Synthesis and Biological Activity of a Novel Pentacyclic Heterocycle [1]

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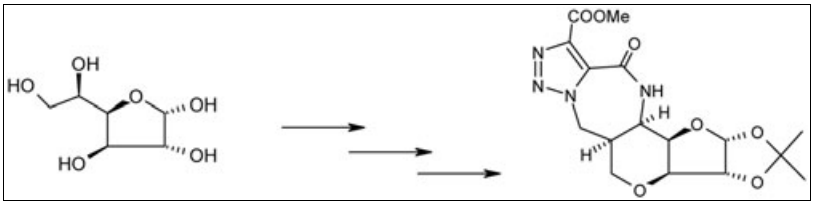

A novel pentacyclic heterocycle has been synthesized starting from D-glucose involving two crucial conversions: the intramolecular cycloaddition of *O*-allyloxy furanaldoxime derived from D-glucose to furanopyran-2-isoxazoline and its diastereoselective reductive cleavage to the corresponding *cis*-1,3-amino alcohol. The antibacterial and antifungal activities of the synthesized heterocycle have been examined.

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INTRODUCTION

Polycyclic heterocycles have gained much importance in recent years as potentially bioactive molecules [2]. Several fused tricyclic and pentacyclic heterocycles are known to exhibit various pharmacological properties including anxiolytic, antigastric, and antiallergic activities [3–6]. In continuation of our work [7,8] on the development and applications of useful synthetic methodologies, we envisioned on the basis of earlier reports [2–6] the construction of a pentacyclic heterocycle **1** to explore its biological properties. Herein we report the synthesis and antibacterial and antifungal activities of this compound.

RESULTS AND DISCUSSION

The retrosynthetic analysis (Scheme 1) reveals that **1** can be synthesized from D-glucose involving two important conversions: (1) the intramolecular cycloaddition of *O*-allyloxy furanaldoxime **5** prepared from D-glucose (**6**) to furanopyran-2-isoxazoline **4** and (2) the diastereoselective reductive cleavage of **4** to *cis*-1,3-amino alcohol **3**.

We initiated the synthesis of **1** starting from D-glucose (**6**) (Scheme 2) by converting it into diacetone-D-glucose (**7**) by reacting with acetone in the presence of anhydrous $CuSO_4$ using a catalytic amount of conc. H_2SO_4 at room temperature for 18 h. *O*-Allylation of **7** was achieved by treatment with allyl bromide utilizing K_2CO_3 in acetone under reflux for 4 h to obtain *O*-allyl diacetone-D-glucose (**8**). The regioselective deprotection of the C-5, C-6 acetonide of this compound was carried out with 0.8% aqueous H_2SO_4 in MeOH for 2 h at room temperature to furnish a diol **9**. The cleavage of the diol with $NaIO_4$ in the presence of saturated aqueous $NaHCO_3$ at room temperature for 4 h yielded the aldehyde **10**, which was readily condensed with $NH_2OH{\cdot}HCl$ in aqueous NaOH at 0°C to room temperature for 1 h to form the corresponding oxime **5**. Compound **5** was treated with diacetoxy iodobenzene at 0°C to room temperature for 1 h to form furanpyranoisoxazoline **4**. The hypervalent iodine generated nitrile oxide from oxime **5** [7,9], and then cycloaddition took place involving the nitrile oxide and the double bond of the allyl group [7,10]. In the next step, isoxazoline **4** was reductively cleaved to form the corresponding 1,3-amino alcohol and the amine group was *in situ* Boc protected in one-pot. To achieve this coversion, **4** was first treated with $NiCl_2{\cdot}6H_2O$ at 0°C followed by addition of $NaBH_4$ in portions to the reaction mixture [8,11]. After 2 h $(Boc)_2O$ was added along with catalytic amount of Et_3N in the same pot to obtain 1,3-amino alcohol **3** exclusively. The stereochemistry of **3** was settled from NOESY experiment which clearly showed that H-5 (δ 4.01, 1H, td, J = 9.5, 4.0 Hz) was related to H-6 (δ 1.74, 1H, m) and H-6 with H-4 (δ 4.30, 1H, m) indicating that H-5 and H-6 are in *cis*-configuration and all the H-4, H-5 and H-6 are α-oriented.

N-Boc protected 1,3-amino alcohol **3** was subsequently reacted with TsCl in the presence of Et_3N at −5°C to room temperature for 2 h to form the *O*-tosyl derivative **11**,

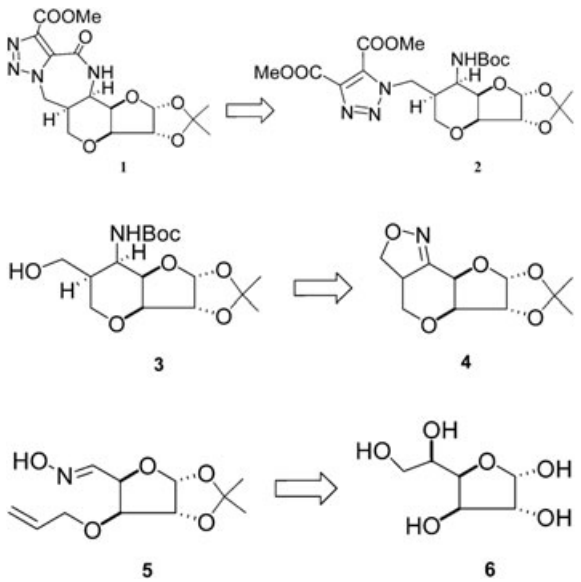
which on treatment with NaN_3 at 70°C for 2 h afforded the *N*-Boc protected 1,3-amino azide **12**. This azide derivative underwent 1,3-dipolar cycloaddition with DMAD at room temperature producing the triazole compound **2**. Finally the treatment of **2** with TFA at 0°C for 0.5 h led to the removal of the protecting group (Boc), and subsequent addition of the excess amount of Et_3N afforded the target heterocycle **1** by intramolecular cycloaddition between free amine and an ester group to generate a new lactam ring.

Reagents and conditions. (i). Acetone, conc. H_2SO_4, anhydrous $CuSO_4$, rt, 18 h, 90%; (ii) allyl bromide, warm K_2CO_3, acetone, reflux, 4 h, 95%; (iii) 0.8% aq. H_2SO_4, MeOH, rt, 2 h, 94%; (iv) $NaIO_4$, DCM, sat. $NaHCO_3$, rt, 4 h, 79%; (v) $NH_2OH{\cdot}HCl$, NaOH in H_2O, 0°C, 1 h, 9%; (vi) $PhI(OAc)_2$, CH_2Cl_2, 0°C to rt, 1 h, 68%; (vii) $NaBH_4$ $NiCl_2{\cdot}6H_2O$ (4:1), MeOH, 0°C to rt, 2 h, $(Boc)_2O$, Et_3N, 0°C to rt, 4 h, 73%; (viii) TsCl, Et_3N, dry DCM, −5°C to rt, 2 h, 81%; (ix) NaN_3, DMF, 70°C, 2 h, 74%; (x) DMAD, $CHCl_2$, rt, 2 h, 89%; (xi) TFA, DCM, 0°C to rt, 0.5 h, excess of Et_3N up to pH = 9, 62%.

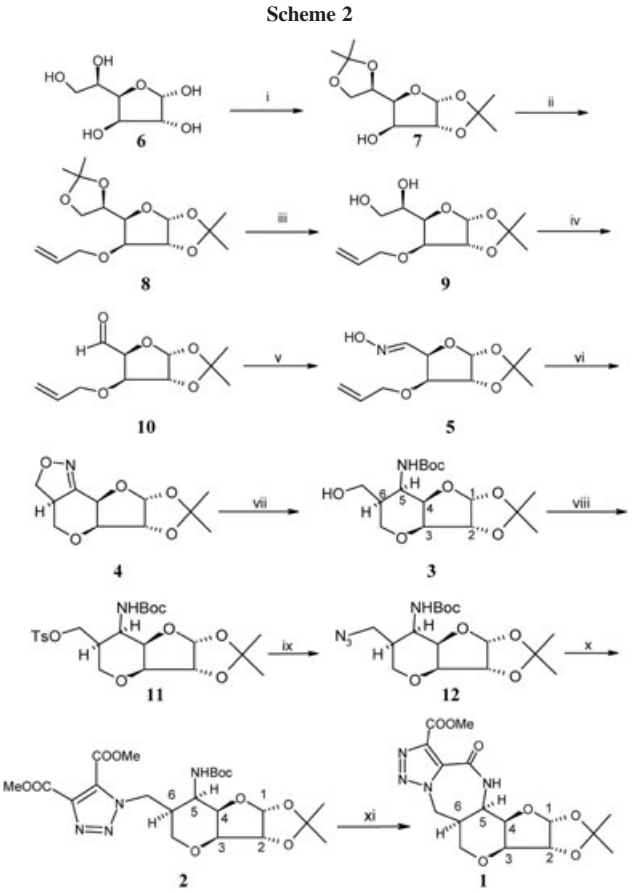
The structures of all the products were settled from their spectral (IR, ^1H and ^{13}C-NMR, and MS) and analytical data. The one- and two-dimensional NMR (^1H-^1H COSY, NOESY, HSQC, and HMBC) spectra of the final product **1** were thoroughly studied to assign correctly all the protons and carbons present in the molecule. The stereo configuration of **1** (H-1 and H-2: β and H-3, H-4, H-5, and H-6: α) was confirmed from NOESY experiment.

The antibacterial and antifungal activities of **1** were examined following the agar cup bioassay method [12] earlier adopted by us [13]. The compound showed moderate antibacterial activity against both Gram-positive and Gram-negative organisms (Table 1). Streptomycin was used as a positive control. However, the compound showed significant activity against some fungi using clotrimazole as a positive control (Table 2).

Scheme 1



Scheme 2



CONCLUSION

In conclusion, we have synthesized a novel pentacyclic heterocycle starting from D-glucose applying simple and convenient protocols. The antibacterial and antifungal activities of the compounds were also evaluated.

EXPERIMENTAL

General methods. IR spectra recorded on a Perkin Elmer RX 1 FT-IR spectrometer, NMR spectra on Gemini 200 MHz spectrometer, and mass spectra on LC-MSD-Trap-SL instrument. Optical rotations were measured with JASCO DIP 300 digital polarimeter. Column chromatography was carried out using silica gel 60–120 mesh (Quingdao Marine Chemicals, China) and thin layer chromatography (TLC) on merck silica gel 60 F_{254} plates.

Experimental procedure. ***Diacetone-D-glucose 7.*** D-Glucose (5.00 g, 27 mmol) and anhydrous copper sulfate (8.83 g, 54 mmol) was taken in a three neck round bottomed flask. Acetone (100 mL) was added to it. Conc. H_2SO_4 (catalytic amount) was added and stirred for 18 h at room temperature. After completion of the

Table 1

Antibacterial activity of compound **1** compared to that of streptomycin against various organisms.[a]

Organism	Compound **1**			Streptomycin		
	25 μg/μL	50 μg/μL	MIC[b]	25 μg/μL	50 μg/μL	MIC[b]
Staphylococcus aureus	14 mm	20 mm	100 μg/μL	8 mm	10 mm	18 μg/μL
Staphylococcus epidermidis	16 mm	22 mm	50 μg/μL	8 mm	10 mm	18 μg/μL
Pseudomonas aeruginosa	14 mm	20 mm	100 μg/μL	8 mm	10 mm	18 μg/μL
Escherichia coli	24 mm	28 mm	25 μg/μL	8 mm	10 mm	18 μg/μL

[a]Inhibitory zone diameters are in mm.
[b]Minimum inhibitory concentration.

reaction (monitored by TLC), reaction mixture was filtered and 2 g of $NaHCO_3$ was added to the filtrate and stirred for another 4 h. Then the compound was extracted with CH_2Cl_2 (3 × 100 mL) and subjected to column chromatography using hexane and ethyl acetate as eluent to obtain pure diacetone-D-glucose **7** as white crystalline solid (6.31 g, 90%, mp: 109–110°C). $[\alpha]_D^{25} = -11.0$ (c = 5.0, EtOH). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 5.87 (1H, d, J = 3.7 Hz), 4.48 (1H, d, J = 3.7 Hz), 4.32–4.10 (3H, m), 4.02–3.90 (2H, m), 2.39 (1H, brs), 1.50 (3H, s), 1.42 (3H, s), 1.34 (3H, s), 1.31 (3H, s). ESIMS: m/z 261 $[M+H]^+$

O-Allyl diacetone-D-glucose 8. A stirred solution of diacetone-D-glucose **7** (6.00 g, 23 mmol), allyl bromide (3.10 mL, 40 mmol), and potassium carbonate (9.10 g, 66 mmol) in distilled acetone (100 mL) was refluxed for 4 h. After the reaction was completed (monitored by TLC), solvent was evaporated under reduced pressure. The reaction mixture was then extracted with ethyl acetate (3 × 30 mL) and water. The organic layer was separated, and the aqueous layer was further washed with EtOAc (2 × 20 mL). The combined organic portion was washed with $NaHCO_3$ solution (30 mL) and dried over Na_2SO_4 and concentrated under reduced pressure. The residue was subjected to column chromatography over silica gel using hexane, EtOAc as eluent to afford *O*-allyl diacetone-D-glucose **8** as a viscous mass (6.57 g, 95%). $[\alpha]_D^{25} = -41.0$ (c = 0.2, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 5.87 (1H, m), 5.82 (1H, d, J = 3.7 Hz), 5.30 (1H, dd, J = 1.5, 15.8 Hz), 5.18 (1H, dd, J = 1.5, 15.8 Hz), 4.49 (1H, d, J = 3.7 Hz), 4.25 (1H, dd, J = 6.0, 7.5 Hz), 4.12–3.86 (6H, m), 1.49 (3H, s), 1.42 (3H, s), 1.32 (3H, s), 1.28 (3H, s). ^{13}C-NMR (50 MHz, $CHCl_3$): δ 133.9, 116.9, 111.4, 108.7, 105.0, 82.6, 81.2, 80.1, 72.2, 71.0, 67.0, 26.6, 26.6, 26.0, 25.1. ESIMS: m/z 323 $[M+Na]^+$.

Table 2

Antifungal activity of compound **1** compared to that of clotrimazole against various fungi.[a]

Fungi	Compound **1**		Clotrimazole	
	25 μg/μL	50 μg/μL	25 μg/μL	50 μg/μL
Candida albicans	12 mm	18 mm	8 mm	10 mm
Saccharomyces cerevisiae	10 mm	18 mm	8 mm	10 mm
Aspergillus niger	14 mm	16 mm	8 mm	10 mm

[a]Inhibitory zone diameters are in mm.

Diol 9. A solution of *O*-allyl diacetone-D-glucose **8** (6.00 g, 20 mmol) in methanol (50 mL) and 0.8% aq. H_2SO_4 (15 mL) was stirred for 3 h. After completion of reaction, solid Ba_2CO_3 was added to the reaction mass to adjust the pH to neutral. It was filtered and filtrate concentrated to a syrupy residue and chromatographed over silica gel using hexane, EtOAc as eluent to obtain diol **9** as a yellowish viscous mass (4.88 g, 94%). $[\alpha]_D^{25} = -21.9$ (c = 0.8, $CHCl_3$). IR (neat): 3435, 2933, 1531 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 5.90 (1H, m), 5.85 (1H, d, J = 3.7 Hz), 5.32 (1H, dd, J = 1.5, 15.8 Hz), 5.21 (1H, dd, J = 1.5, 15.8 Hz), 4.51 (1H, dd, J = 3.7 Hz), 4.19 (1H, dd, J = 5.5, 7.4 Hz), 4.12–3.87 (4H, m), 3.80 (1H, dd, J = 2.9, 8.5 Hz), 3.71 (1H, dd, J = 2.9, 8.5 Hz), 2.83 (1H, brs), 2.52 (1H, brs), 1.48 (3H, s), 1.31 (3H, s). ^{13}C-NMR (50 MHz, $CHCl_3$): δ 113.8, 117.4, 111.4, 104.8, 81.9, 81.3, 79.5, 70.9, 68.6, 64.0, 26.4, 25.9. ESIMS: m/z 543 $[2M+Na]^+$, 261 $[M+H]^+$.

Aldehyde 10. To diol **9** (4.50 g, 17 mmol) in CH_2Cl_2, $NaIO_4$ (7.40 g, 34 mmol) and saturated $NaHCO_3$ (10 mL) were added. The reaction mixture was stirred for 4 h at room temperature. After completion of the reaction indicated by TLC, reaction mixture was further diluted with water (50 mL), and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The organic layer was dried on anhydrous Na_2SO_4 and concentrated at low temperature (below 35°C), and the thick syrupy material aldehyde **10** (3.11 g, 79%) was subjected to perform the next reaction immediately.

Oxime 5. A solution of sodium hydroxide (1.56 g, 39 mmol) in water (20 mL) was cooled to 0°C, and aldehyde **10** (3.00 g, 13 mmol) was slowly added under stirring. Hydroxylamine hydrochloride (1.80 g, 26 mmol) was slowly added to the stirred mixture. After the addition, the mixture was allowed to warm to room temperature. After standing for 1 h, it was cooled on ice bath. Then the reaction mixture was extracted with EtOAc (3 × 100 mL), and the organic layer was subjected to column chromatography over silica gel using hexane and EtOAc as eluent to yield oxime **5** as an yellowish viscous mass (2.90 g, 91%). $[\alpha]_D^{25} = -211.0$ (c = 2.0, $CHCl_3$). IR (neat): 3435, 2933, 1531 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 8.70 (1H, brd, J = 12.5 Hz), 6.89 (1H, d, J = 4.2 Hz), 5.91 (1H, d, J = 3.5 Hz), 5.78 (1H, m), 5.18 (1H, dd, J = 4.9 Hz), 5.14 (1H, dd, J = 3.5 Hz), 4.52 (1H, dd, J = 3.5 Hz), 4.23 (1H, dd, J = 2.8 Hz), 4.05–3.98 (2H, dd, J = 1.4, 4.2 Hz), 1.49 (3H, s), 1.30 (3H, s). ^{13}C-NMR (50 MHz, $CHCl_3$): δ 149.2, 133.7, 117.6, 111.9, 104.7, 82.9, 82.1, 75.5, 71.3, 26.7, 26.1. ESIMS: m/z 266 $[M+Na]^+$, 244 $[M+H]^+$.

Isoxazoline 4. Oxime **5** (2.50 g, 10.2 mmol) dissolved in CH_2Cl_2 (50 mL) was kept on ice bath and stirred, while

diacetoxy iodobenzene (3.96 g, 12.2 mol) was added in three portions. The mixture was stirred for 1 h. Completion of the reaction was indicated by TLC. Water (20 mL) was added to the reaction mixture, and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The organic layer was separated and further washed with saturated solution of $NaHCO_3$ (2 × 20 mL) and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure, and the residue was subjected to column chromatography over silica gel using hexane–EtOAc as eluent to yield the product isoxazoline **4** as white crystals in 68% yield (1.68 g, mp: 124–125°C). $[\alpha]_D^{25}$ = +398.0 (*c* = 0.1, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 5.97 (1H, d, *J* = 3.0 Hz), 4.96 (1H, d, *J* = 2.3 Hz), 4.55 (1H, d, *J* = 3.0 Hz), 4.52 (1H, d, *J* = 2.3 Hz), 4.20 (1H, dd, *J* = 4.5, 6.0 Hz), 3.98 (1H, d, *J* = 2.3 Hz), 3.87 (1H, t, *J* = 9.1 Hz), 3.64 (1H, m), 3.31 (1H, t, *J* = 10.6 Hz), 1.56 (3H, s), 1.34 (3H, s). ^{13}C-NMR (50 MHz, $CHCl_3$): δ 154.1, 112.4, 106.1, 83.2, 82.4, 71.2, 70.6, 69.9, 43.9, 26.7, 26.2. ESIMS: *m/z* 264 $[M+Na]^+$, 242 $[M+H]^+$.

***N*-Boc protected 1,3-amino alcohol 3.** Isoxazoline **4** (1.50 g, 6.2 mmol) was dissolved in 25 mL of distilled MeOH at 0°C on an ice bath. $NiCl_2{\cdot}6H_2O$ (2.90 g, 12.4 mmol) was added, and the mixture was allowed to stir for 5 min. $NaBH_4$ (1.83 g, 49.6 mmol) was added in four to five portions during 15 min. The greenish color of the solution turned to bluish black. The reaction mixture was allowed to stir at room temperature for 2 h. The completion of the reaction was confirmed by TLC. Then, again the reaction mixture was kept on an ice bath. Catalytic amount of triethylamine was added to it along with $(Boc)_2O$, and the reaction mixture was stirred at room temperature for 4 h. The completion of the reaction was indicated by TLC, which turned pinkish after charring with ninhydrin solution. Solvent was evaporated from the reaction mixture and 1*N* HCl solution (5 mL) was added in it. The mixture was extracted with EtOAc (4 × 30 mL). The organic layer was separated, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to column chromatography using hexane and EtOAc as eluent to obtain pure *N*-Boc protected amino alcohol **3** as white solid in yield of 1.56 g (73%, mp: 158–159°C). $[\alpha]_D^{25}$ = +19.4 (*c* = 0.1, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 5.87 (1H, d, *J* = 3.8 Hz), 5.21 (1H, d, *J* = 9.0 Hz), 4.46 (1H, d, *J* = 3.8 Hz), 4.29 (1H, brs), 4.02–3.93 (2H, m), 3.80 (1H, dd, *J* = 3.7, 8.3 Hz), 3.71–3.36 (4H, m), 1.73 (1H, m), 1.54 (3H, s), 1.50 (9H, s), 1.33 (3H, s). ^{13}C-NMR (50 MHz, $CHCl_3$): δ 157.2, 111.9, 105.4, 83.9, 80.4, 79.6, 76.2, 68.5, 59.5, 47.1, 40.0, 28.2, 26.6, 26.0. ESIMS: *m/z* 368 $[M+Na]^+$.

***O*-Tosyl N-*Boc* protected 1,3-amino alcohol 11.** A mixture of *N*-Boc protected 1,3-amino alcohol **3** (1.00 g, 2.8 mmol) and dry CH_2Cl_2 (25 mL) was stirred until complete dilution. The mixture was cooled to −5°C, and catalytic amount of Et_3N was added. Tosyl chloride was slowly added to the mixture and stirred for 2 h at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with saturated NH_4Cl and extracted with CH_2Cl_2 (3 × 20 mL). The organic layer was dried on $NaSO_4$, concentrated under reduced pressure, and subjected to column chromatography using hexane and EtOAc as eluent to obtain pure *O*-tosyl *N*-Boc protected 1,3-amino alcohol **11** as a colorless viscous mass in yield of 1.17 g, 81%. $[\alpha]_D^{25}$ = +61.0 (*c* = 0.7, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 7.78 (2H, d, *J* = 8.0 Hz), 7.32 (2H, d, *J* = 8.0 Hz), 5.82 (1H, d, *J* = 3.0 Hz), 5.01 (1H, d, *J* = 9.8 Hz), 4.43 (1H, d, *J* = 3.0 Hz), 4.17 (1H, m), 4.10–3.61 (6H, m), 3.13 (1H, t, *J* = 11.3 Hz), 2.48 (3H, s), 1.48 (3H, s), 1.42 (9H, s), 1.29 (3H, s). ^{13}C-NMR (50 MHz, $CHCl_3$): δ 155.4, 144.8, 132.5, 129.8, 127.9, 112.0, 104.8, 83.7, 79.8 79.5, 75.7, 68.3, 67.6, 47.7, 37.8, 28.2, 26.6, 26.0, 21.6. ESIMS: *m/z* 500 $[M+H]^+$.

***N*-Boc azido chromane 12.** Sodium azide (0.30 g, 5 mmol) was added under magnetic stirring to a solution of *O*-tosyl *N*-Boc protected 1,3-amino alcohol **11** (1.00 g, 2.0 mmol) in dimethylformamide (15 mL). The mixture was heated to 70°C on a water bath for 2 h. Completion of the reaction was indicated by TLC. The mixture was filtered, and water (5 mL) was added to the filtrate. A white precipitate appeared. It was recovered by filtration and recrystallized from ethanol to yield 0.54 g, 74% of *N*-Boc azido chromane **12** as a viscous mass. $[\alpha]_D^{25}$ = +22.3 (*c* = 0.3, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 5.89 (1H, d, *J* = 3.0 Hz), 5.06 (1H, d, *J* = 9.0 Hz), 4.50 (1H, d, *J* = 3.7 Hz), 4.22 (1H, m), 3.99–3.90 (2H, m), 3.80 (1H, td, *J* = 3.0, 10.0 Hz), 3.53 (1H, dd, *J* = 3.7, 9.0 Hz), 3.23–3.12 (2H, m), 2.01 (1H, m), 1.52 (3H, s), 1.49 (9H, s), 1.32 (3H, s). ESIMS: *m/z* 393 $[M+Na]^+$, 371 $[M+H]^+$.

Triazole 2. A mixture of 0.50 g (1.35 mmol) of *N*-Boc azido chromane **12** and 0.24 mL of DMAD (2.02 mmol) in 10 mL dry CH_2Cl_2 was stirred at room temperature for 2 h. Reaction was monitored by TLC. After completion of the reaction, CH_2Cl_2 was evaporated under reduced pressure. The crude product was subjected to column chromatography to obtain pure triazole compound **2** as colorless viscous mass (0.61 g, 89%). $[\alpha]_D^{25}$ = +11.8 (*c* = 0.8, $CHCl_3$). ^{1}H-NMR (200 MHz, $CDCl_3$): δ 5.86 (1H, d, *J* = 3.7 Hz), 5.25 (1H, d, *J* = 9.5 Hz), 4.78 (1H, dd, *J* = 3.0, 11.0 Hz), 4.48 (1H, d, *J* = 3.7 Hz), 4.42–4.25 (2H, m), 4.01 (3H, s), 3.96 (3H, s), 3.94–3.79 (2H, m), 3.68 (1H, dd, *J* = 3.7, 8.0 Hz), 3.30 (1H, t, *J* = 11.7 Hz), 2.41 (1H, m), 1.52 (3H, s), 1.48 (9H, s), 1.30 (3H, s). ^{13}C-NMR (50 MHz, $CHCl_3$): δ 160.5, 158.6, 155.8, 139.9, 130.0, 112.0, 104.7, 83.6, 80.1, 79.2, 75.5, 67.7, 53.6, 52.2, 49.1, 48.9, 39.0, 28.3, 26.5, 25.8. ESIMS: *m/z* 535 $[M+Na]^+$.

Compound 1. To the compound **2** (0.50 g, 0.97 mmol) in CH_2Cl_2 (50 mL) trifluoro acetic acid (0.096 g, 0.97 mmol) was added and stirred for 0.5 h at 0°C to room temperature. Removal of *N*-Boc protected group was indicated by TLC. Then the reaction mixture was basified with excess of triethyl amine. After completion of the reaction dichloromethane was evaporated under reduced pressure. The crude product was subjected to column chromatography to obtain pure product **1** as a white solid (0.23 g, 62%, mp: 269–270°C). $[\alpha]_D^{25}$ = 0.1, $CHCl_3$). IR (neat): 3421, 1730, 1689 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 6.71 (1H, d, *J* = 6.6 Hz), 5.98 (1H, d, *J* = 3.7 Hz), 4.70–4.39 (4H, m), 3.98 (3H, s), 3.96–3.82 (2H, m), 2.89 (1H, m), 1.50 (3H, s), 1.31 (3H, s). ^{13}C-NMR (50 MHz, $CHCl_3$): δ 159.8, 158.1, 140.0, 133.7, 112.6, 105.8, 83.4, 79.5, 74.2, 67.8, 52.7, 52.5, 49.7, 37.8, 26.7, 26.1. ESIMS: *m/z* 381 $[M+H]^+$. Anal. calcd. For $C_{16}H_{20}N_4O_7$: C, 50.53; H, 5.26; N, 14.74%, Found: C, 50.41; H, 5.32; N, 14.68%.

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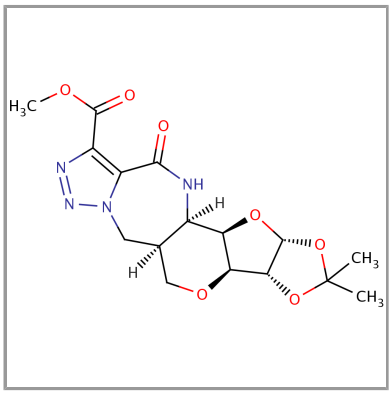

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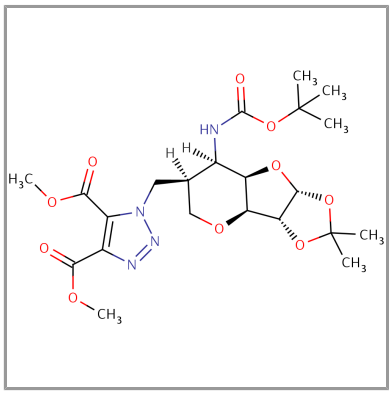

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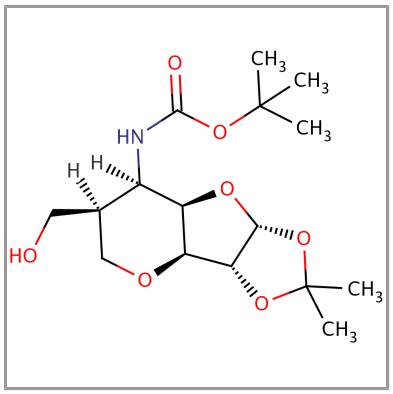

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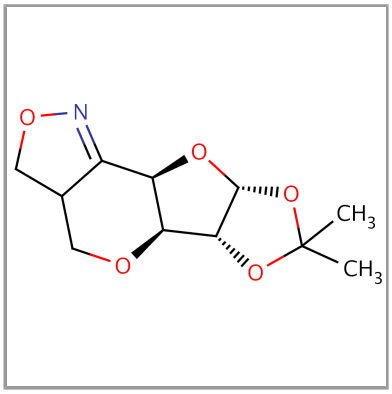

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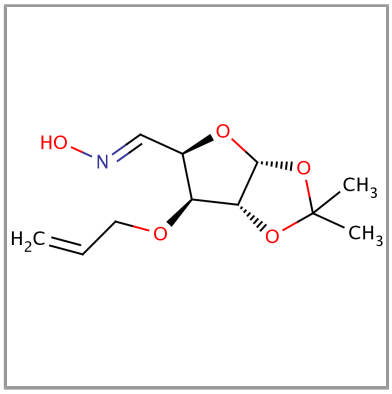

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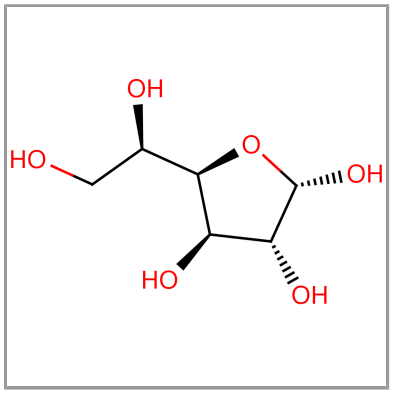

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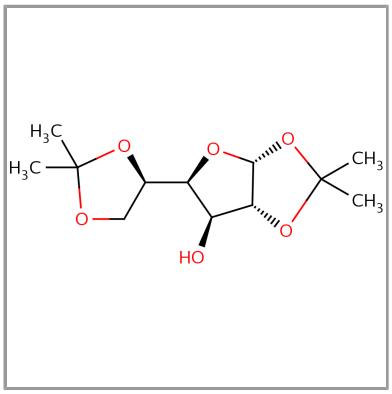

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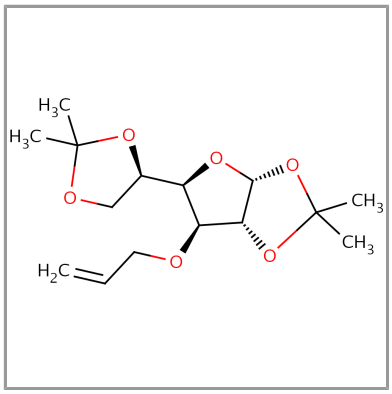

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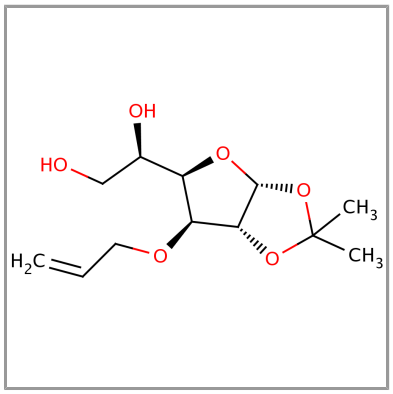

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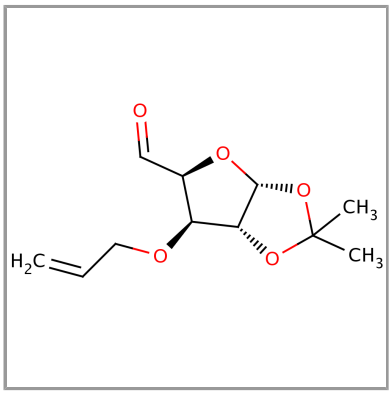

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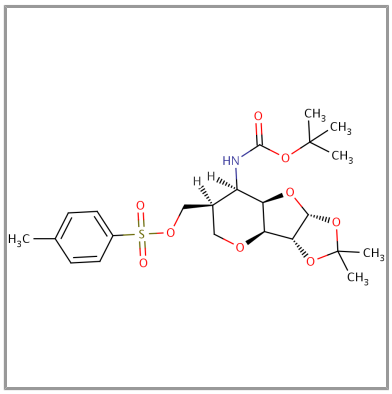

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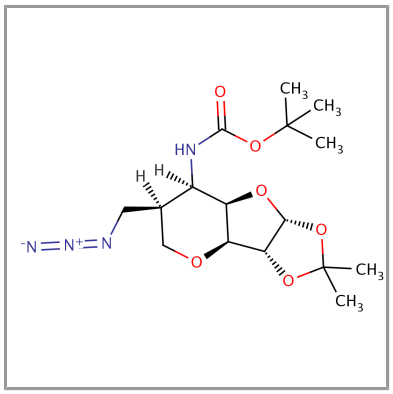

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