Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
ELSEVIER
Tetrahedron 60 (2004) 10269–10275

Diastereoselective Reformatsky reaction of methyl 4-bromocrotonate with 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose: application to novel bicyclic nucleosides

Mukund K. Gurjar,* Dandepally Srinivasa Reddy, Mohan M. Bhadbhade and Rajesh G. Gonnade

National Chemical Laboratory, Pune 411 008, India

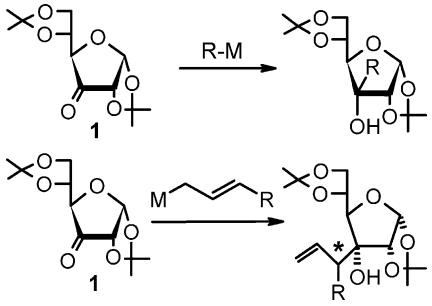
Received 27 May 2004; revised 30 July 2004; accepted 26 August 2004

Abstract—This paper describes an efficient synthetic route for novel bicyclic nucleosides. The stereochemistry of the targeted bicyclic nucleosides was successfully achieved by vinylogous Reformatsky reaction and ring closing metathesis reaction on a carbohydrate backbone.

1. Introduction

Due to the inherent structural complexity associated with carbohydrate precursors, many organometallic C–C bond forming reactions occur with impressive stereoselectivity.[1] For instance, the 3-ulose derivative of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**1**) has been particularly targeted with significant successes.[2] The conformationally rigid 1,2-*O*-isopropylidene functionality of **1** dictates[3] the approach of the nucleophile from the β-face giving rise to the 3-*C*-substituted-D-allose derivative. In most C–C bond forming reactions studied so far, only one new chiral center at C-3 has been created.[4] We were interested in exploring the organometallic reaction of **1** with a specific organometallic reagent which is tuned to produce two new chiral centers as shown in Scheme 1. We believe that this study would be of significant interest for synthesizing novel molecules including bicyclic derivatives.

The design of conformationally restricted nucleosides is a very important approach towards potential antiviral agents and monomers in conformationally restricted oligonucleotides, for potential antisense therapeutic and diagnostic purposes.[5] Anticipating better biological activity, many useful strategies for modification of naturally occurring



Scheme 1.

nucleosides have been developed in the recent past, and the quest for more analogues is still in progress. In particular, nucleoside analogues with bicyclic carbohydrate moieties have been designed as potential antiviral agents. Due to the decrease in conformational freedom introduced by the bicyclic nucleosides, these oligonucleotides have displayed very promising results as compounds with improved recognition of complementary RNA and DNA sequences.[6] Leumann and co-workers introduced the concept of bicyclic oligonucleotides by synthesizing the several bicyclic nucleosides (**2** and its analogues) and incorporating them into oligonucleotides.[7] Since then, numerous approaches for a variety of bicyclic sugar nucleosides have appeared in the literature.[8] Recently, Nielson and co-workers have synthesized various bicyclic nucleoside analogues (**3** and **4**) from diacetone-D-glucose and carried out extensive studies on their ability to incorporate into oligonucleotides.[8a,9] In

Keywords: Bicyclic nucleosides; Vinylogous Reformatsky reaction; Ring closing metathesis; Grubbs' catalyst; Vorbrüggen-type coupling reaction.
* Corresponding author. Tel.: +91-20-25893614; fax: +91-20-25882456; e-mail: gurjar@dalton.ncl.res.in

0040–4020/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2004.08.092

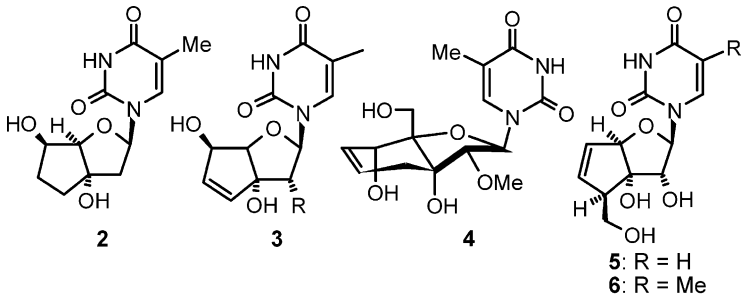


Figure 1.

this report we describe the synthesis of novel bicyclic nucleosides **5**, **6** and their analogues (Fig. 1).[10]

2. Results and discussion

The vinylogous Reformatsky reaction of 3-ulose derivative[11] (**1**) was attempted with methyl 4-bromocrotonate and Zn–Cu couple.[12] This reaction gave two products chromatographically separated on silica gel. The major product obtained in 52% yield was assigned as structure **7** based on the ^{1}H NMR, ^{13}C NMR, mass spectra and elemental analysis. The stereochemical assignment of **7** was confirmed by single crystal X-ray diffraction studies (Fig. 2). The minor product obtained in 26% yield, was given the structure **8** based on spectroscopic and analytical data. The formation of a single diastereomer **7** could be explained by considering the two transition states A and B. The preferred *E*-dienolate of Zn (transition state A) seemed to be more preferred while *Z*-dienolate based transition state B has steric hindrance (Fig. 3).

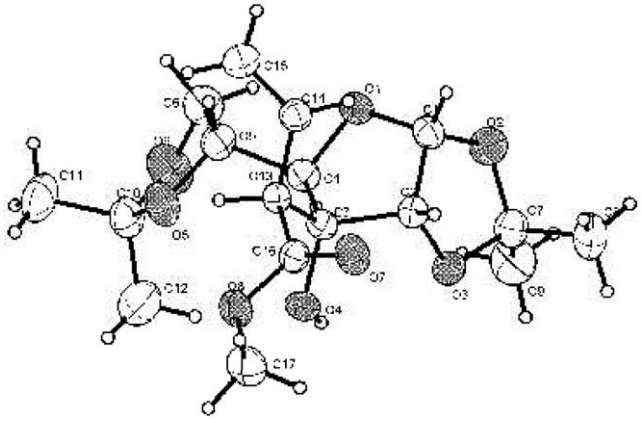


Figure 2. ORTEP diagram of **7**.

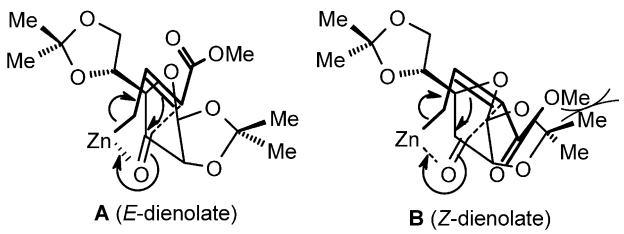
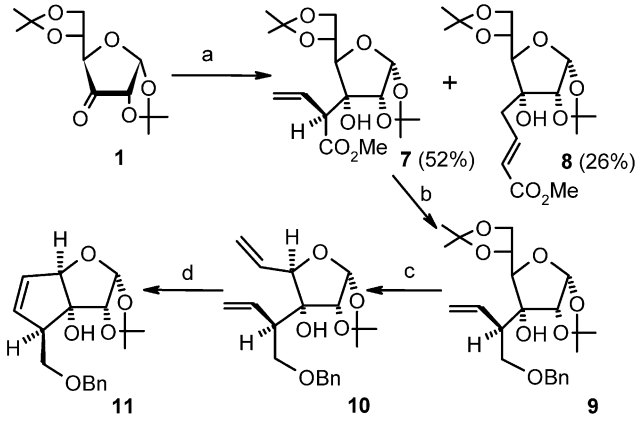


Figure 3. Possible transition states.

The carbomethoxy moiety of **7** was reduced with $LiAlH_4$ and then the resulting hydroxyl group was protected as its benzylic ether (**9**) by using benzyl bromide–Ag_2O. In order to derive the diene **10**, the successive hydrolysis of 5,6-*O*-isopropylidene group with 0.8% H_2SO_4 in methanol, dimesylation of the 5,6-diol derivative with MsCl and $^{i}Pr_2EtN$, and elimination with NaI in ethyl methyl ketone were carried out. The ring closing metathesis reaction of **10** with 4 mol% of Grubbs' 1st generation catalyst in refluxing benzene provided the bicyclic derivative **11** in 87% yield (Scheme 2).[13] The stereochemistry of **11** was unambiguously assigned by NOE studies (Fig. 4). Strong NOE correlations among bridgehead hydroxyl group and the adjacent allylic protons were noticed.

Our final concern was to introduce pyrimidine bases at the anomeric center. The 1,2-*O*-isopropylidene moiety of **11** was cleaved with 60% AcOH followed by acetylation with Ac_2O and Et_3N to afford the triacetylated derivative **12**. The modified Vorbrüggen-type coupling reaction of **12** with



Scheme 2. Reagents and conditions: (a) methyl 4-bromocrotonate, Zn–Cu couple, ether, reflux, 1 h; (b) (i) $LiAlH_4$, ether, 0 °C–rt, 2 h, 83%; (ii) BnBr, Ag_2O, CH_2Cl_2, rt, 1 h, 95%; (c) (i) 0.8% H_2SO_4, MeOH, rt, 24 h, 80%; (ii) MsCl, $^{i}Pr_2EtN$, CH_2Cl_2, 0 °C, 5 min, 95%; (iii) NaI, Et–CO–Me, reflux, 4 h, 83%; (d) Grubbs' catalyst, C_6H_6, reflux, 8 h, 87%.

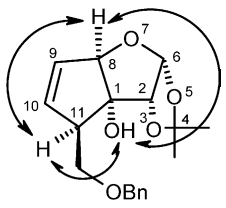
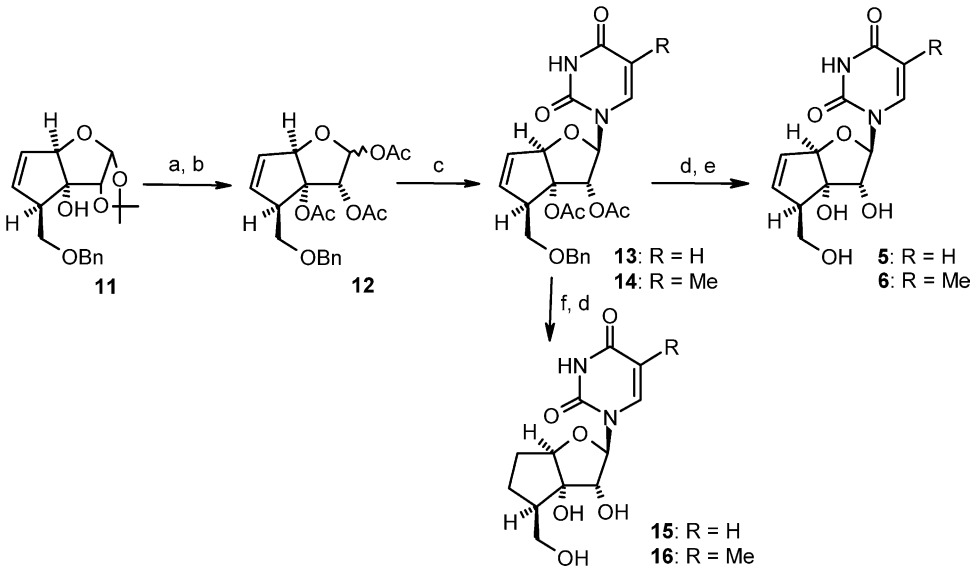


Figure 4. NOE studies on **11**.



Scheme 3. Reagents and conditions: (a) 60% AcOH, reflux, 2 h, 93%; (b) Ac_2O, Et_3N, DMAP, CH_2Cl_2, rt, 1 h, 96%; (c) uracil/thymine, BSA, TMSOTf, CH_3CN, 50 °C, 2 h, 69%/77%; (d) NaOMe, MeOH, 0 °C, 20 min; (e) BCl_3, CH_2Cl_2, −78 °C, 5 h; (f) 20% $Pd(OH)_2$/C, H_2, MeOH, rt, 12 h.

uracil was achieved in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and TMSOTf to afford exclusively the β-nucleoside **13**, attributed to the anchimeric assistance from 4-*O*-acetyl group.[14]

The de-protection of the two acetyl groups under Zemplén reaction condition[15] and the benzylic ether with BCl_3 of **13** afforded **5**. Simultaneously, compound **13** was hydrogenated in the presence of 20% $Pd(OH)_2$/C, followed by deacetylation using NaOMe (Zemplén conditions) to give compound **15**. Similarly, the triacetate **12** was coupled to thymine using *N*,*O*-bis(trimethylsilyl)acetamide and TMSOTf to obtain **14**. Compound **14** was transformed into **6** and **16** as described above (Scheme 3).

In conclusion, we described an elegant methodology to synthesize the novel bicyclic nucleosides having the structural framework of some carbocyclic nucleosides and bridgehead hydroxyl moiety. The biological activity of these novel bicyclic nucleosides is under study and will be published in due course.

3. Experimental

3.1. General

The NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 with TMS as an internal standard on AC-200 MHz, MSL-300 MHz, DRX-500 MHz. Optical rotations were measured with a JASCO DIP 370 digital polarimetrometer. EI Mass spectra were recorded on Finngan MAT-1020. Combustion data were recorded on Elmentar-Vario-EL (Heraeus Company Ltd., Germany). IR spectra were obtained from Perkin–Elmer 68515 PC-FTIR spectrophotometer. Melting points were measured on Buchi 535 melting point apparatus and are uncorrected. Starting materials and reagents were purchased from Aldrich or Lancaster and used as received. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E-Merck silica gel plates (60F-254) with UV, I_2 and anisaldehyde in ethanol as development reagents.

3.1.1. 3-*C*-[(*S*)-1-Carbomethoxy-prop-2-enyl]-1,2;5,6-di-*O*-isopropylidene-α-D-allofuranose (7) and 3-*C*-(3-carbomethoxy-prop-2-enyl]-1,2;5,6-di-*O*-isopropylidene-α-D-allofuranose (8). To a suspension of activated Zn–Cu couple (40.0 g, 611.7 mmol) and iodine (50 mg) in anhydrous ether (140 mL) were gradually added methyl 4-bromocrotonate (45 g, 251.4 mmol) and the solution of **1** (40.0 g, 155.0 mmol in 50 mL of ether) over a period of 30 min. The reaction mixture was heated under reflux for 30 min, cooled and poured over saturated NH_4Cl. The organic layer was separated, washed with brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed on silica gel by using EtOAc–light petroleum (1:7) as eluent to give **7**[16] (28.9 g, 52%) as a colorless solid, mp 88–90 °C; $[\alpha]_D=-42.5$ (*c* 1, $CHCl_3$); ν_{max} ($CHCl_3$) 3462, 2990, 1737, 1384, 1216, 1167, 1075, 1015, 756; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37, 1.45, 1.58 (3s, 12H), 3.32 (s, 1H), 3.74 (s, 3H), 3.78–3.81 (m, 2H), 3.87 (dd, 1H, $J=5.1$, 8.8 Hz), 4.08–4.12 (m, 1H), 4.21 (dt, 1H, $J=9.1$, 5.6 Hz), 5.04 (d, 1H, $J=3.9$ Hz), 5.28–5.35 (m, 2H), 5.61 (d, 1H, $J=4.1$ Hz), 5.83 (ddd, 1H, $J=8.6$, 10.1, 17.5 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.9, 26.0, 26.2, 51.3, 51.4, 67.9, 72.2, 79.5, 79.6, 82.9, 103.5, 109.3, 111.6, 119.6, 130.0, 171.0; EIMS (*m*/*z*) 343 [M^+-15]. Anal. Calcd for $C_{17}H_{26}O_8$: C, 56.97; H, 7.31. Found: C, 56.68; H, 7.52.

Further elution with EtOAc–light petroleum (1:5) gave **8** (14.4 g, 26%) as a colorless solid, mp 106–108 °C; $[\alpha]_D=-25.6$ (*c* 1, $CHCl_3$); ν_{max} ($CHCl_3$) 3440, 3020, 1716, 1376, 1166, 1079, 759; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34, 1.36, 1.45, 1.59 (4s. 12H), 2.30 (dd, 1H, $J=9.1$, 14.7 Hz), 2.78 (s, 1H, OH), 2.80 (ddd, 1H, $J=1.6$, 5.8, 14.7 Hz), 3.75 (s, 3H), 3.78 (m, 1H), 3.87–3.95 (m, 1H), 4.06–4.14 (m, 2H), 4.24 (d, 1H, $J=3.8$ Hz), 5.66 (d, 1H, $J=3.8$ Hz), 5.94 (d, 1H, $J=15.8$ Hz), 7.12 (ddd, 1H, $J=5.4$, 8.8, 15.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.2, 26.4, 26.6, 26.7, 34.9, 51.6, 68.1, 73.2, 78.9, 81.3, 81.9, 103.5,

109.9, 112.8, 124.7, 143.1, 166.3; EIMS (*m/z*) 343 [M^+-15]. Anal. Calcd for $C_{17}H_{26}O_8$: C, 56.97; H, 7.31. Found: C, 56.86; H, 7.27.

3.1.2. 3-*C*-[(*R*)-1-Benzyloxymethyl-prop-2-enyl]-1,2;5,6-di-*O*-isopropylidene-α-D-allofuranose (9). A solution of **7** (28.0 g, 78.0 mmol) and $LiAlH_4$ (4.15 g) in anhydrous ether (150 mL) was stirred for 2 h at rt, quenched with EtOAc and filtered through a plug of Celite. The filtrate was concentrated and purified on silica gel column with EtOAc–light petroleum (1:3) to afford 3-*C*-[(*R*)-1-hydroxymethyl-prop-2-enyl]-1,2;5,6-di-*O*-isopropylidene-α-D-allofuranose (16.8 g, 83%) as a colorless solid, mp 78–80 °C; $[\alpha]_D=-3.4$ (*c* 1.1, $CHCl_3$); ν_{max} ($CHCl_3$) 3401, 2989, 1384, 1217, 1074, 1010, 757; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.38 (s, 6H), 1.45, 1.59 (2s, 6H), 2.72–2.89 (br s, 1H, OH), 2.91–3.07 (m, 1H), 3.12 (s, 1H, OH), 3.68–3.90 (m, 3H), 3.99–4.17 (m, 2H), 4.24–4.36 (m, 1H), 4.50 (d, 1H, *J*=3.9 Hz), 5.17–5.32 (m, 2H), 5.60 (d, 1H, *J*=3.9 Hz), 5.71 (ddd, 1H, *J*=8.7, 10.7, 17.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.3, 26.3, 26.5, 26.6, 47.1, 63.2, 68.4, 72.5, 80.5, 81.0, 84.1, 103.9, 109.7, 112.2, 118.5, 134.3; EIMS (*m/z*) 315 [M^+-15]. Anal. Calcd for $C_{16}H_{26}O_7$: C, 58.17; H, 7.93. Found: C, 57.87; H, 8.18.

The above product (16.0 g, 48.4 mmol), freshly prepared Ag_2O (33.7 g, 145.3 mmol) and benzyl bromide (6.9 mL, 58.0 mmol) in CH_2Cl_2 (50 mL) were stirred for 1 h at rt, filtered through Celite and concentrated. The residue was purified on silica gel by using EtOAc–light petroleum (1:9) to get **9** (19.35 g, 95%) as a syrup: $[\alpha]_D=+13.7$ (*c* 1.1, $CHCl_3$); ν_{max} ($CHCl_3$) 3402, 2936, 1385, 1275, 1217, 1045, 756; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.33, 1.35, 1.44, 1.59 (4s, 12H), 2.85–2.94 (m, 1H), 3.17 (s, 1H, OH), 3.75–3.96 (m, 4H), 4.08–4.16 (m, 1H), 4.25–4.36 (m, 1H), 4.46–4.55 (m, 2H), 4.75 (d, 1H, *J*=7.7 Hz), 5.18–5.29 (m, 2H), 5.62 (d, 1H, *J*=3.8 Hz), 5.75–5.94 (m, 1H), 7.26–7.42 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.2, 26.2, 26.4, 45.6, 68.2, 70.7, 72.4, 72.9, 79.7, 81.0, 83.9, 103.6, 109.2, 111.5, 117.5, 127.1, 127.8, 135.2, 138.2; EIMS (*m/z*) 405 [M^+-15]. Anal. Calcd for $C_{23}H_{32}O_7$: C, 65.70; H, 7.67. Found: C, 65.47; H, 7.58.

3.1.3. 3-*C*-[(*R*)-1-Benzyloxymethyl-prop-2-enyl]-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (10). Compound **9** (16.0 g, 38.0 mmol) and 0.8% H_2SO_4 (20 mL) in MeOH (50 mL) were stirred at rt for 24 h, and then neutralized with solid $NaHCO_3$. The solid was filtered, concentrated and the residue purified on silica gel using EtOAc–light petroleum (1:2) to give 3-*C*-[(*R*)-1-benzyloxymethyl-prop-2-enyl]-1,2-*O*-isopropylidene-α-D-allofuranose (11.6 g, 80%) as a syrup: $[\alpha]_D=-11.4$ (*c* 1, $CHCl_3$); ν_{max} ($CHCl_3$) 3418, 2988, 1385, 1275, 1217, 1087, 1027, 757; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.34, 1.58 (2s, 6H), 2.37–2.53 (br s, 1H, OH), 2.90–3.07 (m, 2H), 3.56–3.88 (m, 6H), 3.91–4.03 (m, 1H), 4.46–4.57 (m, 2H), 4.66 (d, 1H, *J*=3.9 Hz), 5.17–5.27 (m, 2H), 5.57 (d, 1H, *J*=3.9 Hz), 5.66–5.84 (m, 1H), 7.21–7.37 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.0, 26.1, 44.9, 64.3, 68.9, 70.3, 72.8, 80.0, 80.2, 80.7, 103.7, 111.5, 117.7, 127.1, 127.8, 134.3, 137.8; EIMS (*m/z*) 322 [M^+-58]. Anal. Calcd for $C_{20}H_{28}O_7$: C, 63.14; H, 7.42. Found: C, 62.88; H, 7.74.

The above compound (10.0 g, 26.3 mmol), ^{i}Pr$_2$EtN (16 mL, 92.0 mmol), and MsCl (5 mL, 65.7 mmol) in CH_2Cl_2 (40 mL) were stirred at 0 °C for 5 min. The reaction mixture was quenched with saturated Na_2CO_3, water, dried (Na_2SO_4), and concentrated. The crude oily compound was purified on silica gel with EtOAc–light petroleum (1:5) to afford the 5,6-dimesylate derivative (13.4 g, 95%), as a clear oil: $[\alpha]_D=-10.1$ (*c* 1.45, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35, 1.58 (2s, 6H), 3.00–3.04 (m, 1H), 3.06 (s, 3H), 3.13 (s, 3H), 3.56–3.67 (m, 1H), 3.74 (dd, 1H, *J*=5.4, 9.4 Hz), 3.94 (dd, 1H, *J*=3.9, 9.4 Hz), 4.00 (d, 1H, *J*=9.1 Hz), 4.32 (dd, 1H, *J*=5.7, 11.5 Hz), 4.45–4.63 (m, 3H), 4.83 (d, 1H, *J*=3.8 Hz), 5.21–5.41 (m, 2H), 5.55–5.74 (m, 1H), 5.62 (d, 1H, *J*=3.8 Hz), 7.21–7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.0, 26.1, 37.0, 39.0, 44.8, 68.3, 70.6, 72.7, 73.6, 78.8, 79.7, 103.4, 111.8, 118.9, 127.1, 127.9, 133.3, 137.6. Anal. Calcd for $C_{22}H_{32}O_{11}S_2$: C, 49.24; H, 6.01; S, 11.95. Found: C, 48.97; H, 5.77; S, 12.14.

The 5,6-dimesylate (12.0 g, 22.4 mmol) and NaI (33.5 g, 223.6 mol) in 2-butanone (100 mL) were heated under reflux for 4 h and concentrated. The residue was partitioned between EtOAc and saturated aq $Na_2S_2O_3$. The organic layer was washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel with EtOAc–light petroleum (1:9) to afford **10** (6.43 g, 83%) as a syrup: $[\alpha]_D=-15.2$ (*c* 0.95, $CHCl_3$); ν_{max} ($CHCl_3$) 3402, 2933, 1403, 1276, 1092, 1027, 755; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35, 1.58 (2s, 6H), 2.68 (dt, 1H, *J*=9.2, 5.1 Hz), 3.46 (s, 1H, OH), 3.75–3.82 (m, 2H), 4.33 (dt, 1H, *J*=1.4, 2.8 Hz), 4.46–4.53 (m, 2H), 4.59 (d, 1H, *J*=3.9 Hz), 5.09–5.46 (m, 4H), 5.64 (d, 1H, *J*=3.9 Hz), 5.70–6.00 (m, 2H), 7.23–7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.9, 26.0, 44.6, 69.8, 72.6, 79.9, 80.2, 83.8, 103.4, 111.1, 117.1, 117.3, 126.9, 127.7, 131.4, 134.1, 137.7; EIMS (*m/z*) 331 [M^+-15]. Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.56. Found: C, 69.18; H, 7.71.

3.1.4. (1*R*,2*R*,6*R*,8*R*,11*R*)-11-Benzyloxymethyl-1-hydroxy-4,4-dimethyl-3,5,7-trioxatricyclo[6.3.0.0^{2,6}]undec-9-ene (11). Compound **10** (6.0 g, 17.3 mmol) and Grubbs' catalyst (0.57 g, 0.69 mmol) in anhydrous benzene (250 mL) were heated under reflux for 8 h and then evaporated. The residue was purified on silica gel with EtOAc–light petroleum (1:4) to obtain **11** (4.8 g, 87%), as an oil: $[\alpha]_D=+112$ (*c* 1.1, $CHCl_3$); ν_{max} ($CHCl_3$) 3498, 2988, 2935, 2861, 1455, 1383, 1374, 1219, 1166, 1096, 1002, 750, 700; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.37, 1.59 (2s, 6H), 3.06–3.10 (m, 1H), 3.29 (s, 1H, OH), 3.40 (dd, 1H, *J*=7.2, 10.1 Hz), 3.53 (dd, 1H, *J*=4.2, 10.1 Hz), 4.50 (ABq, 2H, *J*=12.1 Hz), 4.61 (d, 1H, *J*=3.8 Hz), 4.75 (d, 1H, *J*=1.9 Hz), 5.62 (d, 1H, *J*=3.8 Hz), 5.85 (dt, 1H, *J*=5.9, 2.7 Hz), 5.89 (dd, 1H, *J*=2.7, 5.9 Hz), 7.29–7.37 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 27.1, 27.4, 54.2, 68.6, 73.2, 80.3, 86.2, 93.1, 106.9, 112.6, 127.9, 128.0, 128.5, 129.8, 136.9, 137.7; EIMS (*m/z*) 318 [M^+]. Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.96. Found: C, 67.96; H, 7.18.

3.1.5. (3*R*/*S*,1*R*,4*R*,5*R*,6*R*)-3,4,5-Triacetoxy-6-benzyloxymethyl-2-oxa-bicyclo[3.3.0]oct-7-ene (12). Compound **11** (2.0 g, 6.3 mmol) and 60% AcOH (15 mL) were heated under reflux for 2 h. The reaction mixture was neutralized with solid Na_2CO_3 and evaporated. The residue was

extracted with EtOAc, dried (Na_2SO_4), concentrated, and purified by silica gel chromatography with EtOAc–light petroleum (1:1) to give (3*R*/*S*,1*R*,4*R*,5*R*,6*R*)-6-benzyloxymethyl-3,4,5-trihydroxy-2-oxa-bicyclo[3.3.0]oct-7-ene (1.63 g, 93%) as a solid: mp 92–94 °C; ν_{max} ($CHCl_3$) 3359, 2936, 1454, 1401, 1366, 1081, 1027, 749, 698; ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.06–3.19 (m, 1H), 3.35 (d, 1H, J= 4.7 Hz, OH), 3.44 (s, 1H, OH), 3.60–3.79 (m, 2H), 3.86 (d, 1H, J=5.8 Hz, OH) 4.07 (t, 1H, J=4.0 Hz), 4.54–4.60 (m, 2H), 5.14 (s, 1H), 5.29–5.33 (m, 1H), 5.57 (d, 1H, J= 6.0 Hz), 5.79 (dt, 1H, J=6.0, 2.1 Hz), 7.28–7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 52.7, 68.8, 72.0, 73.0, 85.6, 92.8, 97.4, 127.5, 128.2, 130.7, 132.8, 137.5. Anal. Calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.39; H, 6.42.

The above product (1.5 g, 5.39 mmol), Ac_2O (3.1 mL, 32.76 mmol), Et_3N (7.5 mL), DMAP (135 mg) in anhydrous CH_2Cl_2 (20 mL) were stirred at rt for 1 h. The reaction mixture was partitioned between water–CH_2Cl_2, the organic layer washed with saturated $NaHCO_3$, water, dried (Na_2SO_4) and concentrated. The residue was purified on silica gel with EtOAc–light petroleum (1:4) as an eluent to obtain **12** (2.1 g, 96%) as an oil: ν_{max} ($CHCl_3$) 3410, 3018, 2958, 1720, 1452, 1374, 1276, 1084, 1027, 756, 714; ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.01, 2.09, 2.13 (3s, 9H), 3.39 (t, 1H, J=5.2 Hz), 3.69–3.74 (m, 2H), 4.49 (ABq, 2H, J= 11.9 Hz), 5.50 (s, 1H), 5.58 (d, 1H, J=4.3 Hz), 5.80–5.89 (m, 2H), 6.29 (d, 1H, J=4.3 Hz), 7.20–7.34 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.1, 20.6, 21.2, 51.4, 68.4, 70.9, 72.9, 90.0, 92.6, 95.2, 95.9, 127.4, 128.1, 135.4, 137.8, 168.6, 169.0, 169.6. Anal. Calcd for $C_{21}H_{24}O_8$: C, 62.37; H, 5.98. Found: C, 62.09; H, 6.12.

3.1.6. (1*R*,3*R*,4*R*,5*R*,6*R*)-4,5-Diacetoxy-6-benzyloxymethyl-3-(uracil-1-yl)-2-oxa-bicyclo[3.3.0]oct-7-ene (13). Compound **12** (0.36 g, 0.89 mmol), uracil (0.20 g, 1.78 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (1.1 mL, 4.45 mmol) in anhydrous CH_3CN (8 mL) were heated under reflux for 15 min, cooled to 0 °C and then TMSOTf (0.32 mL, 1.78 mmol) was added. The reaction mixture was stirred at 50 °C for 2 h, quenched with ice-cold saturated aq $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with water, dried (Na_2SO_4), concentrated, and the residue purified on silica gel with EtOAc–light petroleum (1:1) to give **13** (0.28 g, 69%), as a syrup: $[\alpha]_D$=+16.8 (*c* 0.8, $CHCl_3$); ν_{max} ($CHCl_3$) 3022, 1748, 1693, 1455, 1373, 1240, 1048, 755; ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.02, 2.15 (2s, 6H), 3.26–3.36 (m, 1H), 3.80 (dd, 1H, J=4.3, 10.0 Hz), 4.02–4.13 (m, 1H), 4.50 (ABq, 2H, J=11.2 Hz), 5.03 (dd, 1H, J=2.0, 8.1 Hz), 5.16 (d, 1H, J=1.6 Hz), 5.86–6.01 (m, 3H), 6.17 (d, 1H, J=7.5 Hz), 7.08 (d, 1H, J=8.1 Hz), 7.25–7.37 (m, 5H), 9.62 (br s, 1H, NH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.3, 21.2, 53.2, 68.6, 71.8, 73.1, 86.3, 90.8, 92.2, 103.2, 127.1, 127.7, 128.4, 137.4, 137.7, 139.3, 150.8, 162.9, 169.1, 169.9. Anal. Calcd for $C_{23}H_{24}O_8N_2$: C, 60.52; H, 5.30; N, 6.14. Found: C, 60.29; H, 5.00; N, 6.32.

3.1.7. (1*R*,3*R*,4*R*,5*R*,6*R*)-4,5-Dihydroxy-6-hydroxymethyl-3-(uracil-1-yl)-2-oxa-bicyclo[3.3.0]oct-7-ene (5). To a solution of **13** (0.21 g, 0.46 mmol), 1 M methanolic NaOMe (50 μL) in MeOH (3 mL) were stirred at 0 °C for 20 min. The reaction mixture was neutralized with concd HCl, filtered and concentrated. The residue was purified by silica gel column chromatography with MeOH–CH_2Cl_2 (1:9) to afford (1*R*,3*R*,4*R*,5*R*,6*R*)-6-benzyloxymethyl-4,5-dihydroxy-3-(uracil-1-yl)-2-oxa-bicyclo[3.3.0]oct-7-ene (0.145 g, 85%), as a solid: mp 150–152 °C; $[\alpha]_D$=−24 (*c* 0.95, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.10 (t, 1H, J=6.5 Hz), 3.72 (d, 2H, J=6.5 Hz), 4.07 (br s, 1H, OH), 4.25 (d, 1H, J=7.2 Hz), 4.53 (s, 2H), 4.60 (br s, 1H, OH), 5.05 (s, 1H), 5.66 (d, 1H, J=8.2 Hz), 5.82 (dd, 2H, J=6.4, 12.3 Hz), 6.13 (d, 1H, J=7.6 Hz), 7.25–7.35 (m, 6H), 10.0 (br s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$+MeOD): δ 52.8, 68.1, 73.1, 74.8, 85.4, 88.3, 92.8, 102.6, 127.5, 128.1, 130.0, 134.5, 137.5, 139.5, 151.1, 163.8. Anal. Calcd for $C_{19}H_{20}O_6N_2$: C, 61.28; H, 5.41; N, 7.52. Found: C, 61.09; H, 5.42; N, 7.69.

The above product (0.125 g, 0.34 mmol) in anhydrous CH_2Cl_2 (4 mL) was stirred at −78 °C and then a 1 M solution of BCl_3 in CH_2Cl_2 (0.53 mL, 0.67 mmol) was added dropwise. After being stirred for 5 h at −78 °C the mixture was treated with MeOH (3 mL) and water (0.2 mL) and stirred at rt for 1 h. The solvents were removed under vacuum and the residue purified on silica gel using MeOH–CH_2Cl_2 (1:9) to afford **5** (0.09 g, 95%) as a solid: mp 62–64 °C; $[\alpha]_D$=−47.4 (*c* 0.75, MeOH); ν_{max} ($CHCl_3$) 3204, 3019, 1693, 1462, 1400, 1272, 1216, 1105, 757; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.67–2.72 (m, 1H), 3.47 (dd, 1H, J=9.0, 10.6 Hz), 3.77 (dd, 1H, J=5.2, 10.6 Hz), 4.00 (d, 1H, J=8.4 Hz), 4.74 (s, 1H), 5.68 (dd, 1H, J=2.0, 8.1 Hz), 5.80 (dt, 1H, J=1.8, 6.2 Hz), 5.90 (d, 1H, J=6.2 Hz), 5.92 (d, 1H, J=8.1 Hz), 7.42 (d, 1H, J=8.1 Hz), 11.35 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 55.5, 59.3, 72.6, 84.5, 86.8, 92.2, 102.4, 130.1, 135.0, 140.2, 150.9, 162.9. Anal. Calcd for $C_{12}H_{14}O_6N_2$: C, 51.06; H, 4.99; N, 9.92. Found: C, 51.19; H, 4.81; N, 9.69.

3.1.8. (1*R*,3*R*,4*R*,5*R*,6*R*)-4,5-Dihydroxy-6-hydroxymethyl-3-(uracil-1-yl)-2-oxa-bicyclo[3.3.0]octane (15). Compound **13** (0.11 g, 0.24 mmol) and 20% $Pd(OH)_2$ (0.025 g) in MeOH (4 mL) were stirred under a H_2 atmosphere for 12 h, filtered through a pad of Celite and concentrated. The residue was purified on silica gel with EtOAc–light petroleum (4:1) to give (1*R*,3*R*,4*R*,5*R*,6*R*)-4,5-diacetoxy-6-hydroxymethyl-3-(uracil-1-yl)-2-oxa-bicyclo[3.3.0]octane (0.075 g, 84%) as a syrup: $[\alpha]_D$=−30.4 (*c* 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.89–1.98 (m, 4H), 2.05, 2.13 (2s, 6H), 2.43–2.53 (m, 1H), 3.79 (dd, 1H, J=5.7, 11.2 Hz), 4.06 (dd, 1H, J=4.0, 11.2 Hz), 4.77 (d, 1H, J=2.7 Hz), 5.74 (d, 1H, J=7.4 Hz), 5.77 (dd, 1H, J= 2.2, 7.4 Hz), 6.07 (d, 1H, J=7.5 Hz), 7.52 (d, 1H, J= 7.5 Hz), 9.45 (br s, 1H, NH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 20.4, 21.2, 26.3, 29.4, 49.9, 60.8, 71.5, 87.2, 87.3, 90.6, 102.9, 140.0, 150.6, 163.3, 169.6, 170.1. Anal. Calcd for $C_{16}H_{20}O_8N_2$: C, 52.17; H, 5.47; N, 7.60. Found: C, 52.29; H, 5.76; N, 7.71.

The above product (0.07 g, 0.19 mmol) 1 M methanolic NaOMe (20 μL) in MeOH (4 mL) were stirred for 20 min and worked up as described above to give **15** (0.04 g, 74%) as a solid: mp 185–187 °C; $[\alpha]_D$=−20.2 (*c* 1, MeOH); ν_{max} (MeOH) 3361, 2945, 2833, 1698, 1451, 1402, 1113, 1029; ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.54–1.65 (m, 2H), 1.70–1.83 (m, 2H), 1.88–1.94 (m, 1H), 3.41 (dd, 1H, J=8.7, 10.5 Hz), 3.72 (dd, 1H, J=4.7, 10.5 Hz), 3.88 (d, 1H,

J=8.2 Hz), 4.12 (d, 1H, J=6.7 Hz), 4.90–5.07 (br s, 1H, OH), 5.11–5.27 (br s, 1H, OH), 5.66 (d, 2H, J=8.8 Hz), 7.67 (d, 1H, J=8.8 Hz), 11.34 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 27.0, 29.3, 51.6, 60.1, 70.9, 83.2, 85.3, 88.5, 102.0, 140.6, 150.8, 162.7. Anal. Calcd for $C_{12}H_{16}O_6N_2$: C, 50.70; H, 5.67; N, 9.85. Found: C, 50.49; H, 6.02; N, 9.69.

3.1.9. (1*R*,3*R*,4*R*,5*R*,6*R*)-4,5-Diacetoxy-6-benzyloxymethyl-3-(thymin-1-yl)-2-oxa-bicyclo[3.3.0]oct-7-ene (14). Compound **12** (0.50 g, 1.23 mmol), thymine (0.31 g, 2.47 mmol), *N*,*O*-bis(trimethylsilyl)acetamide (1.5 mL, 6.18 mmol) in anhydrous CH_3CN (10 mL) were heated under reflux for 15 min, cooled to 0 °C and then TMSOTf (0.45 mL, 2.47 mmol) was added. The reaction mixture was stirred at 50 °C for 2 h, quenched with ice-cold saturated aq $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with water, dried (Na_2SO_4), concentrated, and the residue purified on silica gel with EtOAc–light petroleum (1:1) to give **14** (0.45 g, 77%) as a colorless syrup: $[\alpha]_D$=−20.9 (*c* 1.7, $CHCl_3$); ν_{max} ($CHCl_3$) 3195, 3030, 2929, 1748, 1694, 1466, 1371, 1234, 1097, 753; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.61 (s, 3H), 2.01, 2.15 (2s, 6H), 3.35–3.40 (m, 1H), 3.75 (dd, 1H, J=5.1, 10.2 Hz), 3.96 (dd, 1H, J=3.2, 10.2 Hz), 4.53 (ABq, 2H, J=11.9 Hz), 5.2 (s, 1H), 5.88–5.99 (m, 3H), 6.24 (d, 1H, J=7.7 Hz), 7.08 (d, 1H, J=1.3 Hz), 7.28–7.34 (m, 5H), 9.22 (br s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.0, 20.2, 21.2, 52.4, 68.2, 71.9, 72.8, 86.1, 90.9, 91.7, 111.7, 127.3, 127.5, 128.2, 134.5, 136.9, 137.7, 150.9, 163.5, 169.2, 169.9. Anal. Calcd for $C_{24}H_{26}O_8N_2$: C, 61.27; H, 5.57; N, 5.95. Found: C, 60.94; H, 5.81; N, 5.83.

3.1.10. (1*R*,3*R*,4*R*,5*R*,6*R*)-4,5-Dihydroxy-6-hydroxymethyl-3-(thymin-1-yl)-2-oxa-bicyclo[3.3.0]oct-7-ene (6). To a solution of **14** (0.16 g, 0.34 mmol), 1 M methanolic NaOMe (46 μL) in MeOH (3 mL) were stirred at 0 °C for 20 min. The reaction mixture was neutralized with concd HCl, filtered and concentrated. The residue was purified by silica gel column chromatography with MeOH–CH_2Cl_2 (1:9) to give (1*R*,3*R*,4*R*,5*R*,6*R*)-6-benzyloxymethyl-4,5-dihydroxy-3-(thymin-1-yl)-2-oxa-bicyclo[3.3.0]oct-7-ene (0.11 g, 88%) as colorless syrup: $[\alpha]_D$=−51.6 (*c* 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.86 (s, 3H), 3.12 (br s, 1H), 3.73 (d, 2H, J=6.4 Hz), 4.23 (d, 1H, J=7.2 Hz), 4.54 (s, 2H), 5.06 (s, 1H), 5.83 (ABq, 2H, J=5.9 Hz), 6.10 (d, 1H, J=7.4 Hz), 7.12 (s, 1H), 7.27–7.36 (m, 5H), 9.56 (br s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.5, 52.7, 68.5, 73.5, 75.6, 86.6, 89.1, 93.1, 111.4, 127.8, 127.9, 128.5, 130.6, 134.2, 134.9, 137.6, 151.5, 163.7. Anal. Calcd for $C_{20}H_{22}O_6N_2$: C, 62.17; H, 5.74; N, 7.25. Found: C, 62.12; H, 5.86; N, 7.52.

The above product (0.065 g, 0.168 mmol) in anhydrous CH_2Cl_2 (3 mL) was stirred at −78 °C and then a 1 M solution of BCl_3 in CH_2Cl_2 (0.42 mL, 0.42 mmol) was added dropwise. After being stirred for 5 h at −78 °C the mixture was treated with MeOH (3 mL) and water (0.2 mL) and stirred at rt for 1 h. The solvents were removed under vacuum and the residue purified on silica gel using MeOH–CH_2Cl_2 (1:9) to afford **6** (0.04 g, 80%) as a solid: mp 90–92 °C; $[\alpha]_D$=−57.1 (*c* 0.75, MeOH); ν_{max} ($CHCl_3$) 3391, 2947, 2835, 1675, 1450, 1404, 1111, 1027; ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.80 (s, 3H), 2.69–2.73 (m, 1H), 3.50 (dt, 1H, J=9.9, 5.6 Hz), 3.79 (dt, 1H, J=9.9, 4.8 Hz), 4.05 (t, 1H, J=7.7 Hz), 4.58 (t, 1H, J=5.0 Hz), 4.73 (s, 1H, OH), 5.21 (d, 1H, J=6.9 Hz, OH), 5.45 (s, 1H, OH), 5.79–5.81 (m, 1H), 5.90–5.93 (m, 2H), 7.29 (s, 1H), 11.33 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 11.9, 55.6, 59.3, 72.0, 84.3, 86.5, 92.0, 109.8, 129.8, 134.9, 135.4, 150.9, 163.4. Anal. Calcd for $C_{13}H_{16}O_6N_2$: C, 52.70; H, 5.44; N, 9.45. Found: C, 52.52; H, 5.76; N, 9.52.

3.1.11. (1*R*,3*R*,4*R*,5*R*,6*R*)-4,5-Dihydroxy-6-hydroxymethyl-3-(thymin-1-yl)-2-oxa-bicyclo[3.3.0]octane (16). Compound **14** (0.20 g, 0.42 mmol) and 20% $Pd(OH)_2$ (0.035 g) in MeOH (6 mL) were stirred under a H_2 atmosphere for 12 h. After the usual work up, (1*R*,3*R*,4*R*,5*R*,6*R*)-4,5-diacetoxy-6-hydroxymethyl-3-(thymin-1-yl)-2-oxa-bicyclo[3.3.0]octane (0.15 g, 92%) was isolated as a colorless syrup: $[\alpha]_D$=−28.7 (*c* 1.2, $CHCl_3$); ν_{max} ($CHCl_3$) 3462, 3020, 1745, 1694, 1469, 1373, 1241, 1057, 755; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.92 (s, 3H), 1.93–1.96 (m, 4H), 2.07, 2.12 (2s, 6H), 2.45–2.54 (m, 1H), 2.60–2.74 (m, 1H, OH), 3.81 (dd, 1H, J=5.8, 11.3 Hz), 4.01–4.09 (m, 1H), 4.76 (d, 1H, J=2.6 Hz), 5.76 (d, 1H, J=6.8 Hz), 6.05 (d, 1H, J=6.8 Hz), 7.31 (s, 1H), 9.48–9.62 (m, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.2, 20.2, 21.1, 26.3, 29.3, 49.8, 60.7, 71.1, 86.9, 90.5, 111.1, 135.6, 150.7, 163.7, 169.4, 170.0. Anal. Calcd for $C_{17}H_{22}O_8N_2$: C, 53.40; H, 5.80; N, 7.33. Found: C, 53.54; H, 5.52; N, 7.56.

The above compound (0.12 g, 0.31 mmol) and 1 M methanolic NaOMe (0.1 mL) in MeOH (2 mL) were stirred for 20 min and worked up as described above to give **16** (0.075 g, 80%) as a solid: mp 182–184 °C; $[\alpha]_D$=−32.9 (*c* 0.8, MeOH); ν_{max} (MeOH) 3369, 2946, 2834, 1704, 1450, 1404, 1111, 1029, 758; ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.56–1.60 (m, 1H), 1.65–1.80 (m, 2H), 1.82 (s, 3H), 1.81–1.85 (m, 1H), 1.89–1.96 (m, 1H), 3.45 (dt, 1H, J=9.6, 5.5 Hz), 3.73 (dt, 1H, J=9.6, 4.4 Hz), 3.92 (t, 1H, J=7.7 Hz), 4.1 (d, 1H, J=6.1 Hz), 4.32 (t, 1H, J=4.9 Hz, OH), 4.97 (s, 1H, OH), 5.13 (d, 1H, J=6.9 Hz, OH), 5.65 (d, 1H, J=8.5 Hz), 7.49 (s, 1H), 11.32 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ 11.7, 27.0, 29.3, 51.7, 60.1, 70.5, 83.2, 85.0, 88.4, 109.7, 135.8, 150.9, 163.4. Anal. Calcd for $C_{13}H_{18}O_6N_2$: C, 52.34; H, 6.08; N, 9.39. Found: C, 52.12; H, 6.36; N, 9.37.

Acknowledgements

D.S.R. thanks CSIR, New Delhi for financial support in the form of Senior Research Fellowship.

References and notes

1. Hanessian, S. *Total Synthesis of Natural Products: The Chiron Approach*; Pergamon: Oxford, 1983.
2. Vasella, A. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Otto salle Verlag GmbH: Frankfurt am Main, 1980; Vol. 2, pp 173–267.
3. (a) Yoshimura, J. In *Carbohydrate Chemistry and*

Biochemistry; Tipson, S., Horton, D., Eds.; Acacemic: New York, 1984; Vol. 42, pp 69–134. (b) Stütz, E. A. In *Topics in Current Chemistry*; Springer: Heidelberg, 2001; pp 1–345.

4. For examples where two new chiral cenres have been generated see: (a) Kishida, M.; Yamauchi, N.; Sawada, K.; Ohashi, Y.; Eguchi, T.; Kakinuma, K. *J. Chem. Soc., Perkin Trans. 1* **1997**, 891–895. (b) Bouifraden, S.; Lavergne, J.-P.; Martinez, J.; Viallefont, P.; Riche, C. *Tetrahedron: Asymmetry* **1997**, *8*, 949–955. (c) González, Z.; González, A. *Carbohydr. Res.* **2000**, *329*, 901–906.
5. For reviews see: (a) Kool, E. T. *Chem. Rev.* **1997**, *97*, 1473–1488. (b) Herdewijn, P. *Biochim. Biophys. Acta* **1999**, *1489*, 167–179. (c) Leumann, C. J. *Bioorg. Med. Chem.* **2002**, *10*, 841–854.
6. For a recent review on the use of bicyclic nucleosides in oligonucleotides see: Meldgaard, M.; Wengel, J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3539–3554.
7. (a) Tarköy, M.; Bolli, M.; Schweizer, B.; Leumann, C. *Helv. Chim. Acta* **1993**, *76*, 481–510. (b) Bolli, M.; Lubini, P.; Leumann, C. *Helv. Chim. Acta* **1995**, *78*, 2077–2096. (c) Leumann, C.; Bolli, M. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 694–696.
8. (a) Freitag, M.; Thomasen, H.; Christensen, N. K.; Petersen, M.; Nielsen, P. *Tetrahedron* **2004**, *60*, 3775–3786 and references therein. (b) Obika, S.; Sekiguchi, M.; Osaki, T.; Shibata, N.; Masaki, M.; Hari, Y.; Imanishi, T. *Tetrahedron Lett.* **2002**, *43*, 4365–4368. (c) Lescop, C.; Huet, F. *Tetrahedron* **2000**, *56*, 2995–3003. (d) Oh, J.; Lee, C. R.; Chun, K. H. *Tetrahedron Lett.* **2001**, *42*, 4879–4881. (e) Kværnø, L.; Wengel, J. *J. Org. Chem.* **2001**, *66*, 5498–5503. (f) Sørensen, M. H.; Nielsen, C.; Nielsen, P. *J. Org. Chem.* **2001**, *66*, 4878–4886. (g) Wang, G.; Gunic, E. *Nucleosides Nucleotides* **1999**, *18*, 531–536. (h) Singh, S. K.; Kumar, R.; Wengel, J. *J. Org. Chem.* **1998**, *63*, 6078–6079. (i) Obika, S.; Nanbu, D.; Hari, Y.; Morio, K.; In, Y.; Ishida, T.; Imanishi, T. *Tetrahedron Lett.* **1997**, *38*, 8735–8738. (j) Steffens, R.; Leumann, C. J. *J. Am. Chem. Soc.* **1999**, *121*, 3250–3255. (k) Obika, S.; Morio, K.; Nanbu, D.; Imanishi, T. *Chem. Commun.* **1997**, 1643–1644. (l) Obika, S.; Morio, K.; Hari, Y.; Imanishi, T. *Chem. Commun.* **1999**, 2423–2424.
9. Ravn, J.; Nielsen, P. *J. Chem. Soc., Perkin Trans. 1* **2001**, 985–993.
10. For our earlier efforts on the synthesis of novel nucleosides see: Gurjar, M. K.; Maheshwar, K. *J. Org. Chem.* **2001**, *66*, 7552–7554.
11. Garegg, P. J.; Samuelsson, B. *Carbohydr. Res.* **1978**, *67*, 267–270.
12. (a) Rice, L. E.; Boston, M. C.; Finklea, H. O.; Suder, B. J.; Frazier, J. O.; Hudlicky, T. *J. Org. Chem.* **1984**, *49*, 1845–1848. (b) Fürstner, A. *Synthesis* **1989**, 571–590. (c) Rathke, M. W., Weipert, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H. Eds.; Pergamon: Oxford, 1991, Vol. 2, pp 277–299.
13. For recent reviews: (a) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450. (b) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29. (c) Fürstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3012–3043. (d) Kotha, S.; Sreenivasachary, N. *Ind. J. Chem. B* **2001**, *40*, 763–780.
14. (a) Niedballa, U.; Vorbrüggen, H. *J. Org. Chem.* **1974**, *39*, 3654–3660. (b) Vorbrüggen, H.; Krolikewiez, K.; Bennua, B. *Chem. Ber.* **1981**, *114*, 1234–1255. (c) Vorbrüggen, H.; Höfle, G. *Chem. Ber.* **1981**, *114*, 1256–1268.
15. Zemplén, G.; Kunz, A. *Ber.* **1923**, *56B*, 1705.
16. The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as deposition No. CCDC-233198. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk].