Indian Journal of Chemistry
Vol. 45B, May 2006, pp. 1325-1327

Note

Synthesis of novel unsaturated purine nucleoside

Virendra Singh

Department of Chemistry, Lucknow University, Lucknow 226 007, India

E-mail: nirvirendra@rediffmail.com

Received 22 July 2004; accepted (revised) 21April 2005

5′-Silylated derivative of N^6-*n*-propyladenosine **1** has been converted to bisxanthate **2** by reaction with CS_2 followed by alkylation.The bisxanthate affords 2′, 3′-didehydro-2′, 3′-dideoxy-N^6-*n*-propyladenosine **4** on reduction with tri-*n*-butyltin hydride and desilylation.

Keywords: N^6-*n*-propyladenosine, bisxanthate, propyladenosine

IPC: **Int.Cl.[8] C 07 D**

Dideoxynucleosides and their unsaturated derivatives have been prepared for their chemotherapeutic properties[1-4]. Some of them have been proved to be potent anti-HIV agents[1,2]. 2′,3′-Unsaturated nucleosides have been synthesized directly from the corresponding ribonucleosides via their reaction with acetoxyisobutyrylhalides, followed by reductive elimination of the 2′(3′)-acetoxy-3′,(2′)-halogeno derivative[5-9]. Barton[10,11] *et al* carried out deoxygenation of the dithiocarbonates or thionocarbonates of nucleosides for the preparation of 2′,3′-dideoxynucleosides in good yield.

Results and Discussion

Olefinic carbohydrates and aminoglycosides from the corresponding vic-diols via their bisxanthates have been prepared by Hayashi[12] and Barton[13, 14] *et al*. This procedure with some modifications has been used for the synthesis of the title nucleoside. The reaction of 5′-O-silyl-N^6-*n*-propyladenosine **1** with carbondisulphide and alkylation with CH_3I affords bisxanthate **2** as the only reaction product. The compound **2** on treatment with tri-*n*-butyltin hydride afforded **3** which on removal of silyl group with tetra-*n*-butyl ammonium fluoride gave a very good yield of the unsaturated nucleoside viz. 2′, 3′-didehydro-2′, 3′-dideoxy- N^6-*n*-propyladenosine **4** (**Scheme I**). The nucleoside was finally characterized by elemental analysis and ^{1}H NMR spectroscopy.

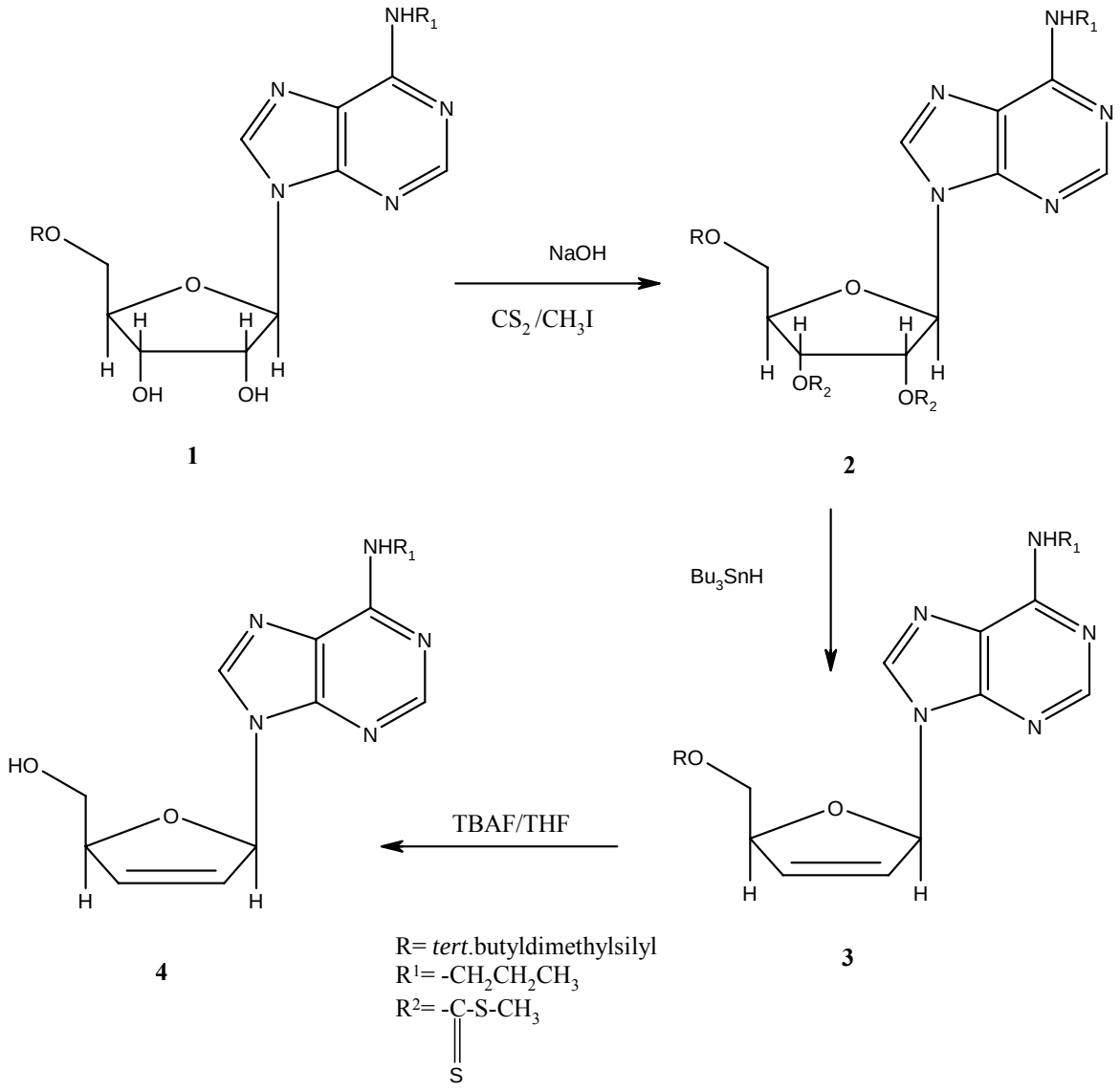
Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were recorded on a Bruker DR×300 spectrometer using TMS as internal standard. Microanalysis was carried on a Carlo Erba 1008 instrument. All the chemicals used were of AR grade (Sigma, BDH and E. Merck).

5′-O-*tert*.Butyldimethylsilyl-N^6-*n*-propyladenosine 1. To a stirred suspension of N^6-*n*-propyladenosine (0.587 g, 1.9 mmoles) and imidazole (4.5 mmoles) in DMF (10 mL) was added *tert*.butyldimethylsilylchloride (0.338 g, 2.25 mmoles) and the reaction mixture was stirred with the exclusion of moisture for 18 hr. The solvent was removed under reduced pressure and the residue was purified on a silica gel column using $CHCl_3$-MeOH (33:1) to obtain 0.667g (83%) of 5′-O-*tert*.butyldimethylsilyl-N^6-*n*-propyladenosine as a colourless solid, m. p. 169-70°C.

5′-O-(*tert*.Butyldimethylsilyl)-2′,3′-bis-O-[[(β-cyanoethyl)thio]thiocarbonyl]-N^6-*n*-propyladenosine 2. Compound **1 (**0.498 g, 1.18 mmoles**)** was reacted with CS_2 (0.297 g, 3.96 mmoles) in the presence of 5 *N* aqueous NaOH (3 mL) in DMSO (5 mL) and alkylated with CH_3I (0.368 g, 2.59 mmoles). Chromatographic purification on a silica gel column using $CHCl_3$: MeOH (55:1) afforded 0.551g (72%) of the product **2**, m.p. 128-29°C, (Found: C, 45.74; H, 6.18; N, 11.55; S, 21.16. Calcd for $C_{23}H_{37}N_5O_4S_4Si$: C, 45.74; H, 6.17; N, 11.59; S, 21.23%, ^{1}H NMR ($CDCl_3$): δ, 0.03 (6H, s, Me_2Si), 0.95 (9H, s, Me_3CSi), 2.51 (3H, s, SCH_3), 2.58 (3H, s, SCH_3), 4.00 (2H, m, 5′-H), 4.51 (1H, m, 4′-H), 6.43-6.62 (3H, m, 1′, 2′ and 3′-H), 8.19 (1H, s, 8-H), 8.36 (1H, s, 2-H).

5′-O-(*tert*.Butyldimethylsilyl)-2′,3′-didehydro-2′, 3′-dideoxy-N^6-*n*-propyladenosine 3. Compound **2 (**0.432 g, 71 mmoles **)** was treated with tri-*n*-butyltin hydride (0.833 g, 2.86 mmoles) in the presence of azobisisobutyronitrile (0.05 g) in toluene (8 mL) at reflux. The solvent was evaporated and the residue was partitioned between acetonitrile and hexane. Evaporation of acetonitrile and purification of the residue by column chromatography using $CHCl_3$-MeOH (35:1) yielded 0.251g (90%) of the product as colourless solid; .m. p. 109-10°C (Found: C, 58.55; H, 8.03; N, 17.95. Calcd for $C_{19}H_{31}N_5O_2Si$: C, 58.57; H, 8.02; N,



1 **2** **3** **4**

Scheme I

17.97%); ^{1}H NMR(DMSO-d_6): δ 0.02 (6H, s, Me_2Si), 0.83 (9H, s, Me_3CSi), 3.70 (2H, d, *J*=3.94 Hz, 5′-H) 4.78-4.98 (1H, m, 4′-H), 6.22 (1H, dt, *J*=1.5, 6.14 Hz, 2′-H), 6.42 (1H, dt, *J*=1.5, 6.14 Hz, 3′-H), 6.95 (1H, m, 1′-H), 0.90 (3H, t, *J*=5.0Hz, $NHCH_2CH_2CH_3$), 1.52 (2H, m, CH_2), 2.89 (2H, t, *J*=5.0Hz, CH_2), 8.10 (1H, S, 8-H), 8.17 (1H, s, 2-H).

2′, 3′-Didehydro-2′, 3′-dideoxy-N^6-*n*-propyladenosine 4. A solution of compound **3** (0.236 g, .60 mmoles) in THF was deprotected with 1*M* solution of tetra-*n*-butylammonium fluoride (1.23 mL) in THF. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on a silica gel column using $CHCl_3$-MeOH (36:1) as the eluent to obtain 0.148g (89%) final yield of the product **4**. m.p. 151-52°C, (Found: C, 56.70; H, 6.23; N, 25.41. Calcd for $C_{13}H_{17}N_5O_2$: C, 56.71, H, 6.22; N, 25.43%); ^{1}H NMR (DMSO-d_6): δ 3.56 (2H, dd, *J*=4.0, 5.26Hz, 5′-H), 4.78-5.00 (2H, m, 4′-H and OH), 6.12 (1H, ddd, *J*=1.44, 1.74, 5.84 Hz, 2′-H), 6.45 (1H, ddd, *J*=1.44, 1.74, 5.84 Hz, 3′-H), 6.93 (1H, m, 1′-H), 0.92 (3H, t, *J*=5.0 Hz, $NHCH_2CH_2CH_3$), 1.56 (2H, m, CH_2), 2.98 (2H, t, *J*=5.0Hz, CH_2), 8.14 (1H, s, 8-H), 8.15 (1H, s, 2-H).

Acknowledgement

The author is thankful to UGC for the award of a major research project and the Head of the department for providing research facilities.

References

1 Hamamoto U, Nakashima H, Matsui A, Matsuda T, Ueda T & Yamamotor N, *Antimicrob Agents Chemother*, 31, **1987**, 907.

2 Lin T S, Schinazi R F & Prusoff W H, *Biochem Pharmacol,* 36, **1987**, 2713.

3 Mitsuya H & Broder S, *Proc Natl Acad Sci* USA, 83, **1986**, 1911.

4 Balzarini J, Kang G J, Dalal M, Herdewijn P, De Clerq E, Broder S & John D G, *Mol Pharmacol*, 32, **1987**, 162.

5 Classon B, Garegg P J & Samuelson B, *Acta Chem Scand Ser B*, 36, **1982**, 251.

6 Russel A F, Greenberg S & Moffatt J G, *J Am Chem Soc*, 95, **1973**, 4025.

7 Robins M J, Hansske F, Low N H & Park J I, *Tetrahedron Lett*, 25, **1984**, 367.

8 Jain T C, Jenkins I D, Russel A F, Verheyden J P H & Moffatt J G, *J Org Chem,* 39, **1974**, 30.

9 Barett A G M, Barton D H R & Bielski R J, *J Chem Soc Perkin Trans 1*, **1979**, 2378.

10 Verheyden J P & Moffatt J G, *Chem Abstr,* 81, **1974**, 63942.

11 Webb R R, Wos J A, Martin J C & Brodfuehrer P R, *Nucleosides Nucleotides*, 7, **1988**, 147.

12 Samukov V V & Ofitserov V L, *Bioorg Khim*, 9, **1983**, 132.

13 Hayashi T, Iwaoka T, Takeda N & Ohki E, *Chem Pharm Bull*, 26, **1978,** 1786.

14 Barrett A G M, Barton D H R, Bielski R & Mc Combie S W, *J Chem Soc Chem Commun,* **1977**, 866.