, 2H), 3.62 (dd, *J* = 6.4, 3.9 Hz, 1H), 3.36 (ddd, *J* = 8.3, 5.6, 3.2 Hz, 1H), 3.21 (dd, *J* = 13.2, 5.5 Hz, 1H), 3.00 (dd, *J* = 13.2, 7.8 Hz, 1H); ^{1}H-NMR (500 MHz, CD_3OD) δ 7.41 (d, *J* = 7.8 Hz, 2H), 7.30 (td, *J* = 8.3, 7.9, 1.9 Hz, 2H), 7.20 (dd, *J* = 8.3, 6.5 Hz, 1H), 5.94 – 5.79 (m, 1H), 5.28 (d, *J* = 16.8 Hz, 1H), 5.15 (d, *J* = 10.5 Hz, 1H), 4.43 (dt, *J* = 5.9, 3.0 Hz, 1H), 4.38 (dd, *J* = 7.0, 4.7 Hz, 1H), 3.53 (t, *J* = 6.0 Hz, 1H), 3.26 – 3.20 (m, 1H), 3.12 – 3.00 (m, 2H), 1.45 (s, 3H), 1.29 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.15 (alkene CH), 135.80 (aromatic C), 129.49 (2 aromatic CH), 128.96 (2 aromatic CH), 126.24 (aromatic CH), 116.44 (alkene CH_2), 113.65 (-*C*(CH_3)$_2$), 85.08, 84.32 (each CH-O), 66.66 (CH-N), 63.20 (CH-N), 38.01 (CH_2S), 27.21 (-C(*C*H_3)$_2$), 25.17 (-C(*C*H_3)$_2$); ^{13}C NMR (126 MHz, CD_3OD) δ 137.39 (CH), 135.61 (C) 129.56 (2 C), 128.65 (2 C), 126.06 (C), 115.79 (CH_2), 84.93 (CH), 84.55 (CH), 66.74 (CH1), 63.10 (CH), 36.67 (CH), 26.04 (CH_3), 23.92 (CH_3)

HRMS (ESI): m/z calc for $C_{16}H_{22}NSO_2$: 292.1371, found: 292.1374 $[M+H]^+$.

(3aS,6aR)-2,2,6-Trimethyl-4-vinyl-3a,6a-dihydro-4H-[1,3]dioxolo[4,5-c]pyrrole 22

Compound **12** (50 mg, 0.239 mmol) was dissolved in toluene (5 mL) and heated at reflux for 12 h. The solvent was removed and chromatography (3:2 hexane-EtOAc) gave imine **22** (4 mg, 10 %) as a clear oil

R_f = 0.38 (EtOAc-hexane, 1:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81 (ddd, *J* = 17.0, 10.4, 6.2 Hz, 1H), 5.19 – 5.10 (m, 2H), 4.89 (d, *J* = 5.4 Hz, 1H), 4.67 (d, *J* = 6.0 Hz, 1H), 4.45 (d, *J* = 5.4 Hz, 1H), 2.14 (s, 3H, CH_3), 1.37 (s, 3H, -C(CH_3)$_2$), 1.35 (s, 3H, -C(CH_3)$_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 174.35 (C=N), 136.08 (alkene CH), 116.38 (alkene CH_2), 112.13 (*C*(CH_3)$_2$) , 86.82 (CHO), 82.48 (CHO), 77.82 (CH-N), 26.94 (C(*C*H_3)$_2$), 25.91 (C(*C*H_3)$_2$), 16.95 (CH_3)

HRMS (ESI): m/z calc for $C_{10}H_{16}NO_2$: 182.1181, found: 182.1189 $[M+H]^+$

(2*S*,3*S*,4*R*,5*R*)-2-Vinylpiperidine-3,4,5-triol hydrochloride 25 (1(*S*)-1-*C*-vinyl-1,5-dideoxy-1,5-imino-ribitol hydrochloride)

Compound **13** (50 mg, 0.296 mmol) was dissolved in DMF (5 mL) and stirred at 90 °C for 30 mins. AcOH (85µL, 1.47 mmol) was then added

followed by water (25 mL) after 10 mins and the solvent was removed under reduced pressure. The residue was then stirred in dilute HCl overnight and volatile materials removed under reduced pressure. Flash chromatography (8:2:0.1:0.1 CH_2Cl_2-MeOH-aq NH_3-H_2O) gave the free amine (2*S*,3*S*,4*R*,5*R*)-2-vinylpiperidine-3,4,5-triol (42 mg, 91 %) as a yellow foam. Reaction of the free amine (10 mg, 0.063 mmol) with 2M HCl gave the title hydrochloride salt **25** (10 mg, 85 %) as a yellow foam. The ^{13}C-NMR spectroscopic data for this HCl salt were in good agreement with those reported (75 MHz) previously by Wrodnigg and co-workers.[30]

$[\alpha]_D^{20}$ +5.51 (***c*** 0.29, H_2O)

^{1}H NMR (500 MHz, D_2O) δ 5.80 – 5.65 (m, 1H, alkene H), 5.52 – 5.41 (2H, overlapping alkene H), 4.07 (br s, 1H), 3.90 (dddd, *J* = 11.6, 5.0, 2.6, 0.9 Hz, 1H), 3.67 – 3.64 (2H, overlapping signals), 3.16 (dd, *J* = 12.1, 4.9 Hz, 1H), 3.02 (t, *J* = 11.9 Hz, 1H)

^{13}C NMR (126 MHz, D_2O) δ 129.51 (alkene CH), 124.68 (alkene CH_2), 69.59 (CH-O), 68.18 (CH-O), 64.55 (CH-O), 56.09 (CH-N), 41.34 (CH_2N)

HRMS (ESI): m/z calc for $C_7H_{13}NO_3Cl$: 194.0584, found: 194.0590 $[M-H]^{\cdot}$

(2S,3S,4R,5R)-5-Azido-2-vinylpiperidine-3,4-diol 26

Compound **13** (50 mg, 0.296 mmol) was dissolved in DMF (5 mL) and stirred at 90 ˚C for 30 mins. NaN_3 (95 mg, 1.47 mmol) and AcOH (25µL, 0.44 mmol) were added and water (25 mL) was added after 10 mins and the solvent was removed under reduced pressure. Flash chromatography (100:1 EtOAc-aq NH_3) gave the title compound **26** (19 mg, 35 %) as a yellow foam

R_f = 0.6 (100:1 EtOAc-aq NH_3)

^{1}H NMR (500 MHz, CD_3OD): δ 5.89 (ddd, *J* = 17.4, 10.7, 6.5 Hz, 1H), 5.27 (d, *J* = 17.7 Hz, 1H), 5.20 (d, *J* = 10.5 Hz, 1H), 4.10 (d, *J* = 2.7 Hz, 1H), 3.30 – 3.25 (2H, overlapping signals), 3.17 (dd, *J* = 9.8, 2.8 Hz, 1H), 2.98 (t, *J* = 11.7 Hz, 1H), 2.86 (dd, *J* = 12.1, 4.9 Hz, 1H)

^{13}C NMR (126 MHz, CD_3OD) δ 137.18 (alkene CH), 115.98 (alkene CH_2), 72.46 (CH-O), 70.48 (CH-O), 59.38 (CH-N_3), 56.83 (CH-N), 41.75 (CH_2-N)

HRMS (ESI): m/z calc for $C_7H_{13}N_4O_2$: 185.1039, found: 185.1045 $[M+H]^+$

(2S,3S,4S,5R)-5-(Phenylthio)-2-vinylpiperidine-3,4-diol 27 and (2R,3R,4S,5S)-2-((phenylthio)methyl)-5-vinylpyrrolidine-3,4-diol 28

Compound **13** (0.05 g, 0.296 mmol) was dissolved in DMF (5 mL) and stirred at 90 ˚C for 30 mins. Thiophenol (0.15 mL, 1.47 mmol) was then added followed by H_2O (25 mL) after 10 mins and the solvent was removed under reduced pressure. Flash chromatography (100:1 EtOAc-aq NH_3) gave the title compounds **27** (35 mg, 48%) and **28** (24 mg, 32 %) as a white solids.

Data for **27**

R_f = 0.64 (100:1 EtOAc-aq NH_3)

^{1}H NMR (500 MHz, CD_3OD) δ 7.47 – 7.41 (m, 2H, aromatic H), 7.34 – 7.26 (m, 2H, aromatic H), 7.26 – 7.20 (m, 1H, aromatic H), 5.90 (ddd, *J* = 17.2, 10.6, 6.5 Hz, 1H), 5.26 (dt, *J* = 17.5, 1.5 Hz, 1H), 5.18 (dt, *J* = 10.6, 1.4 Hz, 1H), 4.10 (t, *J* = 2.6 Hz, 1H), 3.38 – 3.25 (2H, overlapping signals), 3.22 (dd, *J* = 10.0, 2.8 Hz, 1H), 2.96 (t, *J* = 12.2 Hz, 1H), 2.86 (dd, *J* = 12.5, 4.7 Hz, 1H)

^{13}C NMR (126 MHz, CD_3OD): δ 137.43 (alkene CH), 135.07 (aromatic C), 130.94 (2 aromatic CH), 128.68 (2 aromatic CH), 126.49 (aromatic CH), 115.81 (alkene CH_2), 73.42 (CH-O), 70.75 (CH-O), 57.03 (CH-N), 49.94 (CH-S), 44.40 (CH_2N)

HRMS (ESI): *m/z* calc for $C_{13}H_{18}NO_2S$: 252.1058, found: 252.1051 $[M+H]^+$

Data for **28**

R_f = 0.31 (100:1 EtOAc-aq NH_3)

^{1}H NMR (500 MHz, CD_3OD): δ 7.39 (d, *J* = 7.6 Hz, 2H, aromatic H), 7.29 (t, *J* = 7.7 Hz, 2H, aromatic H), 7.18 (t, *J* = 7.4 Hz, 1H, aromatic H), 5.84 (ddd, *J* = 17.7, 10.2, 7.9 Hz, 1H), 5.28 (d, *J* = 16.9 Hz, 1H), 5.18 (d, *J* = 10.3 Hz, 1H), 4.10 (t, *J* = 3.9 Hz, 1H), 3.81 (dd, *J* = 8.6, 4.0 Hz, 1H), 3.60 (t, *J* = 8.2 Hz, 1H), 3.42 (td, *J* = 7.1, 3.6 Hz, 1H), 3.33 – 3.24 (m, 1H), 3.04 (dd, *J* = 13.3, 7.1 Hz, 1H)

^{13}C NMR (126 MHz, CD_3OD): δ 136.8 (alkene CH), 135.9 (aromatic C), 129.0 (2 aromatic CH), 128.6 (2 aromatic CH), 125.8 (aromatic CH), 116.9 (alkene CH_2), 77.3 (CH-O), 71.7 (CH-O), 63.7 (CH-N), 58.3 (CH-N), 32.9 (CH_2S)

HRMS (ESI): m/z calc for $C_{13}H_{18}NO_2S$: 252.1058, found: 252.1056 $[M+H]^+$

3aS,4S,8aS)-2,2-Dimethyl-4-((phenylthio)methyl)-3a,5,6,8a-tetrahydro-4H-[1,3]dioxolo[4,5-c]azepine 32 and (3aR,4S,8aR)-2,2-dimethyl-4-((phenylthio)methyl)-3a,5,6,8a-tetrahydro-4H-[1,3]dioxolo[4,5-c]azepine 33

Compound **15** (0.05 g, 0.239 mmol) was dissolved in DMF (20 mL) and the solution was heated to 110 °C and stirred for 2 h. PhSH (0.12 mL, 1.2 mmol) was then added and the mixture was allowed to attain room temp and left overnight. The reaction mixture was then diluted with Et_2O and washed with satd NH_4Cl, dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. Flash chromatography (4:1 hexane-EtOAc) gave **32** (23 mg, 33 %) and **33** (4 mg, 5 %), both as clear oils

Data for **32**

R_f **=** 0.21 (hexane-EtOAc, 4:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (s, 2H, aromatic H), 7.30 – 7.25 (m, 2H, aromatic H), 7.17 (t, *J* = 7.4 Hz, 1H, aromatic H), 5.99 (dt, *J* = 10.7, 2.2 Hz, 1H), 5.95 – 5.90 (m, 1H), 4.58 – 4.43 (m, 1H), 3.54 – 3.42 (2H, overlapping signals), 3.35 (t, *J* = 8.8 Hz, 1H), 3.20 (dd, *J* = 16.2, 5.0 Hz, 1H), 3.04 (td, *J* = 9.1, 2.4 Hz, 1H), 2.94 (dd, *J* = 13.4, 9.2 Hz, 1H), 1.40 (s, 3H, -C(CH_3)$_2$), 1.39 (s, 3H, -C(CH_3)$_2$)

^{13}C NMR (126 MHz, $CDCl_3$): δ 136.10 (aromatic C), 131.33 (alkene CH), 130.53 (alkene CH), 129.00 (2 aromatic CH), 128.89 (2 aromatic CH), 125.93 (aromatic CH), 109.16 (*C*(CH_3)$_2$), 80.97 (CH-O), 79.03, (CH-O) 60.73 (CH-N), 44.63 (CH_2-N), 37.00 (CH_2-S), 26.98 (C(*C*H_3)$_2$), 26.80 (C(*C*H_3)$_2$)

HRMS (ESI): m/z calc for $C_{16}H_{22}NO_2S$: 292.1371, found: 292.1366 $[M+H]^+$

Data for **33**

R_f = 0.13 (hexane-EtOAc, 4:1)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 (d, *J* = 7.2 Hz, 2H, aromatic H), 7.29 (t, *J* = 7.6 Hz, 2H, aromatic H), 7.19 (q, *J* = 6.6, 5.8 Hz, 1H, aromatic H), 5.85 (d, *J* = 11.1 Hz, 1H), 5.75 (ddt, *J* = 10.9, 5.6, 2.3 Hz, 1H), 4.86 (d, *J* = 9.1 Hz, 1H), 4.04 (dd, *J* = 9.5, 6.9 Hz, 1H), 3.58 – 3.49 (2H, overlapping signals), 3.46 (ddd, *J* = 10.1, 6.9, 2.5 Hz, 1H), 3.32 (dq, *J* = 17.9, 2.9 Hz, 1H), 2.80 (dd, *J* = 13.7, 10.7 Hz, 1H), 1.43 (s, 3H, -C(CH_3)$_2$), 1.43 (s, 3H, -C(CH_3)$_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 135.70 (aromatic C), 131.46 (alkene CH), 129.41 (2 aromatic CH), 128.99 (2 aromatic CH), 128.23 (alkene CH), 126.19 (aromatic CH), 109.13 (-*C*(CH_3)$_2$), 80.90 (C-5), 75.13 (C-4), 53.93 (C-6), 45.87 (C-1), 34.60 (C-7), 27.18 (-C(*C*H_3)$_2$), 26.73 (-C(*C*H_3)$_2$)

HRMS (ESI): m/z calc for $C_{16}H_{22}NSO_2$: 292.1371, found: 292.1363 $[M+H]^+$

Triethyl((1-(5-ethynyl-2,2-dimethyl-1,3-dioxolan-4-yl)allyl)oxy)silane 35

Iodide **9** (13 g, 28.36 mmol) was dissolved in a solution of THF-H_2O (9:1, 125 mL). Activated zinc (18.55 g, 283.6 mmol) was suspended in the solution and the mixture was sonicated at 40 °C for 2 h. The zinc was filtered off, washing with Et_2O (110 mL). The combined organic layers were subsequently washed with H_2O (90 mL), satd $NaHCO_3$ (90 mL), brine (90 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure to give the intermediate aldehyde (6.81 g, 80 %) as a clear oil. $TMSCH_2N_2$ (12.5 mL, 2 M in Et_2O) was added slowly to LDA in THF (25.0 mL of 1 M in THF) at -78°C under argon and the mixture stirred for 1 h. The aldehyde intermediate **34** (1 g, 3.33 mmol) in anhydrous THF (60 mL) was subsequently added to this and the mixture stirred at -78 ˚C for a further hour. The reaction was allowed to attain 0 ˚C and then stirred for 30 min. Satd. NH_4Cl solution (100 mL) was added and the mixture stirred for 2 h and was subsequently concentrated. EtOAc (75 mL) was added to the concentrate which was then washed with H_2O (50 mL). The aqueous layer was extracted with EtOAc (3 x 75 mL) and the combined organic layers were dried over Na_2SO_4, filtered and the solvent then removed under reduced pressure. Flash chromatography (1:40 EtOAc-hexane) gave alkyne **35** (0.65 g, 55 %, two steps) as a clear oil

R_f = 0.58 (EtOAc-hexane, 1:20)

FTIR 3310, 2987, 2954, 2877, 1458, 1415, 1380, 1370, 1338, 1227, 1145, 1123, 1078, 1046, 1004, 973, 930, 866, 839, 780, 726, 690, 671 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$) δ 5.89 (ddd, *J* = 17.0, 10.5, 5.2 Hz, 1H, alkene H), 5.47 (dt, *J* = 17.1, 1.9 Hz, 1H, alkene H), 5.20 (dt, *J* = 10.8, 1.6 Hz, 1H, alkene H), 4.58 (dd, *J* = 5.2, 2.2 Hz, 1H) 4.48 (ddt, J = 8.3, 5.2, 1.5 Hz, 1H), 3.84 (dd, *J* = 8.3, 5.3 Hz, 1H), 2.51 (d, *J* = 2.0 Hz, 1H, alkyne H), 1.54 (s, 3H, $C(CH_3)_2$), 1.33 (s, 3H, $C(CH_3)_2$), 0.97 (t, *J* = 7.8 Hz, 9H, -Si(CH_2CH_3)), 0.70 – 0.59 (m, 6H, -Si(CH_2CH_3))

^{13}C NMR (126 MHz, $CDCl_3$) δ 136.3 (alkene CH), 117.1 (alkene CH_2), 110.6 ($C(CH_3)_2$), 81.5 (CH-O), 80.5 (alkyne C), 75.4 (alkyne CH), 73.2 (CH-O), 67.0 (CH-O), 27.6 ($C(CH_3)_2$), 26.2 ($C(CH_3)_2$), 6.7 (-Si(CH_2CH_3)$_3$), 4.9 (-Si(CH_2CH_3)$_3$)

HRMS (ESI): m/z calc for $C_{16}H_{27}O_3Si$:295.1729, found: 295.1739 $[M-H]^-$;

(*E*)-4-(3-Azidoprop-1-en-1-yl)-5-ethynyl-2,2-dimethyl-1,3-dioxolane 36

To **35** (1.3 g, 4.38 mmol) in anhydrous THF (35 mL) TBAF in THF (13.2 mL, 1 M in THF) was charged slowly and solution stirred at room temp overnight. The mixture was then treated with 3M NaOH (20 mL) and stirred for 15 min. The layers were separated and aqueous layer extracted with EtOAc. All the organic portions were combined and then dried over Na_2SO_4, filtered and solvent removed under reduced pressure. Flash chromatography (1:4 EtOAc-hexane) gave the intermediate alcohol (0.63 g, 79 %) as a clear oil (Rf 0.16, 1:4 EtOAc-hexane). To this alcohol (0.76 g, 4.17 mmol) in THF (25 mL) PPh_3 (1.86 g, 7.10 mmol) was added and mixture was cooled to 0 °C. DIAD (1.4 mL, 7.10 mmol) and DPPA (1.53 mL, 7.10 mmol) were then charged slowly and solution allowed to attain room temp and left overnight. the solvent was removed under reduced pressure and then flash chromatography (40:1, hexane-EtOAc) gave the title compound **36** (0.52 g, 60 %) as a clear oil

R_f = 0.4 (EtOAc-hexane, 1:20)

FTIR 3295, 2988, 2935, 2099, 1371, 1223, 1160, 1118, 1045, 971, 863, 781 cm^{-1}

^1H NMR (600 MHz, $CDCl_3$) δ 6.03 – 5.87 (2H, overlapping signals, alkene H), 4.82 (dd, J = 5.8, 2.2 Hz, 1H), 4.60 (t, J = 6.3 Hz, 1H), 3.84 (d, J = 5.5 Hz, 2H), 2.56 (d, J = 2.2 Hz, 1H, alkyne H), 1.58 (s, 3H, $(CH_3)_2$), 1.39 (s, 3H, $C(CH_3)_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 130.0 (alkene CH), 128.7 (alkene CH), 110.7 (-$C(CH_3)_2$), 79.4 (alkyne C), 78.0 (CH-O), 76.5 (alkyne CH), 69.1 (CH-O), 52.0 (CH_2N_3), 27.6 ($C(CH_3)_2$), 26.0 ($C(CH_3)_2$)

HRMS (ESI): m/z calc for $C_{20}H_{27}N_6O_4$:415.2094, found: 415.2079 $[2M+H]^+$;

(3bR,6aS,7S)-5,5-Dimethyl-7-vinyl-3b,6a-dihydro-7H-[1,3]dioxolo[4',5':3,4]pyrrolo[1,2-c][1,2,3]triazole 37 and (3bR,6aS,7R)-5,5-dimethyl-7-vinyl-3b,6a-dihydro-7H-[1,3]dioxolo[4',5':3,4]pyrrolo[1,2-c][1,2,3]triazole 38

Allylic azide **36** (0.33 g, 1.59 mmol) was heated in toluene at 100 ˚C for 3 h and the solvent was removed under reduced pressure. Flash chromatography (3:2 hexane-EtOAc) gave **37** (0.13 g, 40 %) as a clear oil and **38** (79 mg, 24 %) as a clear waxy solid

Data for **37**

R_f = 0.52 (EtOAc-hexane, 1:1)

FTIR 2989, 2939, 1376, 1259, 1210, 1182, 1155, 1128, 1096, 1058, 989, 929, 868, 825, 804, 688 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ 7.70 (s, 1H, triazole H), 5.94 (ddd, J = 16.9, 10.5, 6.3 Hz, 1H, alkene H), 5.56 (d, J = 5.5 Hz, 1H, alkene H), 5.39 (d, J = 10.5 Hz, 1H), 5.24 – 5.18 (2H, overlapping signals), 5.15 (d, J = 5.8 Hz, 1H), 1.42 (s, 3H, $C(CH_3)_2$), 1.27 (s, 3H, $C(CH_3)_2$)

^{13}C NMR (151 MHz, $CDCl_3$) δ 140.1 (triazole C), 131.9 (alkene CH), 128.6 (triazole CH), 119.8 (alkene CH_2), 113.7 ($C(CH_3)_2$), 89.7 (CH-O), 71.7 (CH-O), 66.7 (CH-N), 27.0 ($C(CH_3)_2$), 25.8 ($C(CH_3)_2$)

HRMS (ESI): m/z calc for $C_{10}H_{14}N_3O_2$: 208.1086, found: 208.1085 $[M+H]^+$

Data for **38**

R_f = 0.35 (EtOAc-hexane, 1:1)

FTIR 3111, 2994, 1450, 1371, 1212, 1154, 1128, 1100, 1083, 1055, 1003, 986, 952, 888, 846, 709, 689 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$) δ 7.68 (s, 1H, triazole H), 6.05 (ddd, J = 17.8, 10.2, 8.1 Hz, 1H, alkene H), 5.66 (d, J = 17.2 Hz, 1H, alkene H), 5.59 (d, J = 10.3 Hz, 1H, alkene H), 5.57 (d, J = 5.7 Hz, 1H), 5.41 (t, J = 5.6 Hz, 1H), 5.02 (dd, J = 8.0, 5.3 Hz, 1H), 1.42 (s, 3H, $C(CH_3)_2$), 1.28 (s, 3H, $C(CH_3)_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 139.60 (triazole C), 129.25 (alkene CH), 128.78 (triazole CH), 122.60 (alkene CH_2), 113.95 ($C(CH_3)_2$), 86.21 (CH-O), 72.05 (CH-O), 64.51 (CH-N), 26.85 ($C(CH_3)_2$), 25.84 (-$C(CH_3)_2$)

HRMS (ESI): m/z calc for $C_{10}H_{14}N_3O_2$: 208.1086, found: 208.1081 $[M+H]^+$

(4R,5S,6S)-6-Vinyl-5,6-dihydro-4H-pyrrolo[1,2-c][1,2,3]triazole-4,5-diol 39

Compound **37** (84.0 mg, 0.40 mmol) was dissolved in 1M HCl (10 mL) and the mixture stirred for 1 h. The solvent was removed under reduced pressure and flash chromatography (CH_2Cl_2-MeOH, 17:3) gave the triazole **37** (61 mg, 90 %) as a white solid

(R_f 0.1, EtOAc); $[\alpha]_D^{20}$ -4.5 (*c* 0.75, $CHCl_3$)

^1H NMR (500 MHz, CD_3OD) δ 7.73 (s, 1H, triazole H), 6.02 (ddd, *J* = 17.5, 10.3, 7.5 Hz, 1H, alkene H), 5.57 – 5.45 (2H, overlapping signals, alkene H), 5.06 (d, *J* = 5.1 Hz, 1H), 4.88 (d, *J* = 6.9 Hz, 1H), 4.48 (t, *J* = 5.6 Hz, 1H)

^{13}C NMR (126 MHz, CD_3OD) δ 141.21 (triazole C), 132.00 (alkene CH), 128.08 (triazole CH), 120.24 (alkene CH_2), 80.70 (CH-O), 66.57 (CH-O), 63.96 (CH-N)

HRMS (ESI): *m/z* calc for $C_7H_{10}N_3O_2$:168.0773, found: 168.0778 $[M+H]$

(4R,5S,6R)-6-Vinyl-5,6-dihydro-4H-pyrrolo[1,2-c][1,2,3]triazole-4,5-diol 40

Compound **38** (34 mg, 0.16 mmol) was dissolved in 1M HCl (5 mL) and the mixture stirred for 1 h. The removal of the solvent under reduced pressure and subsequent flash chromatography (CH_2Cl_2:MeOH 17:3) gave **40** (25 mg, 92 %) as a clear oil

R_f = 0.15 (EtOAc); $[\alpha]_D^{20}$ -15.7 (*c* 0.83, MeOH)

^1H NMR (500 MHz, CD_3OD) δ 7.70 (s, 1H, triazole H), 6.06 (ddd, *J* = 17.8, 10.3, 8.3 Hz, 1H, alkene H), 5.50 (d, *J* = 17.2 Hz, 1H, alkene H), 5.45 (d, *J* = 10.4 Hz, 1H, alkene H), 5.19 – 5.08 (2H, overlapping signals), 4.81 (t, *J* = 5.6 Hz, 1H)

^{13}C NMR (126 MHz, CD_3OD) δ 141.58 (triazole C), 131.61 (alkene CH), 127.75 (triazole CH), 120.43 (alkene CH_2), 77.47 (CH-O), 65.14 (CH-O), 64.84 (CH-N)

HRMS (ESI): *m/z* calc for $C_7H_{10}N_3O_2$:168.0773, found: 168.0775 $[M+H]^+$

(2S,3R,4S,5S)-2-((Phenylthio)methyl)-5-vinylpyrrolidine-3,4-diol hydrochloride 41

Compound **21** (4 mg, 0.01 mmol) was treated with 2M HCl as described for **25** and this gave the title compound (3 mg) as a white solid

^1H NMR (500 MHz, CD_3OD): δ 7.54 – 7.39 (m, 2H, aromatic H), 7.37 (dd, *J* = 8.5, 7.0 Hz, 2H, aromatic H), 7.35 – 7.25 (m, 1H, aromatic H), 5.96 (ddd, *J* = 17.1, 10.3, 8.4 Hz, 1H, alkene H), 5.58 – 5.48 (overlapping signals, 2H, alkene H), 4.09 (t, *J* = 5.0 Hz, 1H), 4.05 (dd, *J* = 6.5, 4.8 Hz, 1H), 4.00 – 3.93 (m, 1H), 3.56 – 3.44 (2H, overlapping signals), 3.17 (dd, *J* = 14.5, 9.7 Hz, 1H)

^{13}C NMR (126 MHz, CD_3OD) δ 133.291 (1 aromatic C), 130.29 (2 aromatic CH), 130.16 (alkene CH), 129.11 (2 aromatic C), 127.15 (aromatic C), 122.58 (alkene CH_2), 73.67 (CH-O), 72.95 (CH-O), 65.20 (CH-N), 62.57 (CH-N), 33.79 (CH_2S)

HRMS (ESI): m/z calc for $C_{13}H_{17}NO_2SCl$: 286.0669, found: 286.0660 $[M-H]^-$

(2R,3R,4S,5S)-2-((Phenylthio)methyl)-5-vinylpyrrolidine-3,4-diol hydrochloride 42

Compound **17** (10 mg, 0.034 mmol) was dissolved in 2M HCl as for **25** and the mixture stirred at room temp overnight. Removal of the volatile materials under reduced pressure gave **42** (9 mg) as a white solid

$[\alpha]_D^{20}$ -58.8 (***c*** 0.35, H_2O)

^1H NMR (500 MHz, CD_3OD) δ 7.46 (d, *J* = 7.7 Hz, 2H, aromatic 2H), 7.35 (t, *J* = 7.6 Hz, 2H, aromatic H), 7.27 (t, *J* = 7.3 Hz, 1H, aromatic H), 5.93 (ddd, *J* = 17.0, 10.2, 8.7 Hz, 1H, alkene H), 5.52 (d, *J* = 17.0 Hz, 1H, alkene H), 5.49 (d, *J* = 10.3 Hz, 1H, alkene H), 4.20 (t, *J* = 3.4 Hz, 1H), 4.07 (dd, *J* = 9.4, 3.5 Hz, 1H), 3.96 (t, *J* = 9.0 Hz, 1H), 3.75 (ddd, *J* = 9.1, 6.2, 3.2 Hz, 1H), 3.46 (dd, *J* = 14.3, 6.1 Hz, 1H), 3.22 (dd, *J* = 14.2, 8.7 Hz, 1H)

^{13}C NMR (126 MHz, CD_3OD) δ 133.95 (aromatic C), 130.82 (alkene CH), 129.80 (2 aromatic CH), 129.02 (2 aromatic CH), 126.82 (aromatic CH), 122.35 (alkene CH_2), 75.37 (CH-O), 70.59 (CH-O), 63.16 (CH-N), 59.52 (CH-N), 30.59 (CH_2S)

HRMS (ESI): m/z calc for $C_{13}H_{17}NO_2SCl$: 286.0669, found: 286.0676 $[M-H]^-$

(2R,3R,4S,5R)-2-((Phenylthio)methyl)-5-vinylpyrrolidine-3,4-diol hydrochloride 43 Compound **20** (5 mg, 0.034 mmol) was treated with 2M HCl as described for **25** and gave **43** (4 mg) as a white solid

^1H NMR (500 MHz, CD_3OD) δ 7.50 – 7.44 (m, 2H, aromatic H), 7.35 (dd, *J* = 8.5, 6.9 Hz, 2H, aromatic H), 7.27 (t, *J* = 7.4 Hz, 1H, aromatic H), 6.10 (ddd, *J* = 17.1, 10.4, 9.0 Hz, 1H, alkene H), 5.54 – 5.45 (overlapping signals, 2H, alkene CH_2), 4.35 (dd, *J* = 6.2, 4.1 Hz, 1H), 4.26 (dd, *J* = 5.3, 4.2 Hz, 1H), 4.00 (dd, *J* = 9.1, 5.3 Hz, 1H), 3.65 (dt, *J* = 10.6, 5.4 Hz, 1H), 3.49 (dd, *J* = 14.6, 4.6 Hz, 1H), 3.22 – 3.15 (m, 1H)

^{13}C NMR (126 MHz, CD_3OD) δ 134.00 (aromatic C), 129.94 (2 aromatic C), 129.37 (alkene CH), 129.01(2 aromatic CH), 126.81 (aromatic CH), 122.57 (alkene CH_2), 72.07 (CH-O), 70.76 (CH-O), 63.04 (CH-N), 59.32 (CH-N), 31.35 (CH_2S)

HRMS (ESI): m/z calc for $C_{13}H_{17}NO_2SCl$: 286.0669, found: 286.0681 $[M-H]^-$

(2R,3R,4S,5S)-2-((Phenylselanyl)methyl)-5-vinylpyrrolidine-3,4-diol hydrochloride 44

Reaction of **19** (20 mg, 0.06 mmol) with 2M HCl as described for **25** gave **44** (18 mg) as a white solid

$[\alpha]_D^{20}$ -38.0 (***c*** 0.1, H_2O)

^1H NMR (500 MHz, CD_3OD) δ 7.79 – 7.41 (m, 2H, aromatic H), 7.40 – 7.11 (m, 3H, aromatic H), 5.95 (ddd, *J* = 17.0, 10.2, 8.6 Hz, 1H, alkene H), 5.51 (d, *J* = 16.9 Hz, 1H, alkene H), 5.48 (d, *J* = 10.2 Hz, 1H, alkene H), 4.23 (t, *J* = 3.3 Hz, 1H), 4.09 (dd, *J* = 9.4, 3.5 Hz, 1H), 3.97 (t, *J* = 9.0 Hz, 1H), 3.78 (td, *J* = 7.6, 3.1 Hz, 1H), 3.35 (dd, *J* = 13.0, 7.7 Hz, 1H), 3.14 (dd, *J* = 13.0, 7.6 Hz, 1H)

^{13}C NMR (126 MHz, CD_3OD) δ 132.80 (2 aromatic CH), 130.87 (alkene CH), 129.15 (2 aromatic CH), 128.31 (aromatic C), 127.45 (aromatic CH), 122.30 (alkene CH_2), 75.51 (CH-O), 70.72 (CH-O), 63.32 (CH-N), 60.47 (CH-N), 22.83 (CH_2Se)

HRMS (ESI): m/z calc for $C_{13}H_{17}NO_2SeCl$: 334.0113, found: 334.0120 $[M-H]^-$

(2S,3S,4S,5R)-5-(Phenylthio)-2-vinylpiperidine-3,4-diol hydrochloride 45

Reaction of **27** (11 mg, 0.044 mmol) with 2M HCl as described for **25** gave **45** (11 mg) as a white solid

$[\alpha]_D^{20}$ -10.0 (***c*** 0.1, H_2O)

^1H NMR (500 MHz, D_2O): δ 7.49 – 7.41 (m, 2H, aromatic H), 7.36 – 7.26 (m, 3H, aromatic H), 5.73 (ddd, *J* = 17.1, 10.6, 7.8 Hz, 1H, alkene H), 5.49 – 5.43 (overlapping signals, 2H, alkene CH_2), 4.17 (t, *J* = 2.4 Hz, 1H), 3.71 (dd, *J* = 10.7, 7.8 Hz, 1H), 3.66 (dd, *J* = 10.6, 2.4 Hz, 1H), 3.47 (ddd, *J* = 12.7, 4.8, 2.2 Hz, 1H), 3.26 (dd, *J* = 12.7, 4.7 Hz, 1H), 3.23 – 3.14 (m, 1H)

^{13}C NMR (126 MHz, D_2O) δ 132.48 (2 aromatic CH), 131.46 (aromatic C), 129.68 (alkene CH), 129.55 (2 aromatic CH), 128.48 (aromatic CH), 124.59 (alkene CH_2), 69.19 (CH-O), 68.54 (CH-O), 56.16 (CHN), 45.49 (CH-S), 41.73 (CH_2N)

HRMS (ESI): *m/z* calc for $C_{13}H_{17}NO_2SCl$: 286.0669, found: 286.0671 $[M-H]^-$

Acknowledgment

The research was supported by NUI Galway (College of Science PhD scholarship to RC) and a Science Foundation Ireland IvP award to PVM (grant number 12/IA/1398 co-funded by the European Regional Development Fund under grant number 14/SP/2710).

Supporting Information

YES (this text will be updated with links prior to publication)

Primary Data

YES (this text will be updated with links prior to publication)

References

(1) For a review of the applications of organic azides see Bräse, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem. Int. Ed.* **2005**, *44*, 5188.

(2) For reviews on intramolecular 1,3-dipolar cycloaddition in synthesis see (a) Nair, V.; Suja, T. D. *Tetrahedron,* **2007**, *63*, 12247; (b) Padwa, A. In "1,3-Dipolar Cycloaddition Chemistry"; Padwa, A. Ed; Wiley-Interscience: New York, **1984**, *2*, 316.

(3) (a) Huisgen, R.; *Angew. Chem.* **1963**, *75*, 604. (b) Huisgen, R. *Angew. Chem. Int. Ed.* **1963**, *11*, 633.

(4) For allylic azide rearrangement used in tandem with intramolecular Schmidt reactions: Liu, R.; Gutierrez, O.; Tantillo, D. J.; Aubé, J. *J. Am. Chem. Soc.* **2012**, *134*, 6528.

(5) Gagneux, A.; Winstein, S.; Young, W. G. *J. Am. Chem. Soc.* **1960**, *82*, 5956.

(6) Zhou, Y.; Murphy, P. V. *Org. Lett.* **2008**, *10*, 3777.

(7) Moynihan, L.; Chadda, R.; McArdle P.; Murphy, P. V. *Org. Lett.* **2015**, *17*, 6226.

(8) (a) Bräse, S.; Banert, K.; Organic Azides: Syntheses and Applications; Wiley: Germany, **2009**. (b) Kadaba, P. K.; Stevenson, P. J.; P-Nnane, I.; Damani, L. A. *Bioorg. Med. Chem.* **1996**, *4*, 165.

(9) For allylic azide rearrangement followed by copper promoted intermolecular azide-alkene cycloaddition: see Feldman, A. K.; Colasson, B.; Sharpless, K. B.; Fokin, V. V. *J. Am. Chem. Soc.* **2005,** *127*, 13444.

(10) Mishra, A.; Hutait, S.; Bhowmik, S.; Rastogi, N.; Roy, R.; Batra, S. *Synthesis* **2010**, 2731.

(11) Skaanderup, P. R.; Poulsen, C. S.; Hyldtoft, L.; Jørgensen, M. R.; Madsen, R. *Synthesis*, **2002**, 1721.

(12) (a) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *62*, 1990. (b) Skaanderup, P. R.; Hyldtoft, L.; Madsen, R.; *Monatshefte für Chemie* **2002**, *133*, 467.

(13) (a) Brock, E. A.; Davies, S. G.; Lee, J. A.; Roberts, P. M.; Thomson, J. E. *Org. Lett.* **2011**, *13*, 1594. (b) Palmer, A. M.; Volker, J. *Eur. J. Org. Chem.* **2001**, 1293.

(14) Kaburagi, Y.; Kishi, Y. *Org. Lett.* **2007**, *9*, 723–726.

(15) Vekariya, R. H.; Liu, R.; Aubé, J. *Org. Lett.* **2014**, *16*, 1844-47.

(16) (a) Yamakado, Y., Ishiguro, M., Ikeda, N. & Yamamoto, H. J. Am. Chem. Soc. 1981, 103, 5568–5570. (b) Colvin, E. W.; Hamill, B. J. *J. Chem. Soc. Chem. Commun.* **1973**, 151.

(17) For a recent example of synthesis of sugars fused to triazoles and their biological relevance see Putapatri, S. R.; Kanwal, A.; Sridhar, B.; Banerjee, S. K.; Kantevari, S. *Org. Biomol. Chem.*, **2014**, *12*, 8415.

(18) Evidence that there is a relationship between ^{13}C-NMR chemical shifts and stereochemistry has been demonstrated. For an example see Lee, J.; Kobayashi, Y.; Tezuka, K.; Kishi, Y. *Org. Lett.* **1999**, *1*, 2177.

(19) Zoidi, M.; Gonzalez Santana, A.; Torvisco, A.; Tysoe, C.; Siriwardena, A.; Withers, S. G.; Wrodnigg, T. M. *Carbohydr. Res.* **2016**, *429*, 62.

(20) Huisgen, R. *J. Org. Chem.* **1968**, *33*, 2291.

(21) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.

(22) For selected syntheses of bioactive hydroxylated pyrrolidines see (a) Card, P. J. Hitz, W. D. *J. Org. Chem.* **1985**, *50*, 891. (b) Trost, B. M.; Horne, D. B.; Woltering, M. J. *Chem. Eur. J.* **2006**, *12*, 6607. (c)

García-Moreno, M. I.; Aguilar, M.; Ortiz Mellet, C.; García Fernández, J. M. Org. Lett. 2006, 8, 297–299. (d) Ayers, B. J.; Ngo, N.; Jenkinson, S.; Martínez, R. F.; Shimada, Y.; Adachi, I.; Weymouth-Wilson, A. C.; Kato, A.; Fleet. G. W. J. J. Org. Chem. 2012, 77, 7777–7792.

(23) For selected syntheses of iminosugars from our group see (a) McDonnell, C.; Cronin, L.; O' Brien, J. L; Murphy, P. V. J. Org. Chem. 2004, 69, 3565-68. (b) Murphy, P. V.; O' Brien, J. L.; Gorey-Feret, L. J.; Smith, III, A. B. Tetrahedron, 2003, 59, 2259-71.

(24) For recent selected applications of iminosugars see (a) Clark, N.; Metcalf, M. C.; Best, D.; Fleet, G. W. J.; Garman, S. C. Proc. Natl Acad. Sci. (USA), 2012, 109, 17400-17405. (b) Ghisaidoobe, A. T.; van den Berg, R. J. B. H. N.; Butt, S. S.; Strijland, A.; Donker-Koopman, W. E.; Scheij, S.; van den Nieuwendijk, A. M. C. H.; Koomen, G.-J.; van Loevezijn, A.; Leemhuis, M.; Wennekes, T.; van der Stelt, M.; van der Marel, G. A.; van Boeckel, C. A. A.; Aerts, J. M. F. G.; Overkleeft, H. S. J. Med. Chem. 2014, 57, 9096–9104. (c) Lopez, O.; Qing, F.-L.; Ortiz Mellet, C. M. Pedersen, M. Bols, Bioorg. Med. Chem. 2013, 21, 4755-4761. (d) E. M. Sanchez-Fernandez, R. Risquez-Cuadro, C.; Garcia Fernandez, J. M.; Nieto, P. M.; Angulo, J. Chem. Eur. J. 2012, 18, 8527-8539. (e) Decroocq, C.; Stauffert, F.; Pamlard, O.; Oulaidi, F.; Gallienne, E.; Martin, O. R.; Guillou, C.; Compain, P. Bioorg. Med. Chem. Lett. 2015, 25, 830-833. (f) Sayce, A. C.; Alonzi, D. S.; Killingbeck, S. S.; Tyrrell, B. E.; Hill, M. L.; Caputo, A. T.; Iwaki, R.; Kinami, K.; Ide, D.; Kiappes, J. L.; Beatty, P. R.; Kato, A.; Harris, E.; Dwek, R. A.; Miller, J. L.; Zitzmann, N.; PLOS Neglected Tropical Diseases, 2016, 10, e0004524; (g) Barron, S.; Murphy, P. V. Med. Chem. Commun. 2014, 5, 1150-1158.

(25) P. Compain and O. R. Martin, Iminosugars: From Synthesis to Therapeutic Applications, Wiley-VCH, Weinheim, Germany, **2007**, 63.

(26) Gossan, D. P. A.; Alabdul M., Abdulmagid; K.-Y.; Philomene A.; Behr, J.-B.; Ahibo, A. C.; Djakoure, L. A.; Harakat, D.; Voutquenne-Nazabadioko, L. Phytochemistry, **2015**, *109*, 76.

(27) Lieberman, R. L.; D'aquino, J. A.; Ringe, D.; Petsko, G. A. *Biochemistry*, **2009**, *48*, 4816-27.

(28) (a) Murphy, P. V. *Eur. J. Org. Chem.* **2007**, 4177-87. (b) Danieli, E.; Lalot, J.; Murphy, P. V. *Tetrahedron*, **2007**, *63*, 6827. (c) Murphy P. V.; Dunne, J. L. *Curr. Org. Synth.* **2006**, *3*, 403. (d) Chagnault, V.; Lalot, J.; Murphy, P. V. *ChemMedChem*, **2008**, *3*, 1071

(29) Yang, M.; Ye, W.; Schneller, S. W. *J. Org. Chem.* **2004**, *69*, 3993.

(30) Zoidi, M.; Gonzalez Santana, A.; Torvisco, A.; Tysoe, C.; Siriwardena, A.; Withers, S. G.; Wrodnigg, T. M. *Carbohydr. Res.* **2016**, *429*, 62.

---

1. For a review of the applications of organic azides see Bräse, S.; Gil, C.; Knepper, K.; Zimmermann, V. Angew. Chem. Int. Ed. 2005, 44, 5188-5240.

2. For reviews on intramolecular 1,3-dipolar cycloaddition in synthesis see (a) Nair, V.; Suja, T. D. Tetrahedron 2007, 63, 12247-75; (b) Padwa, A. In "1,3-Dipolar Cycloaddition Chemistry"; Padwa, A. Ed; Wiley-Interscience: New York, 1984; Vol 2, p 316.

3 . (a) Huisgen, R.; Angew. Chem. 1963, 75, 604–637. (b) Huisgen, R. Angew. Chem. Int. Ed. 1963, 11, 633–645.

4. For allylic azide rearrangement used in tandem with intramolecular Schmidt reactions: Liu, R.; Gutierrez, O.; Tantillo, D. J.; Aubé, J. J. Am. Chem. Soc. 2012, 134, 6528-6531.

5 Gagneux, A.; Winstein, S.; Young, W. G. J. Am. Chem. Soc. 1960, 82, 5956.

6 Zhou, Y.; Murphy, P. V. Org. Lett. 2008, 10, 3777-81.

7 Moynihan, L.; Chadda, R.; McArdle P.; Murphy, P. V.; Org. Lett. 2015, 17, 6226-6229.

8 (a) Bräse, S.; Banert, K.; Organic Azides: Syntheses and Applications; Wiley: Germany, 2009. (b) Kadaba, P. K.; Stevenson, P. J.; P-Nnane, I.; Damani, L. A. Bioorg. Med. Chem. 1996, 4, 165

9 For allylic azide rearrangement followed by copper promoted intermolecular azide-alkene cycloaddition: see Feldman, A. K.; Colasson, B.; Sharpless, K. B.; Fokin, V. V. J. Am. Chem. Soc. 2005, 127, 13444.

10 Mishra, A.; Hutait, S.; Bhowmik, S.; Rastogi, N.; Roy, R.; Batra, S. Synthesis 2010, 2731-2748.

11 Skaanderup, P. R.; Poulsen, C. S.; Hyldtoft, L.; Jørgensen, M. R.; Madsen, R. Synthesis, 2002, 1721-1727.

12 (a) Bernet, B.; Vasella, A. Helv. Chim. Acta 1979, 62, 1990-2016. (b) Skaanderup, P. R.; Hyldtoft, L.; Madsen, R.; Monatshefte für Chemie 2002, 133, 467-472.

13 (a) Brock, E. A.; Davies, S. G.; Lee, J. A.; Roberts, P. M.; Thomson, J. E. Org. Lett. 2011, 13, 1594–1597. (b) Palmer, A. M.; Volker, J. Eur. J. Org. Chem. 2001, 1293.

14. Kaburagi, Y.; Kishi, Y. Org. Lett. 2007, 9, 723–726.

15. Vekariya, R. H.; Liu, R.; Aubé, J. Org. Lett. 2014, 16, 1844-47.

16. (a) Yamakado, Y., Ishiguro, M., Ikeda, N. & Yamamoto, H. J. Am. Chem. Soc. 1981, 103, 5568–5570. (b) Colvin, E. W.; Hamill, B. J. J. Chem. Soc. Chem. Commun. 1973, 151–152.

17. For a recent example of synthesis of sugars fused to triazoles and their biological relevance see Putapatri, S. R.; Kanwal, A.; Sridhar, B.; Banerjee, S. K.; Kantevari, S. Org. Biomol. Chem., 2014, 12, 8415–8421.

18. Evidence that there is a relationship between chemical shift and stereochemistry in 13C-NMR data has been demonstrated. See Lee, J.; Kobayashi, Y.; Tezuka, K.; Kishi, Y. Org. Lett. 1999, 1, 2177–2180.

19. Zoidi, M.; Gonzalez Santana, A.; Torvisco, A.; Tysoe, C.; Siriwardena, A.; Withers, S. G.; Wrodnigg, T. M. Carbohydr. Res. 2016, 429, 62–70.

20. Hoffmann, R. W. Chem. Rev. 1989, 89, 1841.

21. Huisgen, R.; J. Org. Chem. 1968, 33, 2291-97.

22. For selected syntheses of bioactive hydroxylated pyrrolidines see (a) Card, P. J. Hitz, W. D. J. Org. Chem. 1985, 50, 891–893 (b) Trost, B. M.; Horne, D. B.; Woltering, M. J. Chem. Eur. J. 2006, 12, 6607–6620. (c) García-Moreno, M. I.; Aguilar, M.; Ortiz Mellet, C.; García Fernández, J. M. Org. Lett. 2006, 8, 297–299. (d) Ayers, B. J.; Ngo, N.; Jenkinson, S.; Martínez, R. F.; Shimada, Y.; Adachi, I.; Weymouth-Wilson, A. C.; Kato, A.; Fleet. G. W. J. J. Org. Chem. 2012, 77, 7777–7792.

23. For selected syntheses of iminosugars from our group see (a) McDonnell, C.; Cronin, L.; O' Brien, J. L; Murphy, P. V. J. Org. Chem. 2004, 69, 3565-68. (b) Murphy, P. V.; O' Brien, J. L.; Gorey-Feret, L. J.; Smith, III, A. B. Tetrahedron, 2003, 59, 2259-71.

24. For recent selected applications of iminosugars see (a) Clark, N.; Metcalf, M. C.; Best, D.; Fleet, G. W. J.; Garman, S. C. Proc. Natl Acad. Sci. (USA), 2012, 109, 17400-17405. (b) Ghisaidoobe, A. T.; van den Berg, R. J. B. H. N.; Butt, S. S.; Strijland, A.; Donker-Koopman, W. E.; Scheij, S.; van den Nieuwendijk, A. M. C. H.; Koomen, G.-J.; van Loevezijn, A.; Leemhuis, M.; Wennekes, T.; van der Stelt, M.; van der Marel, G. A.; van Boeckel, C. A. A.; Aerts, J. M. F. G.; Overkleeft, H. S. J. Med. Chem. 2014, 57, 9096–9104. (c) Lopez, O.; Qing, F.-L.; Ortiz Mellet, C. M. Pedersen, M. Bols, Bioorg. Med. Chem. 2013, 21, 4755-4761. (d) E. M. Sanchez-Fernandez, R. Risquez-Cuadro, C.; Garcia Fernandez, J. M.; Nieto, P. M.; Angulo, J. Chem. Eur. J. 2012, 18, 8527-8539. (e) Decroocq, C.; Stauffert, F.; Pamlard, O.; Oulaidi, F.; Gallienne, E.; Martin, O. R.; Guillou, C.; Compain, P. Bioorg. Med. Chem. Lett. 2015, 25, 830-833. (f) Sayce, A. C.; Alonzi, D. S.; Killingbeck, S. S.; Tyrrell, B. E.; Hill,

M. L.; Caputo, A. T.; Iwaki, R.; Kinami, K.; Ide, D.; Kiappes, J. L.; Beatty, P. R.; Kato, A.; Harris, E.; Dwek, R. A.; Miller, J. L.; Zitzmann, N.; PLOS Neglected Tropical Diseases, 2016, 10, e0004524; (g) Barron, S.; Murphy, P. V. Med. Chem. Commun. 2014, 5, 1150-1158.

25. P. Compain and O. R. Martin, Iminosugars: From Synthesis to Therapeutic Applications, Wiley-VCH, Weinheim, Germany, 2007, p. 63.

26. Gossan, D. P. A.; Alabdul M., Abdulmagid; K.-Y.; Philomene A.; Behr, J.-B.; Ahibo, A. C.; Djakoure, L. A.; Harakat, D.; Voutquenne-Nazabadioko, L. Phytochemistry, 2015, 109, 76-83.

27. Lieberman, R. L.; D'aquino, J. A.; Ringe, D.; Petsko, G. A. Biochemistry, 2009, 48, 4816-27.

28. (a) Murphy, P. V. Eur. J. Org. Chem. 2007, 4177-87. (b) Danieli, E.; Lalot, J.; Murphy, P. V. Tetrahedron, 2007, 63, 6827-34. (c) Murphy P. V.; Dunne, J. L. Curr. Org. Synth. 2006, 3, 403-437. (d) Chagnault, V.; Lalot, J.; Murphy, P. V. ChemMedChem, 2008, 3, 1071-76

29. Yang, M.; Ye, W.; Schneller, S. W. J. Org. Chem. 2004, 69, 3993-3996.

30. Zoidi, M.; Gonzalez Santana, A.; Torvisco, A.; Tysoe, C.; Siriwardena, A.; Withers, S. G.; Wrodnigg, T. M. Carbohydr. Res. 2016, 429, 62-70.