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Synthesis of bicyclonucleosides by application of Pd(II)Cl-mediated oxidative cyclization protocol of vinylglucofuranosides†

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Abstract

Synthesis of tetrahydrofurofuran nucleoside (**9**) and tetrahydrofurofuranolactone nucleoside (**10**) from D-glucose is described. Key steps involved oxidative cyclization of vinylglucofuranoside (**11**) and thymidine derivative (**14**) to derive the corresponding advanced intermediates **15** and **17**, respectively.

Keywords : Bicyclic nucleosides, oxidative cyclization, vinylglucofuranoside, antiviral, palladium (II) chloride.

1. Introduction

Current interest in the synthesis of bicyclic nucleoside analogues stems from the discovery of antiviral drug 3′-azido-3′-deoxythymidine (AZT) potent against human immunodeficiency virus (HIV).[1] Oligonucleosides containing bicyclic nucleosides have great affinity for complementary RNA/DNA, since they stabilize duplex formation due to their restricted conformation.[2] It has also been suggested that a C-3′ *exo*-conformation of the bicyclic nucleosides is predictive of antiHIV activity.[2] A series of efforts directed in this direction has earlier resulted in the preparation and bioevaluation of bicyclic nucleoside analogues containing a fused methylene group **1**,[3] oxirane **2**[4] or oxetane **3**[5] and tetrahydrofurofuran templates such as in **4**–**7**.[6–11]

The bicyclic framework in compounds **4** and **5** has been derived from isosorbide,[12] **6** from 3-*O*-mesyl glucofuranosyl derivative, **7** from the internal rearrangement of 3,5,6-*O*-orthoester glucose derivative and **8** from 5,6-*O*-cyclic sulphate sugar derivative.[13]

Due to our interest in the synthesis of nucleoside analogues with potent antiviral activity we wish to describe the synthesis of novel bicyclic tetrahydrofurofuran nucleosides by application of palladium(II) chloride-mediated oxidative cyclization of vinylglucofuranosides.[14] We report now the application of this methodology for the preparation of novel tetrahydrofurofuran nucleoside (**9**) and tetrahydrofuranolactone nucleoside (**10**) starting from D-glucose that can be considered analogous of compounds **4**–**8** (Fig.1).

D-Glucose was transformed to the vinylglucofuranoside derivative **11** by the procedure earlier reported by us.[15] Acid-catalysed hydrolysis of **11** with IR-120 H^+ resin in water at 80°C gave triol, that was converted to a diastereomeric mixture of triacetyl derivative **12** on reaction with Ac_2O/py

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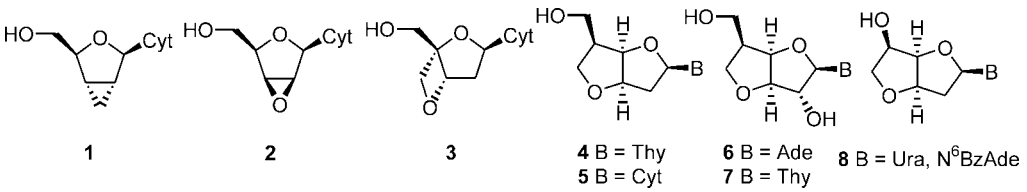
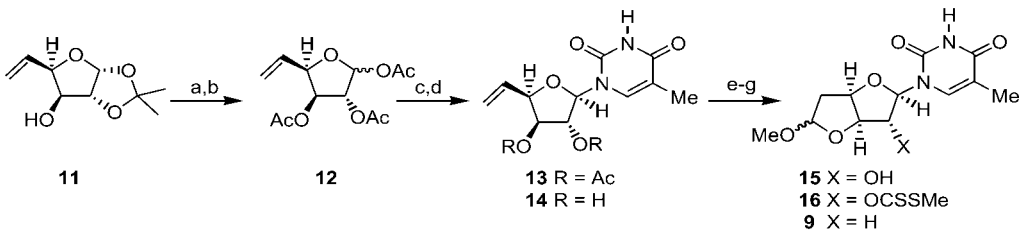


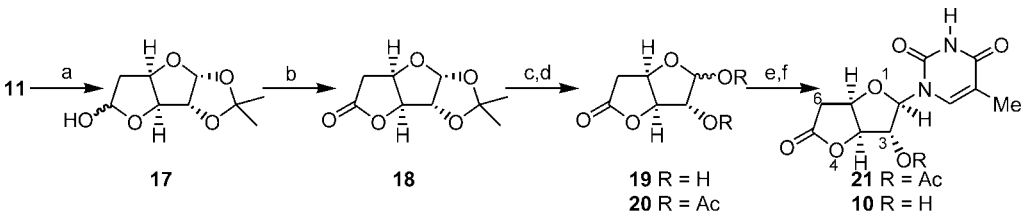
FIG. 1.

(Scheme 1). Compound **12** was characterized from ^{1}H NMR spectrum by the appearance of vinylic protons between δ 5.12 and 5.90 (3H), anomeric proton H-2 (α/β) at δ 6.06 (0.45H, s), δ 6.39 (0.55H, d, J = 3 Hz) and acetyl protons appeared between δ 2.04 and 2.18 integrating for nine protons. Reaction of **12** with *bis*-trimethylsilylthymine and Sn(IV)Cl at room temperature gave the vinylic nucleoside **13**, m.p. 135° C, in 78% yield, which was characterized by ^{1}H NMR spectrum from the appearance of H-1 at δ 6.02 (1H, d, J = 2.5 Hz), H-6 at δ 7.28 (1H, s) and methyl group protons at δ 1.96 (3H, s). Compound **13** on reaction with a catalytic amount of sodium methoxide in methanol at room temperature gave the hydroxy derivative **14** that was characterized from ^{1}H NMR spectrum by the absence of acetyl protons and appearance of H-1 at δ 5.98 (1H, s). Oxidative cyclization of **14** with a catalytic amount of Pd(II)Cl/CuCl/RT in CH_3OH while bubbling oxygen gave a diastereomeric mixture of bicyclic nucleoside **15** as a crystalline solid, m. p. 120° C, which was characterized by ^{1}H NMR spectrum from the appearance of H-5′, 5″ protons between δ 1.64 and 2.14 (2H, m), methoxy protons at δ 2.98, 3.06 (3H, 2s), H-6 at δ 5.24 (0.7H, d, J = 6.2 Hz) and 5.38 (0.3 H, d, J = 5.5 Hz) and H-1 at δ 5.56 (0.3H, s) and δ 5.60 (0.7 H, s). Compound **15** on reaction with CS_2/NaH/MeI in dry THF at 0° C gave the methyl xanthate derivative **16** that on reduction with Bu_3SnH in toluene containing a catalytic amount of AIBN at reflux temperature gave the deoxy bicyclic nucleoside **9** in good yield, which was characterized by ^{1}H NMR spectrum from the appearance of H-2 protons between δ 2.06 and 2.84 (2H, m). After establishing a new route for the synthesis of bicyclic nucleoside **9**, we investigated on the preparation of tetrahydrofuranolactone nucleoside (**10**) by Pd(II)Cl-mediated oxidative cyclization methodology. Accordingly, Pd(II)Cl-mediated oxidative cyclization of **11** was carried out in *N*,*N*-dimethylformamide (DMF)/H_2O (4:1), while bubbling oxygen to obtain a diastereomeric mixture of tetrahydrofurofuran derivative (**17**) in 77% yield (Scheme 2), which was characterized from the appearance of lactal protons between δ 5.40 and 5.62 (1H), and H-5,5′ protons between δ 1.92 and 2.40 (m, 2H). Oxidation of lactol (**17**) with PDC in CH_2Cl_2 at reflux temperature for 2 h gave the lactone **18**, m.p. 73° C, in 85% yield, which was characterized by ^{1}H NMR from the appearance of H-5,5′ protons between δ 2.60 and 2.80 (AB type doublet, 2H) and by the IR spec-



(a) IR 120 H^+, H_2O, 80°C, 4 h; (b) Ac_2O, py; (c) $(TMS)_2$thymine, Sn(IV)Cl, rt, 16 h; (d) catalytic NaOH, MeOH; (e) Pd(II)Cl, CuCl, MeOH, O_2, rt, 10 h; (f) NaH, CS_2, MeI; (g) Bu_3SnH, AIBN, toluene, reflux, 4 h.

Scheme 1.



(a) Pd(II)Cl, CuCl, DMF, H_2O, O_2; (b) PDC, CH_2Cl_2, reflux, 2 h; (c) IR 120 H^+, AcOH, H_2O, 100°C, 4 h; (d) Ac_2O, py; (e) $(TMS)_2$thymine, Sn(IV)Cl, 0°C,12 h; (f) NaOMe (catalytic), MeOH, rt.

Scheme 2.

trum the lactone absorption at 1780 cm^{-1}. Acid-catalyzed hydrolysis of **18** with 50% aqueous acetic acid, IR-120 H^+ resin at 60° C for 4 h gave a diastereomeric mixture of diol **19**, that on reaction with Ac_2O/pyridine gave the diacetate **20** in 87% yield. Coupling of **19** with *bis*-trimethylsilylthymine in CH_2Cl_2 at rt by the use of Sn(IV)Cl as a catalyst gave the nucleoside **21** as a crystalline solid, m.p. 139° C in 60% yield, which was characterized by ^{1}H NMR spectrum from the appearance of methyl group of thymine at δ 1.92 (s, 3H), acetyl protons at δ2.19 (s, 3H), anomeric proton (H-1′,) at δ6.10 (d, J = 3.8 Hz) and H-5,5^{1} at δ2.84–3.15 (dd, 2H, J = 6.5 and 3.5Hz). Compound **21** on deacetylation with a catalytic amount of NaOMe in CH_3OH gave the tetrahydrofuranolactone nucleoside (**10**) as a crystalline solid, m. p. 162° C.

In conclusion, a new family of bicyclic nucleoside analogues of dde and ddA have been prepared from D-glucose using Pd(II)Cl-mediated oxidative cyclization of vinylhydroxy furanoglycosides as a key step.

2. Experimental

^{1}H NMR spectra were measured with a Varian Gemini 200 MHz spectrometer with tetramethylsilane as internal standard for solutions in deuteriochloroform. J values are given in hertz. Optical rotations were measured with a JASCO DIP-370 instrument and $[\alpha]_D^{25}$ values are in units of 10^{-1} deg cm^2 g^{-1}. All melting points are uncorrected. IR spectra were recorded on a Perkin–Elmer 1310 spectrometer. All organic solvents were freshly distilled prior to use. Air sensitive reactions were generally performed under a positive pressure of nitrogen with the glassware flame-dried under vacuum.

2.1. *Diastereomeric mixture of 5,6-dideoxy-5-eno-1,2,3-tri-O-acetyl-α and β -D-glucofuranosides* (**12**)

To a heterogenous solution of **11** (2.95 g, 15.05 mmol) in HOAc-H_2O [(1:1), 7 ml] was added IR-120 H^+ resin (1 ml) and heated to 100° C for 4 h. After completion of the reaction, the reaction mixture was concentrated to a residue and treated with pyridine (6 ml) and Ac_2O (3 ml) to obtain, after work up, the title compound **12** (1.85 g) in 90% yield as a syrup. $[\alpha]_D$ 56.8° (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.04, 2.08, 2.11, 2.14, 2.18 (9H, 5s, 3 x OAc), 4.84 (1H, dd, J=6.0 Hz, and 4.0 Hz, H-4), 5.12–5.45 (4H, m, H-2, 3, 6, 6′), 5.55–5.90 (1H, m, H-5), 6.06 (0.45H, s, H-1β), 6.39 (0.55H, d, J = 4.0 Hz, H-1α). Anal. Calc. for $C_{12}H_{16}O_7$: C, 52.94; H, 5.92. Found: C, 52.78; H, 5.79%.

2.2. *1-(5,6-Dideoxy-5-eno-2,3-di-O-acetyl-β-D-glucofuranosyl)thymine (**13**)*

To a solution of compound **12** (1 g, 3.6 mmol) and silylated thymine (1.19 g, 4.40 mmol) in dry CH_2Cl_2 (30 ml) under N_2 atmosphere at 0° C was added Sn(IV)Cl (1.14 g, 0.51 ml) in dry CH_2Cl_2 (10 ml). The reaction mixture was stirred at rt for 16 h. When TLC showed the formation of a slower moving spot (hexane/MeOH, 1:1), the reaction mixture was diluted with CH_2Cl_2 (20 ml), neutralized with sat. aq. $NaHCO_3$ solution (5 ml) and filtered on a bed of celite. The filtrate was concentrated to obtain the title compound **13** (0.96 g) as a white crystalline solid in 80% yield. m.p. 135° C; $[\alpha]_D$ 38.4° (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.95 (3H, s, C*H*$_3$), 2.52–2.21 (6H, 2s, 2 x OAc), 4.72 (1H, dd, *J*=2.5 Hz, *J*=1.5 Hz, H-4), 5.14 (1H, s, H-2), 5.30 (1H, d, *J*= 5 Hz, H-3), 5.34–5.58 (2H, m, H-6,6), 5.70–5.98 (1H, m, H-5′), 6.02 (1H, d, *J* = 2.5Hz, H-1), 7.31 (1H, s, H-6), 8.95 (1H, s, NH). Anal. Calc. for $C_{15}H_{18}N_2O_7$: C, 52.12; H, 8.28; N, 5.28. Found: C, 52.01; H, 8.29; N, 5.22%.

2.3. *1-(5,6-Dideoxy-5-eno-β-D-glucofuranosyl)thymine (**14**)*

To a solution of **13** (2.0 g, 5.90 mmol) in CH_3OH (10 ml) was added NaOMe (1 ml, 0.1M) and left at rt for 10 h. After completion of the reaction, the reaction mixture was neutralized with IR-120 H^+ resin and filtered to remove the resin. Filtrate was separated and concentrated to obtain the title compound **14** (1.29 g) as a thick syrup in 86% yield. $[\alpha]_D$ 9.8° (c 1.0, CH_3OH); ^{1}H NMR ($CDCl_3$): δ 2.02 (3H, s, CH_3), 4.34 (1H, d, *J* = 4.4Hz, H-3′), 4.45 (1H, s, H-2′), 5.50–5.80 (3H, m, H-6′, H-4′), 5.98 (1H, s, H-1′), 6.10–6.32 (1H, m, H-5′), 7.80 (1H, s, H-6); Anal. Calc. for $C_{11}H_{12}N_2O_5$: C, 52.24; H, 11.14; N, 4.72. Found: C, 51.99; H, 11.07; N, 4.69%.

2.4. *Diastereomeric mixture of 1-(3,6-anhydro-5-deoxy-6R/S-methoxy-β-D-glucofuranosyl)thymine (**15**)*

To a solution of compound **14** (0.50 g, 1.96 mmol) in CH_3OH (7 ml) was added Pd(II)Cl (13 mg) and Cu(I)Cl (0.32 g, 2.3 mmol) and oxygen was bubbled for 10 h at rt. After completion of the reaction, the reaction mixture was concentrated to a residue which was dissolved in $CHCl_3$ (10 ml) and filtered through a bed of silica gel (SiO_2, 60–120 mesh) to obtain the title compound **15** (0.27 g) as an amorphous solid in 51% yield. m.p. 120° C; $[\alpha]_D$ 15.6° (c 1.0, CH_3OH); ^{1}H NMR ($CDCl_3$): δ 1.64–2.12 (2H, m, H-5′), 2.96–3.06 (3H, s, CH_3), 3.61–4.90 (3H, m, H-2′,3′,4′), 5.25 (0.7H, d, *J* = 6.2 Hz, H-6′), 5.35 (0.3H, d, *J* = 5.5 Hz, H-6′), 5.50, 5.60 (1H, 2s, H-1′), 7.2 (1H, s, H-6). Anal. Calc. for $C_{12}H_{16}N_2O_6$: C, 50.70; H, 5.67; N, 9.86. Found: C, 50.58; H, 5.69; N, 9.79%.

2.5. *Diastereomeric mixture of 1-[(3,6-anhydro-5-deoxy-2-O-methylthiocarbonyl)-6R/S-methoxy-β-D-glucofuranosyl]thymine (**16**)*

To a solution of compound **15** (0.40 g, 1.4 mmol) in THF (4 ml) at 0° C was added NaH (0.09 g, 3.60 mmol), followed by CS_2 (0.167 ml, 2.80 mmol) and iodomethane (0.4 g, 2.80 mmol). The reaction mixture was warmed to rt gradually and stirred for an additional 2 h. After completion of the reaction, it was diluted with chilled water (50 ml) and extracted into EtOAc (100 ml). The organic phase was separated, dried and concentrated to a syrupy residue that was filtered on silica gel [SiO_2 60–120 mesh, eluted with hexane:EtOAc (3:7)] to obtain the title compound **16** (440 mg) as syrup in 86.4% yield. $[\alpha]_D$ 15.8° (c 1.0, CH_3OH); ^{1}H NMR ($CDCl_3$): δ 1.98 (3H, s, CH_3), 2.06–2.50 (2H, H-5′), 2.60 (3H, s, SCH_3), 3.40, 3.52 (3H, 2s, OMe), 4.68

(1H, d, J = 2.5 Hz, H-4′), 4.88 (1H, d, J = 4.5 Hz, H-3′), 5.20, 5.28 (1H, 2 d, J = 7.5Hz, H-6′), 5.92, 5.96 (1H, 2 d, J = 2.5 Hz, H-2′), 6.24 and 6.28 (1H, 2s, H-1′), 7.24, 7.59 (1H, 2s, H-6), 8.76, 8.82 (1H, 2s, NH). Anal. Calc. for $C_{14}H_{18}N_2O_6S_2$: C, 44.79; H, 4.72; N, 7.41. Found: C, 44.67; H, 4.69; N, 7.39%.

2.6. *Diastereomeric mixture of 1-(3,6-anhydro-2,5-dideoxy-6R/S-methoxy-β-D-glucofuranosyl) thymine (**9**)*

To a solution of compound **16** (0.46 g, 1.66 mmol) in toluene (4 ml), Bu_3SnH (0.70 g, 2.44 mmol) and a catalytic amount of AIBN were added and refluxed under N_2 atm. for 4 h. The progress of the reaction was monitored by TLC from the appearance of a slower moving spot [hexane:ethyl acetate (7:1)] to obtain the title compound **9** (230 mg) in 65% yield as a syrup. $[\alpha]_D$ 6.2° (c 1.0, CH_3OH); ^{1}H NMR ($CDCl_3$): δ 1.92 (3H, s, CH_3), 2.06–2.84 (4H, m, H-5′, 2′), 3.36, 3.42 (3H, 2s, OCH_3), 4.64 (1H, d, J = 7.5 Hz, H-4′), 4.72–4.86 (1H, m, H-3′), 5.09, 5.19 (1H, d, J = 7.5 Hz, H-6′), 6.09–6.30 (1H, m, H-1′), 7.32 and 7.72 (1H, 2 s, H-6), 9.46 (1H, s, NH). Anal. Calc. for $C_{12}H_{16}N_2O_5$: C, 53.72; H, 6.01; N, 10.44. Found: C, 53.59; H, 6.22; N, 10.48%.

2.7. *Diastereomeric mixture of [3aR, 4aR, 7aS, 7bR]2,2-dimethyl perhydrofuro[2,3:4,5]furo[2,3-d][1,3]dioxol-6(R/S)-ol (**17**)*

To a solution of vinyl furanoside (**11**) (5.9 g, 31.6 mmol) in DMF-H_2O [30 ml, (4:1)] was added Pd(II)Cl (50 mg), Cu(I)Cl (3.8 g, 39.5 mmol) and oxygen was bubbled for 12 h at rt. After completion of the reaction, the reaction mixture was diluted with water and extracted into CH_2Cl_2 (50 ml x 2). The organic phase was separated, dried (Na_2SO_4) and concentrated to obtain the title compound **17** (4.90 g) in 76% yield as a syrup. $[\alpha]_D$ 25.93° (c 1.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.30 & 1.48 (6H, 2s, 2 x CH_3), 1.92–2.40 (2H, m, H-5), 4.72 (1H, d, J = 1.2 Hz, H-7b), 4.90 (1H, m, H-7a), 5.40 (0.6H, d, H-3a), 5.62 (0.4H, t, H-3a), 5.98 (1H, d, J = 2.5 Hz, H-6). Anal. Calc. for $C_9H_{14}O_5$: C, 53.32; H, 6.85. Found: C, 53.19; H, 6.77%.

2.8. *[3aR, 4aR, 7aS, 7bR]-2,2-Dimethyl perhydrofuro[2,3:4,5]furo[2,3-d][1,3]dioxol-6-one (**18**)*

A solution of lactol **17** (3.50 g, 17.0 mmol) in dry CH_2Cl_2 (20 ml) containing pyridinium dichromate (9.71 g, 25.8 mmol) was heated to reflux for 2 h under N_2 atmosphere. After the completion of the reaction, the reaction mixture was filtered, concentrated to a residue and chromatographed [SiO_2, 60–120 mesh, by eluting with hexane/ethyl acetate (1:1)] to obtain the title compound **18** (2.94 g) in 85% yield as a glassy solid. m. p. 72–73° C; $[\alpha]_D$ +36.7° C (c 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.32 and 1.50 (6H, 2 s, 2 x CH_3), 2.60–2.80 (2H, AB-type coupling, H-5,5), 4.80 (2H, m, H-4a,7b), 4.96 (1H, m, H-7a), 5.92 (1H, m, J = 3.40 Hz, H-3a). Anal. Calc. for $C_9H_{12}O_5$: C, 53.79; H, 5.82. Found: C, 53.68; H, 5.77%.

2.9. *Diastereomeric mixture of [3aR, 5R/S, 6R, 6aS]-5,6-dihydroxy perhydrofuro[3,2-b]furan-2-one (**19**)*

To a heterogenous solution of lactone **18** (0.68 g, 3.40 mmol) in HOAc-H_2O [(1:1), 7 ml] was added IR-120 H^+ resin (1 ml) and heated to 100° C for 4 h. After the completion of the reaction, the reaction mixture was filtered to remove the resin and the filtrate was neutralized with saturated aq. $NaHCO_3$ and extracted into ethyl acetate (50 ml x 2). The organic phase was separated, concentrated, dried (Na_2SO_4) and chromatographed [SiO_2, 60–120 mesh eluted with hexane–ethyl

acetate (1:1)] to obtain the title compound **19** (0.37 g) in 68% yield as a syrup. $[\alpha]_D$ –0.22° (c 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.40–2.88 (2H, m, H-3,3), 4.00–4.17 (1H, m, H-6), 4.74–5.00 (2H, m, H-3a, 6a), 5.20 (0.45H, s, H-5), 5.32 (0.55H, d, H-5, *J* = 3.3 Hz). Anal. Calc. for $C_6H_8O_5$: C, 44.70; H, 4.94. Found: C, 44.67; H, 4.88%.

2.10. *Diastereomeric mixture of [3R,3aS,6aR]3-methylcarbonyloxy-5-oxo-perhydrofuro[3,2-b]furan-2-yl acetate (***20***)*

To a solution of diol **19** (1.20 g, 7.70 mmol) in dry CH_2Cl_2 (10 ml) was added pyridine (0.93 ml, 11.50 mmol) and acetic anhydride (0.72 ml, 9.25 mmol) and stirred at rt for 4 h. After completion of the reaction, the reaction mixture was diluted with water (100 ml), washed and extracted into CH_2Cl_2 (50 ml). The organic phase was separated, concentrated to a residue and chromatographed [SiO_2, 60−120 mesh, hexane–ethyl acetate (1:1)] to obtain the title compound **20** (1.63 g) in 87% yield. m.p. 88−90° C; $[\alpha]_D$ +0.6° (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.10–2.20 (6H, 2s, 2 x OAc), 2.75–2.95 (2H, m, H-5,5), 4.95–5.30 (3H, m, H-2,3 and 4), 6.50 (2H, d, H-1, *J* = 3.6 Hz). Anal. Calc. for $C_{19}H_{12}O_7$: C, 49.18; H, 4.95. Found: C, 49.01; H, 4.82%.

2.11. *[2R,3R,3aS,6aR]-2-[5-Methyl-1H,3H-2,4-dioxo-1-pyrimidinyl]-5-oxo-perhydrofuro[3,2-b]furan-3-yl acetate (***21***)*

To a solution of compound **20** (1.28 g, 5.27 mmol) and *bis*-trimethylsilylthymine (1.56 g, 5.8 mmol) in dry CH_2Cl_2 (15 ml) under N_2 atmosphere at 0° C was added Sn(IV)Cl (0.74 ml, 6.30 mmol) in dry CH_2Cl_2 (10 ml) and stirred at rt for 12 h. After the completion of the reaction, the reaction mixture was neutralized with sat. aq. $NaHCO_3$ solution, and filtered on a bed of celite. The filtrate was concentrated to a residue and chromatographed [SiO_2, 60–120 mesh, hexane–ethyl acetate (1:1)] to obtain the title compound **21** (1.10 g) in 67% yield. m. p. 140° C; $[\alpha]_D$ 9.9° (c 0.52, CH_3OH); ^{1}H NMR ($CDCl_3$): δ 1.9 (3H, s, CH_3), 2.19 (s, 3H, OAc), 2.84–3.15 (2H, m, H-6,6), 4.90–5.14 (2H, m, H-3a, 6a), 5.35 (1H, dd, *J* = 3.75 Hz, *J* = 3.0 Hz, H-3), 6.10 (1H, d, H-2), 7.32 (1H, s, H-6′), 11.20 (s, NH). Anal. Calc. for $C_{13}H_{14}N_2O_7$: C, 50.32; H, 4.55; N, 9.03. Found: C, 50.17; H, 4.49; N, 9.07%.

2.12. *1-[2R,3R,3aS,6aR]-3-Hydroxy-5-oxo-perhydrofuro[3,2-b]furan-2-yl)-5-methyl-1H,3H-pyrimidine-2,4-dione (***10***)*

To a solution of **21** (0.11 g, 0.35 mmol) in CH_3OH (2 ml) was added two drops of NaOMe (1 M

solution) and stirred at rt for 4 h. After the completion of the reaction, the reaction mixture was neutralized with IR-120H$^+$ resin (20 mg) and filtered. The filtrate was concentrated to obtain the title compound **10** (59 mg) in 63% yield as a white solid. m. p. 162° C; $[\alpha]_D$ 5.5° (c 0.47, DMSO); ^{1}H NMR ($CDCl_3$): δ 1.90 (3H, s, CH_3), 2.60–2.90 (2H, m, H-6′), 4.55–4.61 (1H, dd, *J* = 2.5 and 1.5Hz, H-3a), 4.80–4.90 (1H, m, H-6a), 4.94 (1H, d, *J* = 5.2 Hz, H-3), 6.10 (1H, d, H-2′), 7.34 (1H, s, H-6), 9.24 (1H, s, NH). Anal. Calc. for $C_{11}H_{12}N_2O_6$: C, 49.25; H, 4.50; N, 10.45. Found: C, 49.12; H, 4.52; N, 10.47%.

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