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Exploitation of in Situ Generated Sugar-Based Olefin Keto-Nitrones: Synthesis of Carbocycles, Heterocycles, and Nucleoside Derivatives

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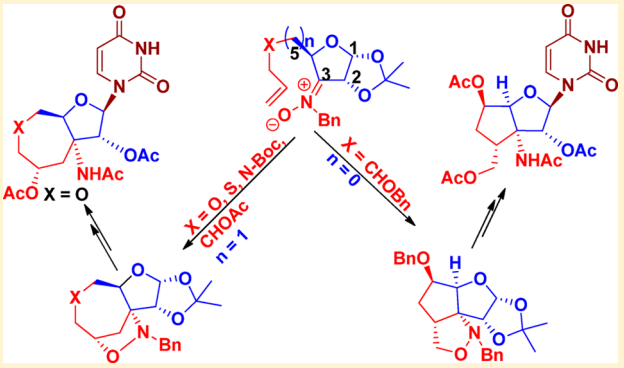
Supporting Information

ABSTRACT: Application of intramolecular 1,3-dipolar nitrone cycloaddition reaction on carbohydrate-derived precursors containing an olefin functionality at C-1 or C-3 or C-5 and a nitrone moiety at C-2 or C-3 as appropriate has resulted in the formation of structurally new cycloaddition products containing furanose-fused oxepane, thiepane, azepane, cyclopentane, cycloheptane, tetrahydrofuran, and pyranose-fused tetrahydrofuran rings. The structure and stereochemistry of these products have been characterized by spectral as well as single-crystal X-ray analyses. Two of the compounds have been transformed to the bicyclic nucleoside derivatives applying Vorbrüggen reaction conditions.



INTRODUCTION

Both the inter- and intramolecular nitrone cycloaddition (INC) reactions provide efficient methods for the synthesis of natural as well as unnatural molecules.[1] However, the method that uses the chirality of natural products as chiral pool generates enantiomerically pure molecules of varying nature and structures.[2] In this perspective, the supremacy of carbohydrates as a chiral pool, is well-established. Various potential chiral auxiliaries,[3] used for the synthesis of chiral molecules, have been generated from carbohydrates through judicious manipulation of the sugar backbone. Attempts to elaborate the synthetic utility of the INC methodology on sugar-based substrates have resulted in generating carbocycles,[4] heterocycles,[5] bicycles,[6] spirocycles,[7] cyclic ethers,[8] alkaloids,[9] amino acids,[10] nucleosides,[11] iminosugars,[12] pseudosaccharides,[13] enzyme inhibitors,[14] precursors for prostaglandin[15] and tetrodotoxin,[16] and other related molecular entities. Nevertheless, the chemistry utilizing this method continues unabated in constructing complex ring systems. Synthetic applications of aldo-nitrones,[17] generated from sugars, have been prevalent, although utilization of the reaction on sugar-based keto-nitrones[18] remains relatively unexplored.

We envisage a strategy that involves an olefin moiety (allyl, homoallyl, *O*-allyl, *S*-allyl, *N*-allyl) at C-5 and a nitrone unit at C-3 (Path A), or an *O*-allyl group at C-1 and a nitrone moiety at C-2 (Path B), or an *O*-allyl group at C-3 and a nitrone function at C-2 (Path C) of sugar-derived substrates that could undergo INC reaction (Figure 1) to generate a diverse nature of carbocycles and heterocycles including tetrahydro-furan (-pyran) rings. The latter two subunits[19] are extensively found

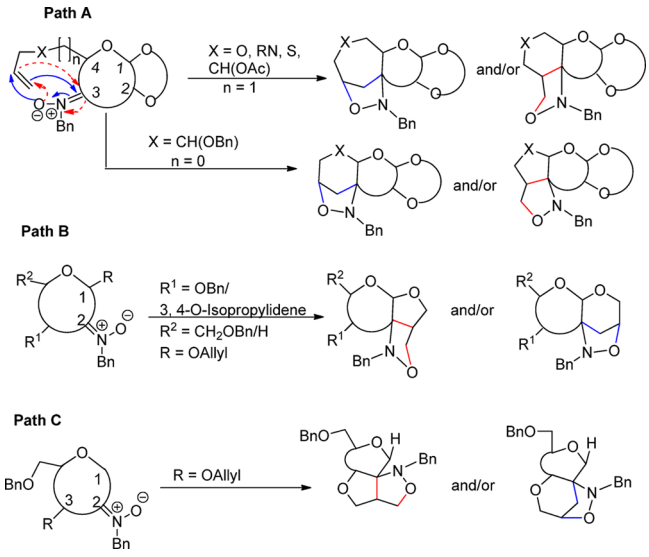


Figure 1. A general strategy for construction of rings using INC reaction.

in a large number of bioactive natural products, such as C_{13}-polyketides,[20] mono and diterpenoids,[21] lignans,[22] and ezomycin octosyl nucleoside,[23] including several synthetic potent HIV-1 protease inhibitors,[24] such as darunavir, UIC-94003, and GRL-0476, while an oxepane ring is present in

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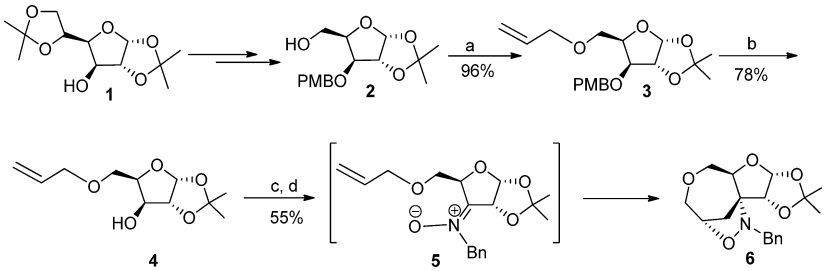
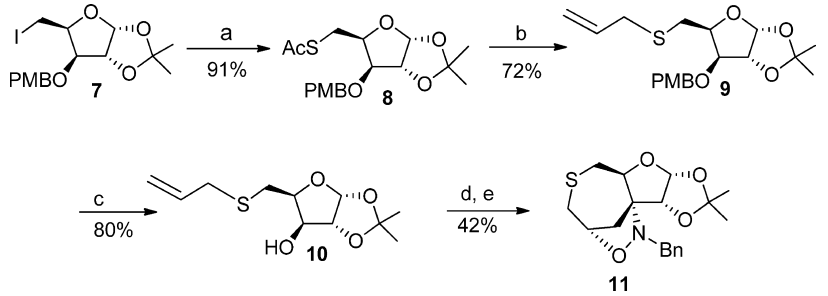
Scheme 1. Construction of Oxepane Ring of 6 on Carbohydrate Backbone[a]



[a]Regents and conditions: (a) allyl bromide, DCM: 50% aq. NaOH (1:1), TBAB, rt, overnight; (b) DDQ, DCM:H_20 (20:1), rt, 2 h; (c) DMP, DCM, 0 °C, 2 h; (d) BnNHOH, toluene, reflux, 10 h.

Scheme 2. Construction of Thiepane Ring of 11 on Sugar Backbone[a]



[a]Reagents and conditions: (a) KSAc, DMF, rt, 3 h; (b) $NaBH_4$, allyl bromide, NaOMe, dry MeOH, 0 °C–rt, 3 h; (c) DDQ, DCM:H_20 (20:1), rt, 2 h; (d) oxalyl chloride, CH_2CI_2, −65 °C, DMSO, 2 h; (e) BnNHOH, toluene, reflux, 10 h.

some biologically important natural molecules,[25] such as heliannuol B and C, sodwanone S, and zoapatanol.[26] Many sulfur heterocycles[27] as well used as drugs display biological and synthetic importances.[28] We report herein the results, obtained from exploration of the INC reaction of carbohydrate-derived keto-nitrones via the strategy as depicted, leading to the formation of new compounds, which contain isoxazolidine-fused oxepane, azepane, thiepane, perhydrofurofuran, and carbocyclic rings of varied sizes. Two of these products have been converted to the bicyclic nucleoside analogues.[29]

RESULTS AND DISCUSSION

Prior to the application of olefin-keto-nitrone cycloaddition reactions on the backbone of carbohydrate derived substrates, preparation of some appropriate precursors from D-glucose was essentially necessary. The success of the strategy solely depended on the appendage of a heteroallyl or allyl moiety, and a hydroxyl group at the proper carbon of the substrates, prepared from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **1**, through simple transformations. The hydroxyl group of the precursor was then oxidized to a ketone, followed by nitrone formation and cycloaddition reaction, furnishing the desired INC product.

Synthesis of Oxygen Heterocycle (via Path A). Allylation of **2**[30] (prepared from **1** in three steps, viz. *p*-methoxybenzylation of the hydroxyl group, selective removal of the 5,6-*O*-isopropylidene protection by acid treatment, vicinal diol cleavage, and reduction of the aldehyde moiety) with allyl bromide in the presence of 50% aqueous sodium hydroxide and tetrabutylammonium bromide (TBAB) as phase transfer catalyst in DCM solvent at room temperature furnished **3** in 96% yield (Scheme 1). Removal of the PMB protection[31] by DDQ in a DCM–H_2O mixture afforded **4** (78%). The hydroxyl group of **4** was oxidized[32] by Dess–Martin periodinane (DMP) in DCM to the corresponding ketone, which, without purification, was treated with *N*-benzyl hydroxylamine (BnNHOH) in refluxing toluene to furnish the isoxazolidinoxepane derivative **6** (55%) through the nonisolable intermediate **5**. There could be two possible ways for the cyclization reaction (Figure 1). The observation of a peak at *m*/*z* 356 $(M + Na)^+$ in the ESI mass spectrum confirmed the molecular weight of **6**. The upfield proton signals at δ 2.24 and 2.74, and a carbon signal at δ 31.6 in the ^1H and ^{13}C NMR spectra clearly indicated the cyclization involving an attack by the oxyanion at the methine terminal of the olefin moiety occurred. The cycloaddition via the other mode of cyclization furnishing the pyran derivative was discarded after analyses of the NMR spectra. The structure as well as the stereochemistry of **6** was further confirmed by the single-crystal X-ray analysis (Figure S1, Supporting Information).

Synthesis of Sulfur Heterocycle (via Path A). The iodide group of **7**, which was prepared from **2** by treatment with I_2/PPh_3/imidazole,[33] was substituted by a thioacetyl group[11c] using KSAc in DMF to produce **8** in 91% yield (Scheme 2). Deprotection of the acetate and subsequent allylation of the thiolate anion in a one-pot reaction using $NaBH_4$/allyl bromide/$NaOCH_3$ in dry MeOH furnished the thioallyl derivative **9** in 72% yield. Sodium borohydride maintained a reductive condition within the reaction mixture in preventing the formation of a disulfide bond. Removal of the PMB protection by DDQ produced **10** (80%). Various attempts including DMP to oxidize the hydroxyl group were unsuccessful due to the oxidation of sulfur. However, Swern oxidation[34] using oxalyl chloride/DMSO/Et_3N in DCM afforded its corresponding ketone, which, without purification, was treated with BnNHOH in refluxing toluene to produce the tetracyclic thiepane product **11** in 42% yield. The stereochemistry of the bridge methylene was assigned on the basis of

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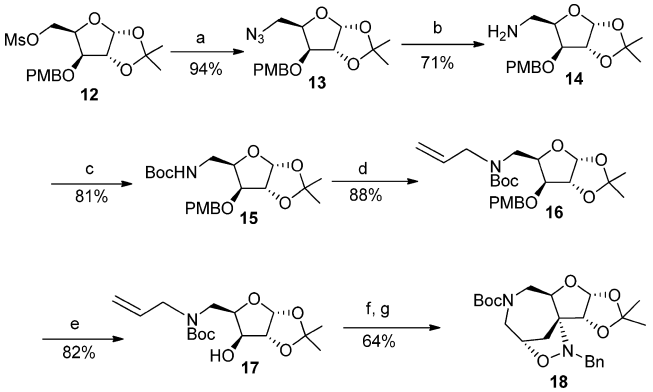
the analogy with the corresponding oxepane derivative **6**, obtained by cycloaddition reaction of the corresponding 5-*O*-allyl nitrone.

Synthesis of Nitrogen Heterocycle (via Path A). In a further manipulation of the strategy, the mesyl functionality of **12** (derived from its corresponding alcohol **2**) was substituted by an azido group by heating with NaN_3 in DMF, furnishing **13** in 94% yield (Scheme 3). Selective reduction of the azido group

Scheme 3. Construction of Azepane Ring in 18 on Sugar Backbone[a]

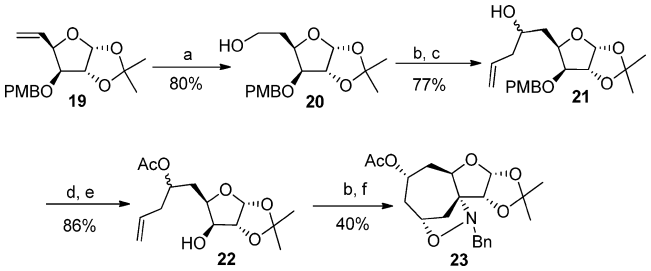


[a]Reagents and conditions: (a) NaN_3, DMF, 80−100 °C, 6 h; (b) PPh_3, moist-THF, reflux, 6 h; (c) $(Boc)_2O$, CH_2Cl_2, rt, 4 h; (d) allyl bromide, NaH, DMF, TBAB, rt, overnight; (e) DDQ, DCM:H_2O (20:1), rt, 2 h; (f) DMP, DCM, 0 °C, 2 h; (g) BnNHOH, toluene, reflux, 12 h.

by Staudinger reaction[35] in moist THF with PPh_3 furnished in 71% yield the primary amine **14**, which was subsequently protected by di-*tert*-butyl dicarbonate to give **15** (81%). N-allylation of **15** using allyl bromide/NaH/TBAB in dry DMF furnished **16** in 88% yield. Deprotection of the PMB group by DDQ furnished the required alcohol precursor **17** (82%). DMP oxidation of the secondary hydroxyl group produced its corresponding ketone, which, upon nitrone formation with BnNHOH in refluxing toluene and subsequent cyclization, furnished the seven-membered tetracyclic azepane heterocycle **18** in 64% yield. All the products showed appropriate NMR spectral data. The stereochemistry of **18** was confirmed indirectly by single-crystal X-ray analysis of one of its derived products **46** (described in Scheme 12).

Synthesis of Carbocycles (via Path A). In a similar approach toward the synthesis of a seven-membered carbocycle, the alkene **19**[36] was readily oxidized to the alcohol **20** (80%) by 9-BBN[37] in THF (Scheme 4). The hydroxyl group was oxidized by DMP to obtain its corresponding aldehyde, which was readily converted to a mixture of the alcohols **21** (1:1 ratio) in 77% yield in two steps using Barbier allylation[38] with allyl bromide in the presence of Zn dust in THF−NH_4Cl. Acetylation of the mixture and removal of the PMB protection by DDQ afforded **22**, a mixture of isomeric products (∼1:1). Oxidation of the hydroxyl group of the mixture of compounds by DMP afforded their corresponding ketones, which were treated with BnNHOH in refluxing toluene to furnish the seven-membered carbocyclic derivative **23** in 40% overall yield. It was interesting to note that only one isomer underwent INC reaction, furnishing only one product. The X-ray analysis of **23** (Figure S2, Supporting Information) confirmed the stereochemistry of the bridge methylene as well as the acetoxy group.

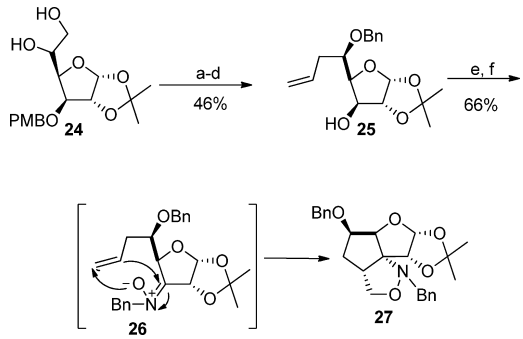
Scheme 4. Construction of Seven-Membered Carbocycle Ring in 23[a]



[a]Reagents and conditions: (a) 9-BBN, THF, 0 °C−rt, overnight, H_20_2, NaOH; (b) DMP, DCM, 0 °C, 2 h; (c) allyl bromide, Zn-dust, THF:NH_4CI (1:5), 0 °C−rt, 12 h; (d) Ac_20, DMAP, py, rt, 8 h; (e) DDQ, DCM:H_20 (20:1), rt, 2 h; (f) BnNHOH, toluene, reflux, 10 h.

The successful formation of the seven-membered carbocycle ring prompted us to replace the homoallyl group by an allyl chain in order to obtain a six-membered carbocyclic ring. To this end, vicinal diol cleavage of **24**, followed by Barberier allylation, hydroxyl group protection, and subsequent PMB deprotection (Scheme 5), furnished **25** (46% overall) as the

Scheme 5. Construction of Five-Membered Carbocycle Ring of 27[a]



[a]Reagents and conditions: (a) $NalO_4$, MeOH, 0 °C,1 h; (b) allyl bromide, Zn-dust, THF:NH_4CI (1:5), 0 °C−rt, 12 h; (c) BnBr, NaH, DMF, TBAB, 0 °C−rt, 6 h; (d) DDQ, DCM:H_20 (20:1), rt, 2 h; (e) DMP, DCM, 0 °C, 2 h; (f) BnNHOH, toluene, reflux, 12 h.

single isomer. The reason for obtaining the only one isomer was due to the approach of the incoming allyl nucleophile from the least hindered α-side. The β-side was hindered by *p*-methoxybenzyl protection at the C-3 position of the sugar ring as well as by blockage of this face due to the formation of a cyclic five-membered transition state[39] through the coordination of unshared electron pairs of oxygen (both carbonyl and ring oxygen) and allylzinc bromide. Oxidation of the hydroxyl group by DMP and subsequent treatment with BnNHOH in refluxing toluene formed the nonisolable nitrone intermediate **26**, which subsequently produced the cyclopentyl tetrahydrofuran derivative **27** (instead of six-membered carbocyclic ring) in 66% yield in two steps. The structure and stereochemistry of the product were confirmed by single-crystal X-ray analysis (Figure S3, Supporting Information). It is important to note that the perhydrocyclopentanofuran skeleton of **27** is present in an HIV protease inhibitor GRL-06579.[24]

Construction of Perhydrofurofuran Ring (via Path B). For the construction of a hexahydrofuro[2,3-*b*]furan ring, the O-allylation at the anomeric center of **28**[40] using allyl alcohol/

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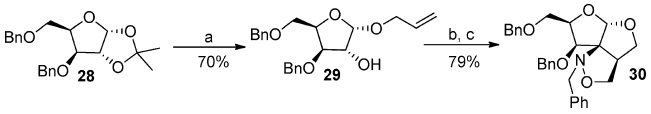
tosic acid afforded **29** (Scheme 6) as the single α-isomer in 70% yield. The S_N2 attack by the allyl alcohol from the β-face was

Scheme 6. Construction of Hexahydrofuro[2,3-*b*]furan Ring of 30[a]

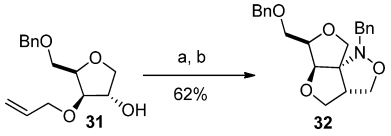


[a]Reagents and conditions: (a) allyl alcohol,TsOH·H_2O, reflux, 6 h; (b) DMP, DCM, 0 °C, 2 h; (c) BnNHOH, toluene, reflux,12 h.

hindered by the steric hindrance of the two bulky benzyl groups at C-3 and C-5, and therefore, the attack took place from the opposite α-face. Oxidation of the hydroxyl group by DMP, and subsequent nitrone generation by reaction with BnNHOH and cyclization, afforded the INC product **30** (79% in two steps). The structure and stereochemistry of **30** were confirmed by single-crystal X-ray analysis (Figure S4, Supporting Information).

In a comparable fashion for the synthesis of a hexahydrofuro-[3,4-*b*]furan ring (via Path C), the 1-deoxy sugar derivative **31**[41] upon oxidation of the hydroxyl group by DMP, followed by nitrone generation using BnNHOH and its in situ cyclization, smoothly afforded the isoxazolidine-fused bisfuran derivative **32** in 62% yield (Scheme 7). The product was

Scheme 7. Construction of Hexahydrofuro[3,4-*b*]furan Ring of 32[a]

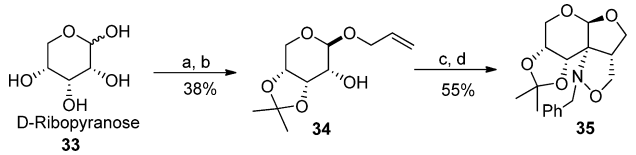


[a]Reagents and conditions: (a) DMP, DCM, 0 °C, 2 h; (b) BnNHOH, toluene, reflux, 6 h.

characterized by NMR spectral analyses, and its stereochemistry at the ring juncture was determined by single-crystal X-ray analysis of one of its derived products **42**.

Synthesis of Perhydropyranofuran Ring (via Path B). Based on the success in creating a furanofuran ring by INC reaction, an application of the strategy to construct a pyranofuran ring from the sugar-derived precursor was attempted. Thus, D-ribopyranose (**33**) was subjected to anomeric O-allylation using *p*-TSA in allyl alcohol, followed by acetonide formation by reaction with 2,2-dimethoxypropane/conc. H_2SO_4/Ag_2CO_3 in acetone, affording **34** (β-isomer) as the major isomer in 38% yield (Scheme 8). The

Scheme 8. Construction of Perhydropyranofuran Ring of 35[a]

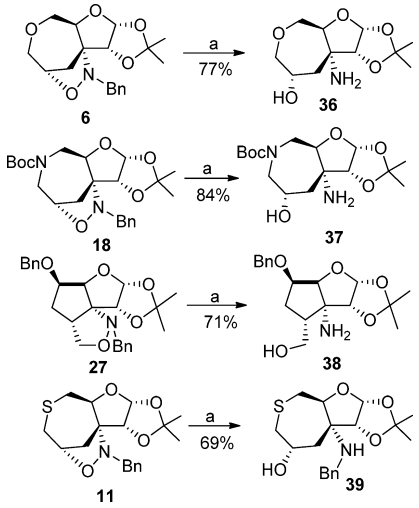


[a]Reagents and conditions: (a) allyl alcohol, TsOH, reflux, 4 h; (b) 2,2-dimethoxypropane, acetone, cone. H_2SO_4, $AgCO_3$, 12 h; (c) DMP, DCM, 0 °C, 3 h; (d) BnNHOH, toluene, reflux, 12 h.

hydroxyl group was oxidized by DMP reagent to its corresponding ketone, which, upon reaction with BnNHOH, yielded the isoxazolidine-fused pyranofuran derivative **35** in 55% yield in two steps. The structure as well as the stereochemistry of the product was confirmed by single-crystal X-ray analysis (Figure S5, Supporting Information).

Cleavage of Isoxazolidine Rings of the INC Products. Installation of nucleoside bases at the anomeric center of the INC products for the synthesis of bicyclic nucleoside derivatives required cleavages of the isoxazolidine rings and removal of the acetonide protection. Thus, treatment of the INC products **6**, **18**, and **27** with molybdenum hexacarbonyl ($Mo(CO)_6$) in refluxing aqueous MeCN[42] cleaved the isoxazolidine rings and removed the N-Bn protection to produce the corresponding amino alcohols **36**–**38** in ~70–80% yield (Scheme 9). However, the O-Bn group of **27** was not

Scheme 9. Cleavage of the N–O Bond and Benzyl Protection from 6, 11, 18, and 27[a]



[a]Reagents and conditions: (a) $Mo(CO)_6$, MeCN: H_2O (15:1), reflux,12 h.

cleaved by the catalyst and the product **38** contained the O-Bn protection. On the other hand, only the isoxazolidine ring cleavage occurred in **11**, furnishing **39** having an NHBn group at quaternary C-3 of the sugar moiety. Therefore, the hydrogenolytic method of cleavage using hydrogen gas over Pd/C was tried to remove the isoxazolidine ring as well as the benzyl protection of the INC products in one-pot.

Cleavage of the isoxazolidine rings and deprotection of the benzyl groups of **30** and **32** using hydrogen gas over Pd/C were successfully completed via catalytic hydrogenation reaction over Pd/C (10%) in MeOH to the corresponding amino alcohols, which, upon acetylation with Ac_2O/Py/DMAP, produced their corresponding bisfuran derivatives **40** and **41** in 74% and 71% yields (Scheme 10). However, deprotection of the N-Bn of **39** by hydrogenation reaction was unsuccessful due to sulfur poisoning of the catalyst.

At this stage, it was felt that the free amino alcohol could be trapped by an aldehyde to a crystalline cyclized product to confirm the stereochemistry of the INC product **32**, shown in Scheme 7. Thus, the dihydroxy amino alcohol **42**, obtained after hydrogenation reaction upon **32** in MeOH, was treated with an aqueous solution of acetaldehyde to isolate **43** as a crystalline solid in 57% yield (Scheme 11). The doublet signal

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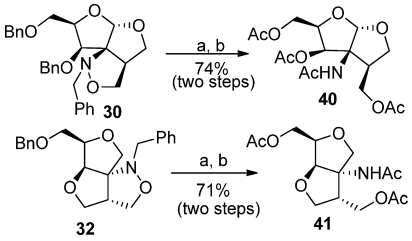
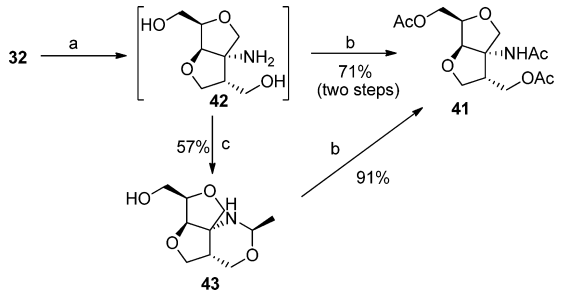
Scheme 10. Hydrogenolysis of Isoxazolidine Rings and Benzyl Groups of 30 and 32[a]



[a]Reagents and condition: (a) 10% Pd/C, H_2, MeOH, rt, 12 h; (b) Ac_20, pyridine, DMAP, rt, 6 h.

Scheme 11. Reaction of Dihydroxy Amino Alcohol 42 with Acetaldehyde[a]



[a]Reagents and conditions: (a) 10% Pd/C, H_2, MeOH, rt, 12 h; (b) Ac_2O, pyridine, DMAP, rt, 6 h; (c) 40 wt % aq. CH_3CHO.

(δ 1.31) for the methyl protons in the ^{1}H NMR spectrum confirmed the insertion of the acetaldehyde residue. The structure and stereochemistry of the product were confirmed by the single-crystal X-ray analysis (Figure S6, Supporting Information). The adduct **43**, upon treatment with Ac_2O/Py/DMAP, furnished the triacetate bisfuran derivative **41** in 91% yield.

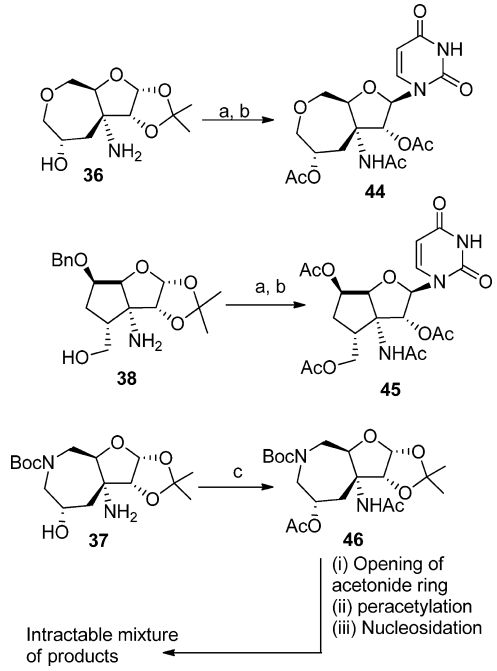
Synthesis of Bicyclic Nucleoside Analogues 44 and 45. Toward the target, deprotection of the 1,2-acetonide moiety from **36** and **38** by acid treatment, followed by peracetylation in a one-pot reaction using Ac_2O–TfOH, afforded their respective acetylated products (anomeric mixture). The mixture, without further purification, was used for installation of a uracil base at the anomeric center via Vorbrüggen glycosidation reaction[43] (uracil, BSA, TMSOTf, MeCN, 50 °C) to furnish their corresponding bicyclic nucleoside derivatives **44** and **45** (Scheme 12).

However, an attempt to introduce a nucleoside base at the anomeric carbon of **46**, derived from **37** by acetylation, failed to produce any desired nucleoside; instead, an intractable mixture of products was obtained. The structure of **46** was confirmed by single-crystal X-ray analysis, which also confirmed the structure of the INC product **18** (Figure S7, Supporting Information). Similarly, installation of the nucleoside base on **11** and **23** using Vorbrüggen reaction through various manipulations was unsuccessful.

CONCLUSIONS

The work presented herein describes a potential application of INC reaction for the stereoselective synthesis of chiral heterocycles and carbocycles of varied nature using keto-nitrone-olefins, which have been derived from D-glucose-based substrates. The structure and stereochemistry of the INC

Scheme 12. Synthesis of Bicyclic Nucleosides Derived from INC Products[a]



[a]Reagents and conditions: (a) Ac_2O, TfOH, AcOH, 0 °C–rt, 2 h; (b) uracil, BSA, TMSOTf, MeCN, 50 °C, 17 h; (c) Ac_2O, pyridine, DMAP, rt, 12 h.

products were confirmed by spectral and single-crystal X-ray analyses. Two of these products have been translated to the corresponding bicyclic nucleoside derivatives using Vorbrüggen glycosidation reaction. However, several problems have occurred during nucleosidation reactions on some of the INC products. The ease of preparation of sugar-based precursors for INC reaction makes the method practical, efficient, and useful. The strategy seems valuable for the synthesis of other ring systems through judicious manipulation of the substrates.

EXPERIMENTAL SECTION

General. Melting points were taken in open capillaries and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ and CD_3OD as solvents using TMS as internal standard. Mass spectra were recorded using EI and ESI mode. Specific rotations were measured at 589 nm. Precoated plates (0.25 mm, silica gel 60 F_{254}) were used for thin-layer chromatography. Column chromatography was performed on silica gel (60–120, 100–200, and 230–400 mesh). All the solvents were distilled and purified as necessary.

(3a*R*,5*R*,6*S*,6a*R*)-5-(Allyloxymethyl)-6-(4-methoxybenzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole (3). TBAB (1.04 g, 3.23 mmol) was added to a solution of **2** (10.0 g, 32.26 mmol) in DCM (80 mL), and the mixture was stirred at room temperature with portionwise addition of 50% aqueous NaOH solution (80 mL). Allyl bromide (3.35 mL, 38.71 mmol) was added to the mixture, and the resulting solution was stirred overnight at room temperature. The organic layer was separated from NaOH solution, washed with brine (3 × 40 mL), dried (Na_2SO_4), and concentrated to an oil, which was purified by column chromatography on silica gel (60–120 mesh) using a mixture of petroleum ether–EtOAc (9:1) as eluent to furnish **3** (10.8 g, 96%) as a colorless liquid. $[\alpha]_D^{25}$ − 38 (*c* 0.39, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s, 3H), 1.48 (s, 3H), 3.68 (d, 2H, *J* = 6.0 Hz), 3.81 (s, 3H), 3.95 (d, 1H, *J* = 2.7 Hz), 3.97–4.09 (m, 2H), 4.36 (m, 1H), 4.45 (d, 1H, *J* = 11.7 Hz), 4.58 (partially merged d, 1H, *J* = 3.3 Hz), 4.61 (d, 1H, *J* = 11.4 Hz), 5.18 (d, 1H, *J* = 10.2 Hz), 5.28 (dd, 1H, *J* = 0.9, 16.7 Hz), 5.84–5.95 (m, 2H), 6.68 (d, 2H, *J* = 8.4 Hz),

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7.24 (d, 2H, J = 11.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.2 (CH_3), 26.7 (CH_3), 55.2 (CH_3), 67.5 (CH_2), 71.6 (CH_2), 72.3 (CH_2), 79.1 (CH), 81.2 (CH), 82.3 (CH), 105.0 (CH), 111.5 (C), 113.8 (2 × CH), 117.1 (CH_2), 129.3 (2 × CH), 129.5 (C), 134.5 (CH), 159.3 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{19}H_{26}NaO_6$, m/z 373.1627, found 373.1656.

(3a*R*,5*R*,6*S*,6a*R*)-5-(Allyloxymethyl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-ol (4). DDQ (6.81 g, 30 mmol) was added to a solution of **3** (7.0 g, 20 mmol) in a mixture of DCM−H_2O (20:1, 42 mL), and the solution was stirred at room temperature for 2 h. After quenching the reaction with a saturated $NaHCO_3$ solution (50 mL), the mixture was extracted with DCM (2 × 50 mL). The combined extract was dried (Na_2SO_4) and concentrated to a residue, which was purified chromatographically on silica gel (100−200 mesh) using petroleum ether−EtOAc (5:1) as eluent to give **4** (3.6 g, 78%) as a colorless oil. $[\alpha]_D^{25}$ − 1 (c 0.44, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s, 3H), 1.49 (s, 3H), 3.77 (d, 1H, J = 2.7 Hz), 3.86−3.98 (m, 2H), 4.04 (dd, 1H, J = 6.0, 12.6 Hz), 4.12 (dd, 1H, J = 5.4, 12.9 Hz), 4.24 (brd, 1H, J = 2.7 Hz), 4.30 (brs, 1H), 4.53 (d, 1H, J = 3.3 Hz), 5.23 (d, 1H, J = 10.8 Hz), 5.29 (d, 1H, J = 17.7 Hz), 5.83−5.94 (m, 1H), 5.99 (d, 1H, J = 3.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.0 (CH_3), 26.6 (CH_3), 68.0 (CH_2), 72.8 (CH_2), 76.1 (CH), 781 (CH), 85.2 (CH), 104.7 (CH), 111.5 (C), 117.9 (CH_2), 133.6 (CH); HRMS (ESI−QToF, positive ion) calcd for $C_{11}H_{18}NaO_5$, m/z 253.1052, found 253.1072.

(3*S*,6a*S*,7a*R*,10a*R*,10b*R*)-1-Benzyl-9,9-dimethylhexahydro-1*H*-3,10b-methano[1,3]dioxolo[4′,5′:4,5]furo[3,2-*c*][1,6,2]-dioxazocine (6). DMP (6.9 g, 16.3 mmol) was added to a solution of **4** (2.5 g, 10.87 mmol) in DCM (20 mL) at 0 °C under N_2, and the solution was stirred for 2 h. The solvent was evaporated, and the residue was extracted with DCM (2 × 40 mL). The extract was washed with a saturated solution of $NaHCO_3$ (30 mL) and 10% $Na_2S_2O_3$ solution (30 mL), dried (Na_2SO_4), and evaporated to furnish a crude ketone. To a solution of this ketone in toluene (60 mL) was added BnNHOH (2.0 g, 16.31 mmol), and the mixture was heated at reflux for 10 h. The solvent was evaporated in rotary evaporator to a gummy residue, which was purified by column chromatography on silica gel (230−400 mesh). Elution with petroleum ether−EtOAc (17:3) furnished **6** (2.0 g, 55%) as a colorless solid. mp 192−193 °C; $[\alpha]_D^{25}$ + 157 (c 0.37, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.36 (s, 3H), 1.60 (s, 3H), 2.24 (t, 1H, J = 10.5 Hz), 2.74 (d, 1H, J = 11.7 Hz), 3.60 (apparent t, 2H, J = 13.8, 17.1 Hz), 3.83 (apparent t, 2H, J = 14.4, 18.0 Hz), 4.20 (m, 3H), 4.60 (s, 1H), 4.70 (brd, 1H, J = 7.5 Hz), 5.94 (s, 1H), 7.30−7.48 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.2 (CH_3), 26.5 (CH_3), 31.6 (CH_2), 57.5 (CH_2), 68.4 (CH_2), 72.6 (CH_2), 76.3 (C), 78.3 (CH), 79.6 (CH), 82.3 (CH), 103.9 (CH), 113.0 (C), 127.3 (CH), 128.4 (2 × CH), 129.1 (2 × CH), 137.7 (C); HRMS (EI, magnetic sector, positive ion) calcd for $C_{18}H_{23}NO_5$, m/z 333.1576, found 333.1575.

(3a*R*,5*S*,6R,6a*R*)-5-(Iodomethyl)-6-(4-methoxybenzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole (7). To a solution of **2** (3.5 g, 11.3 mmol) in toluene (30 mL) were added Ph_3P (4.44 g, 16.95 mmol) and imidazole (1.54 g, 22.6 mmol), and the mixture was heated at 70 °C for 30 min. Iodine (4.3 g, 16.95 mmol) was added to it, and the heating was continued for 3 h. The mixture was cooled, and the solution was washed successively with 30% $Na_2S_2O_3$ solution (20 mL) and water (3 × 10 mL), dried (Na_2SO_4), and evaporated to a crude residue, which was purified by column chromatography on silica gel (100−200 mesh). Elution was made with petroleum ether−EtOAc (9:1) to furnish **7** (4.2 mg, 88%) as a colorless oil. $[\alpha]_D^{25}$ − 60 (c 0.32, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s, 3H), 1.50 (s, 3H), 3.29 (s, 1H), 3.31 (d, 1H, J = 2.7 Hz), 3.81 (s, 3H), 4.08 (d, 1H, J = 3.0 Hz), 4.43−4.53 (m, 2H), 4.61−4.63 (m, 2H), 5.95 (d, 1H, J = 3.6 Hz), 6.89 (d, 2H, J = 8.7 Hz), 7.30 (d, 2H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ − 0.96 (CH_2), 26.2 (CH_3), 26.8 (CH_3), 55.2 (CH_3), 72.3 (CH_2), 81.0 (CH), 81.1 (CH), 81.9 (CH), 105.6 (CH), 111.8 (C), 113.8 (2 × CH), 129.2 (C), 129.6 (2 × CH), 159.4 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{16}H_{21}INaO_5$, m/z 443.0331, found 443.0333.

***S*-(((3a*R*,5*S*,6*R*,6a*R*)-6-(4-Methoxybenzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)methyl)ethanethioate (8).** A solution of **7** (4.5 g, 10.7 mmol) in DMF (75 mL) was stirred at room temperature for 10 min, and then potassium thioacetate (3.66 g, 32.1 mmol) was slowly added to it over a period of 10 min. The mixture was stirred at room temperature for an additional 3 h. The solvent was evaporated to furnish a residue, which was extracted with $CHCl_3$ (3 × 30 mL). The combined extract was washed with brine (50 mL), dried (Na_2SO_4), and evaporated in vacuo. The crude product was purified by column chromatography on silica gel (60−20 mesh) using petroleum ether−EtOAc (9:1) as eluent to furnish **8** (3.6 g, 91%) as a colorless oil. $[\alpha]_D^{25}$ − 61 (c 0.27, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.31 (s, 3H), 1.47 (s, 3H), 2.33 (s, 3H), 3.12 (dd, 1H, J = 6.9, 13.5 Hz), 3.26 (dd, 1H, J = 7.2, 13.5 Hz), 3.81 (s, 3H), 3.88 (d, 1H, J = 3.0 Hz), 4.25 (dt, 1H, J = 3.0, 6.9 Hz), 4.44 (d, 1H, J = 11.4 Hz), 4.49 (merged d, 1H), 4.61 (d, 1H, J = 11.1 Hz), 5.90 (d, 1H, J = 3.6 Hz), 6.89 (d, 2H, J = 8.4 Hz), 7.26 (d, 2H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.2 (CH_3), 26.7 (CH_3), 27.0 (CH_2), 30.4 (CH_3), 55.2 (CH_3), 71.7 (CH_2), 79.1 (CH), 81.5 (CH), 82.1 (CH), 105.0 (CH), 111.6 (C), 113.8 (2 × CH), 129.2 (C), 129.4 (2 × CH), 159.4 (C), 195.2 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{18}H_{24}NaO_6S$, m/z 391.1191, found 391.1187.

(3a*R*,5*S*,6*R*,6a*R*)-5-(Allylthiomethyl)-6-(4-methoxybenzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole (9). To a solution of **8** (2.0 g, 5.43 mmol) in MeOH (50 mL) at 0 °C was added $NaBH_4$ (619 mg, 16.29 mmol) portionwise. After 10 min of stirring, allyl bromide (0.95 mL, 10.86 mmol) was added to the mixture by a syringe. A methanolic solution of NaOMe (28 wt %) (2.7 mL, 10.8 mmol) was added dropwise to the mixture, which was allowed to stir at room temperature for 3 h. The solvent was evaporated in vacuo, and to the residue EtOAc (25 mL) and water (30 mL) were added. The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layer was washed with H_2O (2 × 10 mL) and dried (Na_2SO_4), and the solvent was removed in vacuo. The crude product was purified by column chromatography over silica gel (100−200 mesh) using petroleum ether−EtOAc (9:1) as eluent to obtain **9** (1.44 g, 72%) as a yellow oil. $[\alpha]_D^{25}$ − 68 (c 0.24, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s, 3H), 1.49 (s, 3H), 2.77 (d, 2H, J = 7.2 Hz), 3.17 (d, 2H, J = 6.9 Hz), 3.81 (s, 3H), 3.96 (d, 1H, J = 3.0 Hz), 4.31 (dt, 1H, J = 3.0, 7.2 Hz), 4.47 (d, 1H, J = 3.9 Hz), 4.58 (d, 1H, J = 3.9 Hz), 4.61 (d, 1H, J = 11.7 Hz), 5.07−5.13 (m, 2H), 5.75−5.86 (m, 1H), 5.90 (d, 1H, J = 3.6 Hz), 6.88 (d, 2H, J = 8.7 Hz), 7.26 (d, 2H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.2 (CH_3), 26.7 (CH_3), 28.2 (CH_2), 35.4 (CH_2), 55.2 (CH_3), 71.8 (CH_2), 79.9 (CH), 81.3 (CH), 82.0 (CH), 105.0 (CH), 111.4 (C), 113.7 (2 × CH), 117.2 (CH_2), 129.35 (2 × CH), 129.41 (C), 134.2 (CH), 159.3 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{19}H_{26}NaO_5S$, m/z 389.1399, found 389.1414.

(3a*R*,5*S*,6*R*)-5-(Allylthiomethyl)-2,2-dimethyltetrahydrofuro-[2,3-*d*][1,3]dioxol-6-ol (10). Deprotection of the PMB group was carried out, following the procedure as described for the preparation of **4**, using **9** (1.2 g, 3.28 mmol) and DDQ (1.12 g, 4.92 mmol). The usual work up and purification by column chromatography on silica gel (100−200 mesh) using petroleum ether−EtOAc (17:3) furnished **10** (0.65 g, 80%) as a colorless oil. $[\alpha]_D^{25}$ − 40 (c 0.27, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s, 3H), 1.50 (s, 3H), 2.15 (d, 1H, J = 5.4 Hz), 2.74 (dd, 1H, J = 9.0, 13.2 Hz), 2.86 (dd, 1H, J = 5.4, 13.2 Hz), 3.21 (d, 2H, J = 7.2 Hz), 4.26−4.33 (m, 2H), 4.53 (d, 1 H, J = 3.6 Hz), 5.12−5.88 (m, 2H), 5.74−5.88 (m, 1H), 5.92 (d, 1H, J = 3.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.1 (CH_3), 26.6 (CH_3), 27.9 (CH_2), 35.3 (CH_2), 74.8 (CH), 79.4 (CH), 84.9 (CH), 104.6 (CH), 111.6 (C), 117.6 (CH_2), 133.9 (CH); HRMS (ESI−QToF, positive ion) calcd for $C_{11}H_{18}NaO_4S$, m/z 269.0823, found 269.0836.

(3*S*,6a*S*,7a*R*,10a*R*,10b*S*)-1-Benzyl-9,9-dimethylhexahydro-1*H*-3,10b-methano[1,3]dioxolo[4′,5′:4,5]furo[3,2-*c*][1,6,2]oxathiazocine (11). To a solution of oxalyl chloride (0.35 mL, 4.06 mmol) in dry DCM (7 mL) cooled to −65 °C was added a solution of dry DMSO (0.52 mL, 7.27 mmol) in DCM (2 mL) dropwise under N_2, and the mixture was stirred for15 min. A solution of **10** (0.500 g, 2.03 mmol) in DCM (5 mL) was added to the above mixture over a

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period of 1 h, and the stirring was continued for another 1 h. Et_3N (3 mL) was added to it, and the reaction mixture was allowed to reach room temperature. After quenching the reaction with addition of water (5 mL), the mixture was extracted with DCM (3 × 30 mL). The combined extract was washed with water (2 × 30 mL) and dried (Na_2SO_4), and the solvent was evaporated in vacuo to furnish a crude ketone, which was treated with BnNHOH (0.375 g, 3.05 mmol) in refluxing toluene (20 mL) for 10 h. The usual work up and purification by column chromatography on silica gel (230−400 mesh) and elution with petroleum ether−EtOAc (17:3) furnished **11** (0.300 g, 42%) as a yellow viscous liquid. $[\alpha]_D^{25}$ + 129 (*c* 0.21, $CHCl_3$); ^1H NMR ($CDCl_3$, 600 MHz): δ 1.35 (s, 3H), 1.60 (s, 3H), 2.22 (apparent t, 1H, *J* = 9.6, 11.4 Hz), 2.40 (dd, 1H, *J* = 4.2,14.4 Hz), 2.86 (brd, 1H, *J* = 15.6 Hz), 2.99 (brd, 1H, *J* = 15.0 Hz), 3.22 (dd, 1H, *J* = 2.4,16.8 Hz), 3.28−3.29 (brs, 1H), 3.88−3.90 (brs, 1H), 4.20 (brd, 1H, *J* = 12.0 Hz), 4.47−4.52 (m, 1H), 4.55 (d, 1H, *J* = 3.6 Hz), 5.02 (brs, 1H), 5.93 (d, 1H, *J* = 3.0 Hz), 7.28−7.40 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.2 (CH_3), 26.5 (CH_3), 30.4 (CH_2), 33.1 (CH_2), 34.7 (CH_2), 56.7 (CH_2), 77.2 (CH), 77.9 (CH), 82.6 (CH), 103.8 (CH), 113.1 (C), 127.3 (CH), 128.3 (2 × CH), 129.1 (2 × CH), 137.7 (C), one (C) not discernible; HRMS (ESI−QToF, positive ion) calcd for $C_{18}H_{23}NNaO_4S$, *m*/*z* 372.1245, found 372.1241.

((3a*R*,5*R*,6*S*,6a*R*)-6-(4-Methoxybenzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)methylmethanesulfonate (12). CH_3SO_2Cl (1.3 mL, 17.12 mmol) was added to an ice−cold solution of **2** (3.32 g, 10.7 mmol) in DCM (50 mL). After stirring for 5 min, Et_3N (2.25 mL, 16 mmol) was added dropwise to the mixture and it was stirred at room temperature for 2 h. The organic layer was washed with a saturated solution of $NaHCO_3$ (3 × 10 mL), and water (3 × 10 mL), and then dried (Na_2SO_4), and evaporated to a residue, which was purified by column chromatography on silica gel (60−120 mesh) using petroleum ether−EtOAc (9:1) as eluent to furnish **12** (3.92 g, 94%) as a colorless liquid. $[\alpha]_D^{25}$ − 28 (*c* 0.38, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 1.33 (s, 3H), 1.49 (s, 3H), 3.03 (s, 3H), 3.81 (s, 3H), 3.98 (brs, 1H), 4.34−4.44 (m, 4H), 4.60−4.63 (m, 2H), 5.95 (d, 1H, *J* = 3.6 Hz), 6.89 (d, 2H, *J* = 8.4 Hz), 7.23 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.2 (CH_3), 26.8 (CH_3), 37.05 (CH_3), 55.3 (CH_3), 67.8 (CH_2), 71.6 (CH_2), 77.8 (CH), 80.9 (CH), 81.9 (CH), 105.3 (CH), 112.0 (C), 114.0 (2 × CH), 128.8 (C), 129.6 (2 × CH), 159.6 (C); HRMS (EI, magnetic sector, positive ion) calcd for $C_{17}H_{24}O_8S$, *m*/*z* 388.1192, found 388.1196.

(3a*R*,5*R*,6*S*,6a*R*)-5-(Azidomethyl)-6-(4-methoxybenzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole (13). A mixture of **12** (4.3 g, 11.1 mmol) and NaN_3 (6.63 g, 102.0 mmol) in anhydrous DMF (50 mL) was heated at 80−100 °C for 6 h. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure. The residue was extracted with $CHCl_3$ (3 × 30 mL); the combined extract was washed with water, dried (Na_2SO_4), and evaporated in vacuo. The crude product was chromatographically purified on silica gel (100−200 mesh) using petroleum ether−EtOAc (19:1) as eluent to give **13** (3.51 g, 94%) as a colorless liquid. $[\alpha]_D^{25}$ − 37 (*c* 0.24, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 1.33 (s, 3H), 1.50 (s, 3H), 3.45 (dd, 1H, *J* = 6.6, 12.3 Hz), 3.56 (dd, 1H, *J* = 6.9, 12.3 Hz), 3.81 (s, 3H), 3.92 (d, 1H, *J* = 3.3 Hz), 4.29 (td, 1H, *J* = 3.3, 6.3 Hz), 4.44 (d, 1H, *J* = 11.4 Hz), 4.61 (d, 1H, *J* = 3.9 Hz), 4.62 (d, 1H, *J* = 11.4 Hz), 5.92 (d, 1H, *J* = 3.6 Hz), 6.89 (d, 2H, *J* = 8.4 Hz), 7.24 (d, 2H, merged with $CDCl_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.1 (CH_3), 26.7 (CH_3), 49.1 (CH_2), 55.1 (CH_3), 71.4 (CH_2), 78.6 (CH), 80.9 (CH), 81.9 (CH), 104.9 (CH), 111.7 (C), 113.8 (2 × CH), 128.9 (C), 129.4 (2 × CH), 159.4 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{16}H_{21}N_3NaO_5$, *m*/*z* 358.1379, found 358.1370.

((3a*R*,5*R*,6*S*,6a*R*)-6-(4-Methoxybenzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)methanamine (14). To a mixture of **13** (2.35 g, 7.01 mmol) and Ph_3P (2.75 g, 10.52 mmol) taken in THF (30 mL) was added water (0.20 mL, 10.5 mmol), and the reaction mixture was heated at 110 °C for 6 h. The mixture was extracted with Et_2O (3 × 50 mL), and the combined organic extract was washed with water (100 mL) and brine (100 mL). The solvent was dried (Na_2SO_4) and concentrated to a crude yellow oil, which was purified by column chromatography on silica gel (100−200 mesh) using petroleum ether−EtOAc (1:1) as eluent to furnish **14** (1.54 g, 71%) as a colorless liquid. $[\alpha]_D^{25}$ − 38 (*c* 0.28, $CHCl_3$); ^1H NMR ($CDCl_3$ + D_2O, 300 MHz): δ 1.33 (s, 3H), 1.49 (s, 3H), 2.88 (dd, 1H, *J* = 5.1, 13.2 Hz), 3.01 (dd, 1H, *J* = 6.3, 13.2 Hz), 3.81 (s, 3H), 3.89 (d, 1H, *J* = 3.3 Hz), 4.13 (brd, 1H, *J* = 3.0 Hz), 4.39 (d, 1H, *J* = 11.7 Hz), 4.62 (d, 1H, *J* = 3.6 Hz), 4.65 (d, 1H, *J* = 11.7 Hz), 5.94 (d, 1H, *J* = 3.6 Hz), 6.89 (d, 2H, *J* = 8.7 Hz), 7.25 (merged d, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.2 (CH_3), 26.7 (CH_3), 40.2 (CH_2), 55.2 (CH_3), 71.3 (CH_2), 80.8 (CH), 81.3 (CH), 82.3 (CH), 104.9 (CH), 111.5 (C), 113.9 (2 × CH), 129.2 (C), 129.5 (2 × CH), 159.4 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{16}H_{23}NNaO_5$, *m*/*z* 332.1474, found 332.1473.

***O*-*tert*-Butyl-(((3a*R*,5*R*,6*S*,6a*R*)-6-(4-Methoxybenzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)methyl)carbamate (15).** To a solution of **14** (1.50 g, 4.85 mmol) in DCM (20 mL) was added di-*tert*-butyl dicarbonate (1.10 mL, 4.85 mmol), and the mixture was stirred at room temperature for 4 h. The mixture was diluted with $CHCl_3$ (20 mL) and then extracted with $CHCl_3$ (3 × 50 mL). The combined organic extract was washed with water (50 mL) and brine (50 mL), and dried (Na_2SO_4) and concentrated under reduced pressure to give a crude residue, which was purified by column chromatography on silica gel (60−120 mesh) using petroleum ether−EtOAc (4:1) as eluent to furnish **15** (1.6 g, 81%) as a colorless liquid. $[\alpha]_D^{25}$ − 33 (*c* 0.47, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s, 3H), 1.42 (s, 9H), 1.48 (s, 3H), 3.34 (brs, 1H), 3.49 (brs, 1H), 3.81 (s, 3H), 3.88 (s, 1H), 4.22 (brs, 1H), 4.39 (d, 1H, *J* = 11.4 Hz), 4.60 (s, 1H), 4.62 (d, 1H, merged), 4.73 (brs, 1H), 5.92 (s, 1H), 6.89 (d, 2H, *J* = 7.5 Hz), 7.25 (d, 2H, merged). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.2 (CH_3), 26.7 (CH_3), 28.3 (3 × CH_3), 39.5 (CH_2), 55.2 (CH_3), 71.4 (CH_2), 79.1 (CH), 81.2 (CH), 82.3 (CH), 104.9 (CH), 111.6 (C), 114.0 (2 × CH), 129.1 (C), 129.4 (2 × CH), 155.9 (C), 159.4 (C), one quaternary C was not discernible; HRMS (ESI−QToF, positive ion) calcd for $C_{21}H_{31}NNaO_7$, *m*/*z* 432.1998, found 432.2017.

***O*-*tert*-Butylallyl(((3a*R*,5*R*,6*S*,6a*R*)-6-((4-methoxybenzyl)oxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)methyl)-carbamate (16).** To a solution of **15** (3.10 g, 7.58 mmol) in dry DMF (80 mL) was added TBAB (0.245 g, 0.76 mmol), and the mixture was stirred at 0 °C with portionwise addition of NaH (60% in mineral oil, 0.394 g, 9.85 mmol). After 10 min, allyl bromide (0.85 mL, 9.85 mmol) was added to it, and the resulting mixture was stirred overnight at room temperature. The solvent was evaporated under reduced pressure. The residue was extracted with $CHCl_3$ (3 × 30 mL); the combined extract was washed with water, dried (Na_2SO_4), and evaporated in vacuo. The crude product was purified by chromatography on silica gel (100−200 mesh) using petroleum ether−EtOAc (9:1) as eluent to furnish **16** (3.0 g, 88%) as colorless liquid. $[\alpha]_D^{25}$ + 3 (*c* 0.15, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 1.31 (s, 3H), 1.43 (s, 9H), 1.47 (s, 3H), 3.19−3.44 (m, 2H), 3.81 (s, 3H), 3.91−4.05 (m, 3H), 4.38 (brs, 1H), 4.40 (d, 1H, *J* = 11.7 Hz), 4.57 (brs, 2H), 5.03−5.09 (m, 2H), 5.70−5.80 (m, 1H), 5.92 (s, 1H), 6.88 (d, 2H, *J* = 7.8 Hz), 7.23 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.2 (CH_3), 26.7 (CH_3), 28.3 (3 × CH_3), 46.4 (CH_2), 50.7 (CH_2), 55.2 (CH_3), 71.5 (CH_2), 79.5 (C), 79.9 (CH), 81.9 (CH), 82.0 (CH), 105.0 (CH), 111.4 (C), 113.9 (2 × CH), 115.6 (CH_2), 129.4 (2 × CH), 134.1 (CH), 155.8 (C), 159.4 (C), one quaternary C not discernible; HRMS (ESI−QToF, positive ion) calcd for $C_{24}H_{35}NNaO_7$, *m*/*z* 472.2311, found 472.2299.

***O*-*tert*-Butylallyl-(((3a*R*,5*R*,6*S*,6a*R*)-6-hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)methyl)carbamate (17).** Removal of PMB protection was done, according to the procedure as adopted in the preparation of **4**, using **16** (2.0 g, 4.45 mmol) and DDQ (1.52 g, 6.68 mmol). The usual work up and purification by column chromatography on silica gel (100−200 mesh) using petroleum ether−EtOAc (5:1) afforded **17** (1.2 g, 82%) as a colorless oil: $[\alpha]_D^{25}$ + 49 (*c* 0.23, $CHCl_3$); ^1H NMR ($CDCl_3$ + D_2O, 300 MHz): δ 1.32 (s, 3H), 1.45 (s, 9H), 1.51 (s, 3H), 3.05 (brd, 1H, *J* = 13.8 Hz), 3.62 (brdd, 1H, *J* = 5.1, 15.6 Hz), 3.86 (t, 1H, *J* = 12.3 Hz), 3.95−4.07 (m, 2H), 4.12 (brd, 1H, *J* = 10.2 Hz), 4.60 (s, 1H), 5.12−5.18 (m,

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2H), 5.72−5.77 (m, 1H), 5.92 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.0 (CH_3), 26.7 (CH_3), 28.2 (3 × CH_3), 44.0 (CH_2), 51.3 (CH_2), 73.7 (CH), 78.5 (CH), 81.2 (C), 84.7 (CH), 104.7 (CH), 111.2 (C), 117.1 (CH_2), 133.0 (CH), 156.9 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{16}H_{27}NNaO_6$, m/z 352.1736, found 352.1720.

(3*S*,6a*R*,7a*R*,10a*R*,10b*R*)-*tert*-Butyl-1-benzyl-9,9-dimethylhexahydro-3,10*b*-methano[1,3]dioxolo[4′,5′:4,5]furo[3,2-*c*][1,2,6]oxadiazocine-5(1*H*)-carboxylate (18). Oxidation of **17** (2.2 g, 6.69 mmol) in dry DCM (30 mL) was carried out using DMP (4.26 g, 10.04 mmol) as described in the preparation of **6**. The usual work up afforded a crude ketone, which was treated with BnNHOH (1.23 g, 10.04 mmol) in refluxing toluene (50 mL) for 12 h. The usual work up and purification by column chromatography on silica gel (230−400 mesh) using petroleum ether−EtOAc (17:3) furnished **18** (1.85 g, 64%) as a colorless solid. mp 167−168 °C; $[\alpha]_D^{25}$ + 102 (*c* 0.18, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.34 (s, 3H), 1.46 (s, 9H), 1.60 (s, 3H), 2.19−2.36 (m, 2H), 2.91 (brs,1H), 3.21 (brs,1H), 3.88 (m, 1H), 4.14−4.23 (m, 4H), 4.51 (d, 1H, *J* = 3.0 Hz), 4.76 (brs, 1H), 5.83 (d, 1H, *J* = 3.3 Hz), 7.29−7.41 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.1 (CH_3), 26.5 (CH_3), 28.2 (3 × CH_3), 32.9 (CH_2), 45.4 (CH_2), 49.4 (CH_2), 57.5 (CH_2), 76.2 (CH), 77.2 (CH), 78.6 (C), 80.0 (C), 82.3 (CH), 103.8 (CH), 112.7 (C), 127.3 (CH), 128.3 (2 × CH), 129.2 (2 × CH), 137.8 (C), 156.2 (C); HRMS (EI, magnetic sector, positive ion) calcd for $C_{23}H_{32}N_2O_6$, m/z 432.2260, found 432.2250.

2-((3a*R*,5*R*,6*S*,6a*R*)-6-(4-Methoxybenzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)ethanol (20). A solution of **19** (4.75g, 15.52 mmol) in THF (40 mL) at 0 °C was treated with a solution of 9-BBN (94 mL, 0.5 M in THF, 46.57 mmol), the reaction mixture was allowed to warm up to 20 °C and stirred overnight. The mixture was cooled in an ice−water bath, treated carefully with an aqueous solution of sodium hydroxide (2 N, 50 mL), followed by hydrogen peroxide (50 mL, 30% in water), warmed up to 20 °C, and stirred for 2 h more. The solvent was removed in vacuum to afford a residue, which was partitioned between ether (100 mL) and water (100 mL). The separated ether layer was dried (Na_2SO_4) and concentrated. Chromatographic purification of the residue on silica gel (100−200 mesh) using petroleum ether−EtOAc (3:1) as eluent provided **20** (4.0 g, 80%) as a colorless oil. $[\alpha]_D^{25}$ − 28 (*c* 0.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s, 3H), 1.48 (s, 3H), 1.73−1.87 (m, 1H), 1.98−2.10 (m, 1H), 2.25 (brs, 1H), 3.73 (t, 2H, *J* = 5.7 Hz), 3.80 (s, 3H), 4.28−4.34 (m, 1H), 4.41 (d, 1H, *J* = 11.7 Hz), 4.61 (d, 1H, *J* = 4.2 Hz), 4.63 (d, 1H, *J* = 12.9 Hz), 5.91 (d, 1H, *J* = 3.9 Hz), 6.87 (d, 2H, *J* = 8.7 Hz), 7.24 (d, 2H, *J* = 8.4 Hz), one H not discernible; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.1 (CH_3), 26.5 (CH_3), 30.8 (CH_2), 55.2 (CH_3), 60.1 (CH_2), 71.3 (CH_2), 78.4 (CH), 81.9 (CH), 82.1 (CH), 104.6 (CH), 111.3 (C), 113.8 (2 × CH), 129.3 (2 × CH), 159.3 (C), one C not discernible; HRMS (ESI−QToF, positive ion) calcd for $C_{17}H_{24}NaO_6$, m/z 347.1471, found 347.1463.

1-((3a*R*,5*R*,6*S*,6a*R*)-6-(4-Methoxybenzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)pent-4-en-2-ol (21). To a solution of **20** (2.3 g, 7.10 mmol) in DCM (40 mL) at 0 °C was added DMP (4.34 g, 10.23 mmol) under N_2, and the reaction was stirred for 2 h. The residue was extracted with DCM (2 × 40 mL), and the solvent was washed with a saturated solution of $NaHCO_3$ (50 mL), 10% $Na_2S_2O_3$ solution (50 mL), and brine (50 mL). The organic solvent was dried (Na_2SO_4) and evaporated in vacuo to give an aldehyde. To the crude aldehyde dissolved in NH_4Cl−THF (5:1, 36 mL) at 0 °C was added allyl bromide (1.84 mL, 21.3 mmol), and the reaction mixture was stirred for 5 min. Zn dust (2.7 g,41.2 mmol) was added portionwise to the reaction mixture, which was stirred at room temperature for 12 h. The reaction was quenched with a saturated aqueous $NaHCO_3$ solution (50 mL), and the solvent was evaporated to furnish a residue, which was extracted with $CHCl_3$ (3 × 40 mL). The combined extract was washed with brine (50 mL), dried (Na_2SO_4), and evaporated in vacuo. The crude product was purified by column chromatography on silica gel (100−200 mesh) using petroleum ether−EtOAc (8:2) to furnish **21** (2.0 g, 77%) as a colorless liquid (a mixture of α and β anomers). $[\alpha]_D^{25}$ − 36 (*c* 0.35, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s), 1.48 (s), 1.61−1.78 (m), 1.81−2.05 (m), 2.15−2.35 (m), 3.72−3.77 (m), 3.81 (s), 3.84−3.92 (m), 4.33−4.37 (m), 4.41 (dd, *J* = 6.3, 11.7 Hz), 4.60 (q, *J* = 3.6 Hz), 4.65 (d, *J* = 3.6 Hz), 5.14 (m), 5.74−5.88 (m), 5.9 (d, *J* = 4.2 Hz), 5.92 (d, *J* = 4.2 Hz), 6.88 (d, *J* = 8.7), 7.25 (d, *J* = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.0 (CH_3), 26.4 (CH_3), 34.4 (CH_2), 34.8 (CH_2,), 41.8 (CH_2), 42.3 (CH_2), 55.0 (CH_3), 67.7 (CH), 69.1 (CH_3), 71.1 (CH_2), 77.2 (CH), 78.8 (CH), 81.5 (CH), 81.8 (CH), 82.2 (CH), 104.3 (CH), 104.5 (CH), 111.0 (C), 111.2 (C), 113.6 (CH), 117.3 (CH_2), 117.5 (CH_2), 129.2 (CH), 129.4 (CH), 134.6 (CH), 159.1 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{20}H_{28}NaO_6$, m/z 387.1784, found 387.1781.

1-((3a*R*,5*R*,6*S*,6a*R*)-6-Hydroxy-2,2-dimethyltetrahydrofuro-[2,3-*d*][1,3]dioxol-5-yl)pent-4-en-2-yl acetate (22). To a solution of **21** (1.38 g, 3.8 mmol) in pyridine (20 mL) were added Ac_2O (0.72 mL, 7.58 mmol) and DMAP (pinch), and the mixture was stirred at room temperature for 8 h. Pyridine was evaporated by azeotropic distillation with toluene in rotary evaporator. The residue was extracted with DCM (2 × 50 mL), and the solvent was washed with brine (50 mL), dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography on silica gel (60−120 mesh) using petroleum ether−EtOAc (1:4) as eluent to furnish the triacetylated derivative (1.48 g, 96%) as a thick oil. The removal of the PMB protection was done, following the method as described in **4**, using the oil (1.08 g, 2.66 mmol) and DDQ (0.91 g, 4.01 mmol) in a mixture of DCM (40 mL) and H_2O (2 mL). The usual work up and purification by column chromatography on silica gel (100−200 mesh) using petroleum ether−EtOAc (5:1) as eluent furnished **22** (685 mg, 90%) as a colorless oil. $[\alpha]_D^{25}$ − 10 (*c* 0.55, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.31 (s), 1.48 (s), 1.88−2.03 (m), 2.05 and 2.06 (2*s*), 2.37−2.45 (m), 4.07−4.22 (m), 4.49 and 4.54 (2 × d, *J* = 3.6 Hz), 4.83−4.92 (quint, *J* = 6.0 Hz), 5.04−5.14 (m), 5.69−5.83 (m), 5.88 (t, *J* = 3.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.0 (CH_3), 26.0 (CH_3), 26.5 (CH_3), 31.5 (CH_2), 31.9 (CH_2), 38.6 (CH_2), 38.8 (CH_2), 70.8 (CH), 71.3 (CH), 75.0 (CH), 75.3 (CH), 77.0 (CH), 77.3 (CH), 85.0 (CH), 85.2 (CH), 104.0 (CH), 104.1 (CH), 111.18 (C), 111.21 (C), 117.9 (CH_2), 118.1 (CH_2), 132.9 (CH), 133.1 (CH), 170.9 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{14}H_{22}NaO_6$, m/z 309.1314, found 309.1307.

(3*S*,5*R*,6a*R*,7a*R*,10a*R*,10b*R*)-1-Benzyl-9,9-dimethyloctahydro-3,10*b*-methano[1,3]dioxolo[4′,5′:4,5]furo[3,2-*c*][1,2]-oxazocin-5-yl acetate (23). Oxidation of the hydroxyl group of **22**, followed by nitrone cycloaddition reaction, was carried out, according to the procedure as described in **6**, using **22** (0.64 g, 2.24 mmol) and DMP (1.42 g, 3.4 mmol) for oxidation, and BnNHOH (0.42 g, 3.41 mmol) in refluxing toluene (10 mL) for 10 h for cycloaddition reaction. The usual work up and purification by column chromatography on silica gel (230−400 mesh) using petroleum ether−EtOAc (10:1.5) furnished **23** (0.35 g, 40%) as a colorless solid. mp 186−187 °C; $[\alpha]_D^{25}$ − 80 (*c* 0.11, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.34 (s, 3H), 1.60 (s, 3H), 1.58−1.62 (a merged signal 1H), 2.00 (s, 3H), 2.13−2.31 (m, 5H), 3.81 (brs, 1H), 4.16 (d, 1H, *J* = 13.2 Hz), 4.43 (brs, 1H), 4.49 (d, 1H, *J* = 3.6 Hz), 4.69 (brs, 1H), 5.19 (dt, 1H, *J* = 5.4,10.2 Hz), 5.83 (d, 1H, *J* = 3.6 Hz), 7.27 (t, 1H, *J* = 7.2 Hz), 7.34 (t, 2H, *J* = 7.8 Hz), 7.40 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 21.3 (CH_3), 26.2 (CH_3), 26.4 (CH_3), 33.5 (CH_2), 37.4 (CH_2), 57.4 (CH_2), 66.8 (CH), 73.8 (CH), 82.2 (CH), 103.7 (CH), 113.0 (C), 127.3 (CH), 128.3 (2 × CH), 129.2 (2 × CH), 137.7 (C), 170.2 (C), one CH_2, one CH and one C not discernible; HRMS (EI, magnetic sector, positive ion) calcd for $C_{21}H_{27}NO_6$, m/z 389.1838, found 389.1841.

(3a*R*,5*S*,6*S*,6a*R*)-5-((*R*)-1-(Benzyloxy)but-3-en-1-yl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-ol (25). Sodium metaperiodate (3.89 g, 18.2 mmol) dissolved in water (10 mL) was added to a solution of **24** (5.32 g, 15.2 mmol) in MeOH (150 mL) at 0 °C, and the reaction was stirred for 3 h. The reaction mixture was filtered, and the residue was washed with MeOH (2 × 30 mL). The combined filtrate was evaporated to furnish a residue, which was extracted with DCM (2 × 50 mL) and washed with brine (30 mL). The solvent was dried (Na_2SO_4) and evaporated in vacuo to give a crude aldehyde (4.22 g). The aldehyde (3.5 g) was allylated using allyl

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bromide (2.95 mL, 34.1 mmol), Zn dust (4.45g, 68.16 mmol), and NH_4Cl–THF (5:1, 42 mL) following the procedure as described in the preparation of **21**. The usual work up and purification by column chromatography on silica gel (100–200 mesh) using petroleum ether–EtOAc (4:1) as eluent furnished the hydroxy allyl derivative (β isomer, 2.65 g, 67%) as a colorless liquid. To a cold (0 °C) suspension of NaH (60% in mineral oil, 0.343 g, 8.57 mmol) in dry DMF (10 mL) was added a solution of the above isomer (2.5 g, 7.14 mmol) in DMF (15 mL), and the mixture was stirred for 30 min at 0 °C. Benzyl bromide (1.10 mL, 9.28 mmol) in dry DMF (15 mL) containing TBAB (0.262 g, 0.81 mmol) was added to the reaction mixture, which was then stirred at room temperature for 6 h. The reaction was quenched with a saturated aqueous NH_4Cl solution (25 mL), and the organic solvent was evaporated under vacuum to a residue, which was extracted with EtOAc (3 × 30 mL). The combined organic extract was dried (Na_2SO_4) and evaporated to a residue, which was purified by column chromatography on silica gel (60–120 mesh). Elution was made with a petroleum ether–EtOAc (19:1) mixture to give the benzyl protected olefin derivative (2.65 g, 84%) as a colorless gum. A solution of the above derivative (2.0 g) in DCM–H_2O (20:1, 42 mL) was oxidized by DDQ (1.55 g, 6.82 mmol) following the procedure as described in the preparation of **4**. The usual work up and purification by column chromatography on silica gel (100–200 mesh) using petroleum ether–EtOAc (5:1) produced **25** (1.2 g, 82%) as a colorless oil. $[\alpha]_D^{25}$ − 5 (*c* 0.15, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s, 3H), 1.48 (s, 3H), 2.36–2.45 (m, 2H), 4.04–4.10 (m, 2H), 4.27 (brs, 1H), 4.32 (brs, 1H), 4.51 (d, 1H, *J* = 3.3 Hz), 4.66 (d, 1H, *J* = 11.4 Hz), 4.80 (d, 1H, *J* = 11.4 Hz), 5.11 (d, 1H, *J* = 11.1 Hz), 5.16 (d, 1H, *J* = 18.6 Hz), 5.76–5.90 (m, 1H), 5.98 (d, 1H, *J* = 3.6 Hz), 7.33–7.43 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.1 (CH_3), 26.7 (CH_3), 36.4 (CH_2), 74.0 (CH_2), 75.3 (CH), 78.0 (CH), 80.5 (CH), 85.2 (CH), 104.5 (CH), 111.5 (C), 118.0 (CH_2), 128.0 (3 × CH), 128.4 (2 × CH), 133.5 (CH), 137.6 (C); HRMS (EI, magnetic sector, positive ion) calcd for $C_{18}H_{24}O_5$, *m*/*z* 320.1624, found 320.1619.

(3a*R*,5*R*,5a*S*,6a*R*,9a*R*,9b*R*)-1-Benzyl-5-(benzyloxy)-8,8-dimethyloctahydro[1,3]dioxolo[4″,5″:4′,5′]furo[3′,2′:1,5]cyclopenta[1,2-*c*]isoxazole (27). Oxidation of the hydroxyl group of **25**, followed by INC reaction of the generated ketone, was done, according to the procedure as described in **6**, using **25** (2.0 g, 6.25 mmol), DMP (3.98 g, 9.38 mmol), and dry DCM (30 mL). The usual work up afforded a crude residue. To a solution of this residue in toluene (50 mL) was added BnNHOH (1.15 g, 9.38 mmol), and the mixture was heated at reflux for 12 h. The usual work up and purification by column chromatography on silica gel (230–400 mesh) using petroleum ether–EtOAc (4:1) afforded **27** (1.75 g, 66%) as a colorless solid. mp 120–121 °C; $[\alpha]_D^{25}$ + 14.0 (*c* 0.16, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.36 (s, 3H), 1.58 (s, 3H), 1.87 (dd, 1H, *J* = 7.2, 12.6 Hz), 2.19 (q, 1H, *J* = 10.5 Hz), 2.69 (apparent t, 1H, *J* = 7.2, 7.8 Hz), 3.55 (d, 1H, *J* = 8.7 Hz), 3.86 (d, 1H, *J* = 13.8 Hz), 3.96 (apparent t, 1H, *J* = 6.9, 8.1 Hz), 4.11 (apparent t, 1H, *J* = 6.6, 8.1 Hz), 4.39 (d, 1H, *J* = 14.1 Hz), 4.61 (d, 1H, *J* = 11.7 Hz), 4.67 (merged s, 1H), 4.69 (d, 1H, *J* = 11.7 Hz), 4.77 (s, 1H), 5.88 (s, 1H), 7.30–7.54 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.6 (CH_3), 27.2 (CH_3), 35.2 (CH_2), 48.6 (CH), 57.7 (CH_2), 72.2 (CH_2), 73.1 (CH_2), 79.3 (CH), 80.1 (CH), 81.5 (C), 85.3 (CH), 105.2 (CH), 113.6 (C), 127–128.4 (10 × CH), 138.0 (C), 138.4 (C); HRMS (EI, magnetic sector, positive ion) calcd for $C_{25}H_{29}NO_5$, *m*/*z* 423.2046, found 423.2051.

(2*S*,3*R*,4*R*,5*R*)-2-(Allyloxy)-4-(benzyloxy)-5-((benzyloxy)-methyl)tetrahydrofuran-3-ol (29). To a mixture of **28** (2.5 g, 6.76 mmol) and dry allyl alcohol (50 mL) was added tosic acid (0.20 g, 1.08 mmol), and the mixture was heated at reflux for 6 h. The reaction mixture was neutralized with a saturated $NaHCO_3$ solution (30 mL), and the solvent was removed in vacuo until a syrupy residue was obtained. The residue was extracted with DCM (3 × 40 mL), and the organic layer was washed with H_2O (50 mL), dried, and concentrated to give a mixture of crude product (α and β anomer). The mixture was separated and purified by column chromatography on silica gel (230–400 mesh) using petroleum ether–EtOAc (9:1) as eluent to furnish **29** (1.75 g, 70%) as a colorless oil. $[\alpha]_D^{25}$ − 87 (*c* 0.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.77 (d, 1H, *J* = 7.5 Hz), 3.65 (dd, 1H, *J* = 6.6, 10.5 Hz), 3.73 (dd, 1H, *J* = 4.2,10.5 Hz), 4.03 (dd, 1H, *J* = 4.2, 5.7 Hz), 4.10 (dd, 1H, *J* = 6.3, 12.9 Hz), 4.26 (dd, 1H, *J* = 4.5, 7.8 Hz), 4.33 (dd, 1H, *J* = 5.1, 12.9 Hz), 4.42(dd, 1H, *J* = 5.7, 10.5 Hz), 4.52 (d, 1H, *J* = 12.0 Hz), 4.55 (d, 1H, *J* = 12.0 Hz), 4.62 (d, 1H, *J* = 12.0 Hz), 4.74 (d, 1H, *J* = 12.0 Hz), 5.14 (d, 1H, *J* = 4.8 Hz), 5.20 (d, 1H, *J* = 10.5 Hz), 5.28 (dd, 1H, *J* = 1.2, 17.1 Hz), 5.84–5.97 (m, 1H), 7.27–7.38 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 68.99 (CH_2), 69.0 (CH_2), 71.8 (CH_2), 73.4 (CH_2), 76.9 (CH), 77.4 (CH), 83.5 (CH), 99.9 (CH), 117.6 (CH_2), 127.5–128.3 (10 × CH), 133.7 (CH), 137.9 (C), 138.1 (C); HRMS (ESI–QToF, positive ion) calcd for $C_{22}H_{26}NaO_5$, *m*/*z* 393.1678, found 393.1658.

(3a*S*,5a*S*,7*R*,8*R*,8a*S*)-1-Benzyl-8-(benzyloxy)-7-(benzyloxy)-methylhexahydro-1*H*-furo[2′,3′:2,3]furo[3,4-*c*]isoxazole (30). Oxidation and INC reaction were carried out, according to the procedure as described in **6**, using **29** (0.350 g, 0.95 mmol), DMP (0.606 g, 1.43 mmol), and dry DCM (15 mL). The usual work up furnished a crude ketone, which was dissolved in toluene (10 mL), and then BnNHOH (0.176 g, 1.43 mmol) was added to it. The mixture was heated at reflux for 12 h. The usual work up and purification by column chromatography on silica gel (230–400 mesh) using petroleum ether–EtOAc (3:17) as eluent gave **30** (0.355 g, 79%) as a colorless solid. mp 175–176 °C; $[\alpha]_D^{25}$ − 10 (*c* 0.16, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.91–2.96 (m, 1H), 3.70–3.72 (m, 2H), 3.85 (dd, 1H, *J* = 2.1, 8.7 Hz), 3.93 (dd, 1H, *J* = 3.0, 9.3 Hz), 4.08 (d, 1H, *J* = 14.1 Hz), 4.04–4.11 (merged dd, 1H), 4.20 (d, 1H, *J* = 3.0 Hz), 4.24 (apparent t, 1H, *J* = 7.2, 9.3 Hz), 4.35 (dd, 1H, *J* = 3.0, 6.3 Hz), 4.40 (d, 1H, *J* = 14.7 Hz), 4.49 (d, 1H, *J* = 11.7 Hz), 4.56 (d, 1H, *J* = 11.7 Hz), 4.65 (d, 1H, *J* = 11.1 Hz), 4.91 (d, 1H, *J* = 11.4 Hz), 6.02 (s, 1H), 7.17–7.39 (m, 15H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 53.6 (CH), 58.5 (CH_2), 68.2 (CH_2), 71.9 (CH_2), 73.1 (CH_2), 73.7 (CH_2), 74.8 (CH_2), 80.9 (CH), 83.9 (CH), 86.7 (C), 104.3 (CH), 127.0–128.4 (15 × CH), 137.6 (C), 137.8 (C), 138.3 (C); HRMS (ESI–QToF, positive ion) calcd for $C_{29}H_{31}NNaO_5$, *m*/*z* 496.2100, found 496.2108.

(3a*S*,5a*R*,6*R*,8a*S*)-1-Benzyl-6-((benzyloxy)methyl)hexahydro-1*H*-furo[3′,4′:2,3]furo[3,4-*c*]isoxazole (32). Oxidation, nitrone formation, and in situ cyclization were executed, following the procedure as described in **6**, using **31** (0.550 g, 2.10 mmol), DMP (1.34 g, 3.15 mmol), and dry DCM (20 mL). The usual work up afforded a ketone, which was dissolved in toluene (15 mL), and BnNHOH (0.390 g, 3.15 mmol) was added to it. The mixture was heated at reflux for 6 h. The usual work up and purification by column chromatography on silica gel (230–400 mesh) using petroleum ether–EtOAc (4:1) furnished **32** (0.475 g, 62%) as a colorless solid. mp 170–171 °C; $[\alpha]_D^{25}$ − 37 (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.11–3.13 (m, 1H), 3.67–3.85 (m, 7H), 3.96–3.99 (m, 1H), 4.14–4.19 (m, 2H), 4.24 (d, 1H, *J* = 9.9 Hz), 4.54 (s, 1H), 4.56 (partially merged d, 1H, *J* = 12.0 Hz), 4.64 (d, 1H, *J* = 12.0 Hz), 7.28–7.36 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 54.6 (CH), 55.9 (CH_2), 68.2 (CH_2), 70.6 (CH_2), 72.0 (CH_2), 73.6 (CH_2), 74.6 (CH_2), 82.7 (2 × CH), 87.1 (C), 127.4–128.4 (10 × CH), 137.0 (C), 138.0 (C); HRMS (EI, magnetic sector, positive ion) calcd for $C_{22}H_{25}NO_4$, *m*/*z* 367.1784, found 367.1779.

(3a*R*,7*R*,7a*S*)-6-(Allyloxy)-2,2-dimethyltetrahydro-3a*H*-[1,3]-dioxolo[4,5-*c*]pyran-7-ol (34). A mixture of **33** (10 g, 66.7 mmol), allyl alcohol (150 mL), and *p*-TSA·H_2O (1.27 mg, 6.67 mmol) was heated at reflux for 4 h under N_2. The reaction mixture was filtered, and the filtrate was evaporated in vacuo to a residue, which was extracted with $CHCl_3$ (2 × 50 mL). The combined extract was washed with brine (50 mL), dried (Na_2SO_4), and evaporated to a crude anomeric mixture of the allylated product (11.4 g), which was used without further purification for the next step. A solution of 2,2-dimethoxy propane (9.7 mL, 78.95 mmol) and *p*-TSA·H_2O (1.5 g, 7.89 mmol) in dry acetone (150 mL) was added to the above crude anomeric mixture (10.0 g, 52.6 mmol), and the mixture was stirred under N_2 for 12 h. Silver carbonate (3.26 g, 11.8 mmol) was added, and the mixture was stirred for another 50 min. The heterogeneous mixture was filtered, and the residue was washed with acetone (100 mL). The combined solvent was evaporated under vacuum to a crude mixture (anomers) of products, which were purified by column

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chromatography on silica gel (230−400 mesh) using petroleum ether−EtOAc (4:1) as eluent to furnish (**34**, β-anomer, 4.6 g, 38%) as a colorless gum. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.39 (s, 3H), 1.60 (s, 3H), 2.19 (d, 1H, J = 8.7 Hz), 3.55−3.69 (m, 2H), 3.83 (dd, 1H, J = 3.9, 10.8 Hz), 3.97−4.11 (m, 2H), 4.26 (m, 1H), 4.42 (brs, 1H), 4.75 (d, 1H, J = 3.3 Hz), 5.21 (d, 1H, J = 10.4 Hz), 5.31 (d, 1H, 17.4 Hz), 5.87−5.94 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 25.3 (CH_3), 26.5 (CH_3), 61.8 (CH_2), 68.3 (CH), 69.0 (CH_2), 72.7 (CH), 72.9 (CH), 99.4 (CH), 109.8 (C), 117.5 (CH_2), 133.9 (CH); ESIMS, m/z: 253 $(M + Na)^+$.

(3a*R*,5a*R*,7a*R*,10a*S*,10b*R*)-1-Benzyl-9,9-dimethyloctahydro-[1,3]dioxolo[4″,5″:4′,5′]pyrano[2′,3′:2,3]furo[3,4-*c*]isoxazole (35). Oxidation and subsequent INC reaction were performed, following the procedure as described in **6**, using **34** (1.0 g, 4.35 mmol), DMP (2.03 g, 4.78 mmol), and dry DCM (100 mL). The usual work up produced a crude residue, which was treated with BnNHOH (803 mg, 6.53 mmol) in refluxing toluene (25 mL) for 12 h. The usual work up and purification by a column chromatography on silica gel (230−400 mesh) using petroleum ether−EtOAc (10:1) as eluent gave **35** (800 mg, 55%) as solid material. mp 164−165 °C; $[\alpha]_D^{25}$ + 15 (c 0.11, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.41 (s, 3H), 1.51 (s, 3H), 2.88 (quint, 1H, J = 4.2 Hz), 3.66 (dd, 1H, J = 3.6, 13.2 Hz), 3.76 (dd, 1H J = 3.6, 12.6 Hz), 3.78 (d, 1H, J = 9.0 Hz), 3.85 (dd, 1H, J = 4.2, 9.0 Hz), 3.91 (dd, 1H, J = 4.8, 9.0 Hz), 4.07 (d, 1H, J = 13.8 Hz), 4.33−4.36 (m, 2H), 4.44 (t, 1H, J = 9.0 Hz), 4.71 (d, 1H, J = 6.6 Hz), 5.56 (s, 1H), 7.26−7.43 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.5 (CH_3), 27.0 (CH_3), 51.1 (CH), 57.0 (CH_2), 64.1 (CH_2), 71.9 (CH_2), 72.8 (CH), 74.3 (C), 75.2 (CH_2), 76.2 (CH), 100.2 (CH), 110.0 (C), 127.1 (CH), 128.5 (2 × CH), 128.6 (2 × CH), 138.7 (C); HRMS (EI, magnetic sector, positive ion) calcd for $C_{18}H_{23}NO_5$, m/z 333.1576, found 333.1570.

(3a*R*,4a*S*,8*S*,9a*R*,9b*R*)-9a-Amino-2,2-dimethyloctahydro-[1,3]dioxolo[4′, 5′:4, 5]furo[2, 3-*c*]oxepin-8-ol (36). To a stirred solution of **6** (1.5 g, 4.5 mmol) in CH_3CN−H_2O (15:1, 16 mL) was added $Mo(CO)_6$ (1.80 g, 6.8 mmol), and the mixture was heated at reflux under N_2 for 12 h. The solvent was removed in vacuo, and the residue was dissolved in a DCM−MeOH mixture (15:1) and was passed through a bed of neutral alumina. The solvent was evaporated to give **36** (0.85 g, 77%) as a thick oil. $[\alpha]_D^{25}$ + 31 (c 0.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.35 (s, 3H), 1.55 (s, 3H), 1.95−2.06 (m, 2H), 2.18 (brs, 3H), 3.82 (s, 1H), 3.91 (d, 2H, J = 3.6 Hz), 4.05 (d, 1H, J = 3.6 Hz), 4.07 (d, 2H, J = 2.7 Hz), 4.18−4.20 (m, 1H), 5.87 (d, 1H, J = 3.9 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 26.5 (CH_3), 26.8 (CH_3), 34.1 (CH_2), 64.3 (C), 67.7 (CH_2), 71.3 (CH), 78.7 (CH_2), 81.5 (CH), 86.1 (CH), 103.4 (CH), 112.0 (C); HRMS (EI, magnetic sector, positive ion) calcd for $C_{11}H_{19}NO_5$, m/z 245.1263, found 245.1260.

(3a*R*,4a*R*,8*S*,9a*R*,9b*R*)-*tert*-Butyl-9a-amino-8-hydroxy-2,2-dimethylhexahydro-3a*H*-[1,3]dioxolo[4′,5′:4,5]furo[2,3-*c*]-azepine-6(9b*H*)-carboxylate (37). Cleavage of the N−O bond and debenzylation were carried out, following the procedure as described in **36**, using **18** (1.2 g, 2.78 mmol), $Mo(CO)_6$ (1.1 g, 4.17 mmol), and a CH_3CN−H_2O mixture (15:1, 16 mL). The usual work up provided **37** (0.80 g, 84%) as a yellow oil. $[\alpha]_D^{25}$ + 35 (c 0.23, $CHCl_3$); ^{1}H NMR ($CDCl_3$ + D_2O, 300 MHz): δ 1.32 (s, 3H), 1.46 (s, 9H), 1.54 (s, 3H), 1.82 (apparent t, 2H, J = 16.0 Hz), 3.28 (dd, 1H, J = 3.6, 13.8 Hz), 3.53−3.77 (m, 2H), 3.84−3.92 (m, 1H), 3.96 (s, 1H), 4.07−4.26 (m, 2H), 5.74 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.3 (CH_3), 26.4 (CH_3), 26.6 (CH_3), 28.3 (3 × CH_3), 35.7 (CH_2), 35.9 (CH_2), 47.4 (CH_2), 48.7 (CH_2), 55.0 (CH_2), 56.5 (CH_2), 64.4 (C), 64.9 (C), 69.6 (CH), 70.4 (CH), 77.2 (C), 79.8 (CH), 80.0 (CH), 86.6 (CH), 87.2 (CH), 103.1 (CH), 103.4 (CH), 111.6 (C), 111.8 (C), 155.7 (C), 155.9 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{16}H_{28}N_2NaO_6$, m/z 367.1845, found 367.1827.

((3a*R*,4a*S*,5*R*,7*R*,7a*R*,7b*R*)-7a-Amino-5-(benzyloxy)-2,2-dimethylhexahydro-3a*H*-cyclo-penta[4,5]furo[2,3-*d*][1,3]-dioxol-7-yl)methanol (38). A solution of **27** (1.5 g, 3.55 mmol) in CH_3CN−H_2O (15:1, 16 mL) was treated with $Mo(CO)_6$ (1.87 g, 7.1 mmol), according to the procedure as described in **36**. The usual work up gave **38** (0.85 g, 71%) as a thick oil. $[\alpha]_D^{25}$ + 77 (c 0.11, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.35 (s, 3H), 1.56 (s, 3H), 1.76−1.85 (m, 1H), 1.99−2.10 (m, 2H), 2.32 (brs, 3H), 3.63 (dd, 1H, J = 9.0, 11.1 Hz), 3.73 (dd, 1H, J = 4.8, 11.4 Hz), 4.08 (dt, 1H, J = 3.3, 8.1 Hz), 4.18 (d, 1H, J = 3.3 Hz), 4.41 (d, 1H, J = 3.6 Hz), 4.55 (d, 1H, J = 12.0 Hz), 4.62 (d, 1H, J = 12.0 Hz), 5.94 (d, 1H, J = 3.6 Hz), 7.28−7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.6 (CH_3), 27.1 (CH_3), 31.1(CH_2), 42.4 (CH), 62.8 (CH_2), 69.7 (C), 71.8 (CH_2), 78.5 (CH), 85.6 (CH), 86.9 (CH), 106.1 (CH), 112.5 (C), 127.7 (CH), 127.8 (2 × CH), 128.3 (2 × CH), 138.0 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{18}H_{25}NNaO_5$, m/z 358.1630, found 358.1628.

(3a*R*,4a*S*,8*S*,9a*S*,9b*R*)-9a-(Benzylamino)-2,2-dimethyloctahydrothiepino[4′,3′:4,5]furo[2,3-*d*][1,3]dioxol-8-ol (39). Isoxazolidine ring cleavage of **11** (250 mg, 0.72 mmol) in a mixture of CH_3CN−H_2O (15:1, 8 mL) was done following the procedure as described in **36**, using $Mo(CO)_6$ (285 mg, 1.08 mmol). The usual work up afforded **39** (175 mg, 69%) as a yellow oil. $[\alpha]_D^{25}$ + 40 (c 0.37, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.40 (s, 3H), 1.56 (s, 3H), 2.01 (dd, 1H, J = 1.8, 15.6 Hz), 2.25 (dd, 1H, J = 4.8, 14.4 Hz), 2.82 (dt, 2H, J = 5.4, 14.4 Hz), 3.01 (dd, 1H, J = 4.8,14.4 Hz), 3.31 (dd, 1H, J = 3.6, 15.6 Hz), 3.96 (d, 1H, J = 11.4 Hz), 4.08 (brs, 1H), 4.16 (d, 1H, J = 10.8 Hz), 4.38 (d, 1H, J = 3.0 Hz), 4.47−4.50 (m, 1H), 5.83 (d, 1H, J = 4.2 Hz), 7.28−7.37 (m, 5H), two Hs not discernible; ^{13}C NMR ($CDCl_3$, 150 MHz): δ 26.6 (CH_3), 26.9 (CH_3), 31.1 (CH_2), 33.7 (CH_2), 42.2 (CH_2), 48.0 (CH_2), 70.3 (CH), 71.2 (C), 77.2 (CH), 84.8 (CH), 103.0 (CH), 112.2 (C), 128.4−128.9 (5 × CH), one (C) not discernible; HRMS (ESI−QToF, positive ion) calcd for $C_{18}H_{26}NO_4S$, m/z 352.1583, found 352.1612.

((2*R*,3*R*,3a*S*,4*S*,6a*S*)-3a-Acetamido-3-acetoxyhexahydrofuro-[2,3-*b*]furan-2,4-diyl)bis(methylene)diacetate (40). Pd/C (10%, 100 mg) was added to a solution of **30** (600 mg, 1.27 mmol) in MeOH (20 mL) and hydrogenated with H_2 gas under 1 atmospheric pressure at room temperature for 12 h. The catalyst was filtered off, the solvent was evaporated, and the residue was used in the next step without further purification. The residue (210 mg, 1.02 mmol) was dissolved in pyridine (20 mL), Ac_2O (1.0 mL, 10.2 mmol) and DMAP (pinch) were added to the solution, and the mixture was stirred at room temperature for 6 h. Pyridine was evaporated through azeotropic distillation with toluene under vacuum. The residue was extracted with $CHCl_3$ (3 × 40 mL), the combine extract was washed with brine (50 mL), and dried (Na_2SO_4), and the solvent was evaporated to a residue, which was purified by column chromatography on silica gel (230−400 mesh) using petroleum ether−EtOAc (2:3) as eluent to afford **40** (350 mg, 74% overall) as a thick oil. $[\alpha]_D^{25}$ − 7 (c 0.14, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.03 (s, 3H), 2.08 (s, 3H), 2.09 (s, 3H), 2.12 (s, 3H), 2.73 (quint, 1H, J = 7.2 Hz), 4.00−4.06 (m, 2H), 4.12−4.30 (m, 4H), 4.56 (td, 1H, J = 4.5, 7.8 Hz), 5.49 (d, 1H, J = 3.3 Hz), 5.91 (s, 1H), 5.99 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.4 (CH_3), 20.7 (CH_3), 20.7 (CH_3), 23.0 (CH_3), 45.5 (CH), 61.7 (2 × CH_2), 71.2 (CH_2), 72.8 (C), 76.7 (CH), 78.0 (CH), 110.6 (CH), 170.0 (C), 170.6 (C), 170.96 (C), 170.99 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{16}H_{23}NNaO_9$, m/z 396.1271, found 396.1257.

((3*S*,3a*S*,6*R*,6a*R*)-3a-Acetamidohexahydrofuro[3,4-*b*]furan-3,6-diyl)bis(methylene)diacetate (41). Isoxazolidine ring cleavage, followed by debenzylation and acetylation, was carried out, following the procedure as described in **40**, using **32** (500 mg, 1.36 mmol) in MeOH (20 mL), Pd/C (10%, 80 mg), pyridine (20 mL), Ac_2O (0.81 mL), and DMAP (pinch). The usual work up and purification by column chromatography on silica gel (230−400 mesh) using petroleum ether−EtOAc (1:1) as eluent afforded **41** (305 mg, 71% overall) as a thick oil. $[\alpha]_D^{25}$ − 3 (c 0.07, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.02 (s, 3H), 2.08 (s, 3H), 2.10 (s, 3H), 2.82−2.86 (m, 1H), 3.89−3.95 (m, 2H), 4.00−4.07 (m, 3H), 4.16−4.24 (m, 3H), 4.29 (d, 1H, J = 10.2 Hz), 4.41 (d, 1H, J = 3.6 Hz), 6.20 (brs, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 20.9 (2 × CH_3), 23.2 (CH_3), 47.4 (CH), 62.6 (CH_2), 62.7 (CH_2), 71.4 (C), 72.1 (CH_2), 79.3 (CH_2), 80.2 (CH), 87.9 (CH), 170.6 (C), 170.88 (C), 170.91 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{14}H_{21}NNaO_7$, m/z 338.1216, found 338.1197.

((2*R*,4a*S*,6a*R*,7*R*,9a*S*)-2-Methyloctahydrofuro[3′,4′:2,3]furo-[3,4-*d*][1,3]oxazin-7-yl)methanol (43). Hydrogenolysis of **32** (700

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mg, 1.91 mmol) in dry MeOH (20 mL) was carried out over Pd/C (10%, 100 mg) following the procedure as described in **40**. The usual work up afforded a residue **42** (250 mg, 1.32 mmol), which was dissolved in 40% aqueous CH_3CHO (w/w %), and the mixture was stirred at room temperature for 12 h. The solvent was evaporated, and the residue was extracted with EtOAc (100 mL). The organic layer was washed with brine (50 mL), dried (Na_2SO_4) and evaporated to a residue, which was purified by column chromatography on silica gel (230−400 mesh) using petroleum ether−EtOAc (4:6) as eluent to provide **43** (235 mg, 57%) as a solid material. mp 142−143 °C; $[\alpha]_D^{25}$ + 3 (*c* 0.07, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.31 (d, 3H, *J* = 5.7 Hz), 2.04−2.12 (m, 1H), 2.47 (d, 1H, *J* = 6.6 Hz), 3.50 (d, 1H, *J* = 11.7 Hz), 3.57 (dd, 1H, *J* = 2.7, 9.3 Hz), 3.79−4.13 (m, 8H), 4.27−4.36 (m, 1H), one H not discernible; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.5 (CH_3), 39.9 (CH), 61.6 (CH_2), 68.0 (CH_2), 71.0 (CH_2), 71.3 (C), 81.1 (CH_2), 81.8 (CH), 83.1 (CH), 83.6 (CH); HRMS (ESI−QToF, positive ion) calcd for $C_{10}H_{17}NNaO_4$, *m*/*z* 238.1055, found 238.1028.

Conversion of 43 to 41. To a solution of **43** (210 mg, 0.98 mmol) in pyridine (15 mL) were added Ac_2O (0.7 mL, 7.4 mmol) and DMAP (pinch), and the mixture was stirred at room temperature for 6 h. Pyridine was evaporated through azeotropic distillation with toluene in a rotary evaporator. The residue was extracted with $CHCl_3$ (3 × 40 mL), and the combined extract was washed with brine (50 mL), dried (Na_2SO_4), and evaporated to a crude product, which was purified by column chromatography over silica gel (230−400 mesh) using petroleum ether−EtOAc (1:1) as eluent to afford **41** (280 mg, 91%) as a thick oil.

(2*R*,3*R*,3a*R*,5*S*,8a*S*)-3a-Acetamido-2-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)octahydro-furo[2,3-*c*]oxepine-3,5-diyl)-diacetate (44). Ac_2O (2.20 mL, 23.2 mmol) was added to **36** (0.70 g, 2.9 mmol) dissolved in HOAc (30 mL). The mixture was cooled to 0 °C, TfOH (0.009 mL, 0.1 mmol) was added to it, and the mixture was stirred for 2 h at room temperature. The reaction was quenched with a cold saturated $NaHCO_3$ solution (10 mL), and the mixture was extracted with DCM (3 × 25 mL). The combined solvent was dried (Na_2SO_4), and evaporated to a crude anomeric mixture of products, dried via co-evaporation with anhydrous CH_3CN (2 × 15 mL). Uracil (0.682 g, 6.09 mmol) and *N*,*O*-bis(trimethylsilyl)acetamide (2.13 mL, 8.7 mmol) were added to a solution of the above anomeric mixture in CH_3CN (20 mL), and the mixture was heated at reflux for 45 min until the suspension became a clear solution. The reaction mixture was cooled to 0 °C, and TMSOTf (0.79 mL, 4.35 mmol) was added to it dropwise and heated at 50 °C for 17 h. CH_3CN was evaporated under reduced pressure to a residue, to which was added a saturated NH_4Cl solution (10 mL). The mixture was extracted with DCM (2 × 25 mL). The combined extract was dried (Na_2SO_4), evaporated, and the crude product was purified by column chromatography over silica gel (230−400 mesh) using petroleum ether−EtOAc (2:3) as eluent to furnish **44** (0.550 g, 45%) as a colorless foam. $[\alpha]_D^{25}$ + 58 (*c* 0.23, CH_3OH); ^{1}H NMR (CD_3OD, 300 MHz): δ 2.02 (s, 3H), 2.06 (s, 3H), 2.16 (s, 3H), 2.94 (dd, 1H, *J* = 11.1, 14.4 Hz), 3.44 (dd, 1H, *J* = 10.5, 11.4 Hz), 3.87 (dd, 1H, *J* = 1.8, 14.4 Hz), 4.17−4.24 (m, 3H), 5.06−5.15 (m, 2H), 5.56 (d, 1H, *J* = 7.5 Hz), 5.82 (d, 1H, *J* = 8.1 Hz), 6.26 (d, 1H, *J* = 7.5 Hz), 7.78 (d, 1H, *J* = 8.1 Hz), two Hs were not discernible; ^{13}C NMR (CD_3OD, 75 MHz): δ 20.5 (CH_3), 20.9 (CH_3), 23.5 (CH_3), 37.1 (CH_2), 63.1 (C), 69.2 (CH), 74.9 (CH_2), 76.5 (CH), 76.7 (CH_2), 85.4 (CH), 86.8 (CH), 104.1 (CH), 141.3 (CH), 152.7 (C), 165.9 (C), 171.5 (C), 171.7 (C), 174.0 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{18}H_{23}N_3NaO_9$, *m*/*z* 448.1332, found 448.1306.

(2*R*,3*R*,3a*R*,4*R*,6*R*,6a*S*)-3a-Acetamido-4-(acetoxymethyl)-2-(2,4-dioxo-3,4-dihydro-pyrimidin-1(2*H*)-yl)hexahydro-2*H*-cyclopenta[*b*]furan-3,6-diyldiacetate (45). Nucleosidation on **38** was carried out, following the method as described in **44**, using **38** (0.70 g, 2.1 mmol), Ac_2O (1.98 mL, 21.0 mmol), HOAc (25 mL), and TfOH (0.006 mL, 0.07 mmol) for peracetylation. The usual work up afforded a residue, which was treated with uracil (0.494 g, 4.41 mmol) and *N*,*O*-bis(trimethylsilyl)acetamide (1.54 mL, 6.3 mmol) in refluxing CH_3CN (20 mL). The reaction mixture was cooled to 0 °C, and TMSOTf (0.57 mL, 3.15 mmol) was added to it dropwise and heated at 50 °C for 17 h. The usual work up and purification by column chromatography over silica gel (230−400 mesh) using petroleum ether−EtOAc (3:7) as eluent furnished **45** (0.40 g, 41%) as a foam. $[\alpha]_D^{25}$ + 79 (*c* 0.37, CH_3OH); ^{1}H NMR (CD_3OD, 300 MHz): δ 1.96 (s, 3H), 1.98 (s, 3H), 2.00 (s, 3H), 2.04 (s, 3H), 2.08−2.16 (partially merged m, 1H), 2.27−2.31 (m, 1H), 2.66 (m, 1H), 3.96 (dd, 1H, *J* = 6.6, 8.1 Hz), 4.07 (dd, 1H, *J* = 7.5, 11.1 Hz), 4.15 (d, 1H, *J* = 8.4 Hz), 5.14 (d, 1H, *J* = 5.7 Hz), 5.25−5.26 (m, 1H), 5.76 (d, 1H, *J* = 8.4 Hz), 5.88 (d, 1H, *J* = 8.4 Hz), 7.69 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (CD_3OD, 150 MHz): δ 20.8 (CH_3), 21.0 (CH_3), 21.1 (CH_3), 23.2 (CH_3), 35.1(CH_2), 43.3 (CH), 46.4 (CH), 65.6 (CH_2), 70.3 (C), 72.9 (CH), 78.3 (CH), 85.7 (CH), 104.2 (CH), 141.4 (CH), 152.4 (C), 171.8 (C), 172.0 (C), 172.4 (C), 172.8 (C), 174.6 (C); HRMS (ESI−QToF, positive ion) calcd for $C_{20}H_{25}N_3NaO_{10}$, *m*/*z* 490.1438, found 490.1428.

(3a*R*,4a*R*,8*S*,9a*R*,9b*R*)-*tert*-Butyl-9a-acetamido-8-acetoxy-2,2-dimethylhexahydro-3a*H*-[1,3]dioxolo[4′,5′:4,5]furo[2,3-*c*]-azepine-6(9b*H*)-carboxylate (46). To a solution of **37** (0.85 g, 2.5 mmol) in pyridine (20 mL) were added Ac_2O (1.18 mL, 12.5 mmol) and DMAP (a pinch). The mixture was stirred at room temperature for 12 h. Pyridine was evaporated by azeotropic distillation with toluene under vacuum. The residue was extracted with DCM (2 × 30 mL), and the combined extract was washed with brine (30 mL), dried (Na_2SO_4), and evaporated to a crude residue, which was purified by column chromatography on silica gel (100−200 mesh) using petroleum ether−EtOAc (3:1) as eluent to furnish **46** (0.80 g, 75%) as a crystalline material. mp 178−179 °C; $[\alpha]_D^{25}$ + 53 (*c* 0.16, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.31 (s), 1.37 (s), 1.46 (s), 1.51 (s), 1.53 (s), 1.78 (brt, *J* = 15 Hz), 1.96 (s), 1.98 (s), 2.01 (s), 2.04 (s), 2.88 (brdt, *J* = 4.2,14.1 Hz), 3.11 (dd, *J* = 8.7,13.2 Hz), 3.40 (dd, *J* = 3.9,15.3 Hz), 3.83 (m), 4.08−4.18 (m), 4.30 (t, *J* = 5.7 Hz), 4.71 (d, *J* = 3.0 Hz), 4.76 (d, *J* = 3.6 Hz), 4.80 (brs), 5.05 (brs), 5.77 (d, *J* = 3.3 Hz), 5.83 (m), 6.06 (s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.1 (CH_3), 21.3 (CH_3), 23.6 (CH_3), 26.5 (CH_3), 28.2 (CH_3), 28.3 (CH_3), 32.1 (CH_2), 35.8 (CH_2), 47.8 (CH_2), 49.2 (CH_2), 51.7 (CH_2), 53.2 (CH_2), 62.5 (C), 64.2 (C), 68.5 (CH), 70.6 (CH), 79.6 (CH), 80.2 (C), 80.4 (C), 82.7 (CH), 84.3 (CH), 103.7 (CH), 111.9 (C), 155.6 (C), 155.8 (C), 170.0 (C); HRMS (EI, magnetic sector, positive ion) calcd for $C_{20}H_{32}N_2O_8$, *m*/*z* 428.2159, found 428.2151.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of all the new compounds; ORTEP diagrams; and CIFs of **6**, **23**, **27**, **30**, **35**, **43**, and **46**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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