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A SHORT SYNTHESIS OF 2-VINYLINOSINE

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ABSTRACT

A short and practical synthesis of 2-vinylinosine from readily available materials is described.

INTRODUCTION

2-Substituted derivatives of inosine are conveniently prepared by the excellent procedure of Yamasaki *et al*[1], which consists of the condensation of the commercially available fermentation product 5-amino-1-ß-D-ribofuranosyl-4-imidazolcarboxamide (AICA-riboside) with aliphatic[1] or aromatic[2] esters. This simple method fails, however, in the case of alkali sensitive esters such as methyl acrylate. 2-vinylinosine **6** has, therefore, been prepared from guanosine by Nair *et al*[3] by a novel procedure which, however, requires a total of eight steps.

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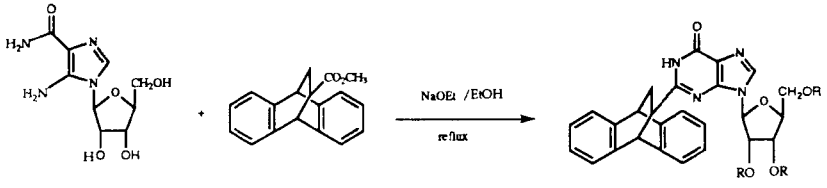
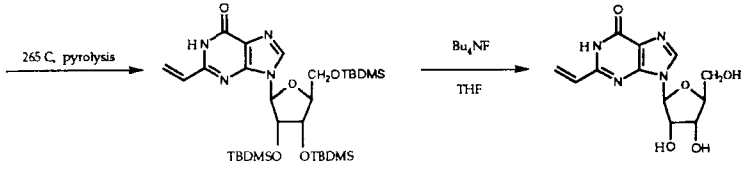
We wish to report that the Yamasaki procedure can be extended to the synthesis of **6** requiring but four steps by protecting the double bond of methyl acrylate as the known Diels-Alder adduct **2**[4,5] with anthracene. This methodology for protecting the sensitive vinyl substituent has been widely used[6,7], but, to our knowledge, not in the field of nucleosides.

The reaction of **1** and **2** proceeded in 90% yield in spite of the proximity of the large tetracyclic substituent attached to the reacting carboxylic ester group in **2**. Pyrolysis of the diastereomeric mixture **3** at 210° or 240° led to mixtures indicating that reversal of the Diels-Alder reaction and cleavage of the glycosidic bond had taken place. On the other hand, pyrolysis of the TBDMS ether **4** at 265° yielded the riboside **5** in 50% yield, which on desilylation afforded pure vinylinosine in 67% yield.



1 **2** **3**, R = H; **4**, R = TBDMS



5 **6**

EXPERIMENTAL:

2-[(9",10"-Dihydro-9",10"-ethano) anthracen-11"-yl] inosine (3).

To a solution of ethanolic sodium ethoxide [prepared from 0.82 g (36 mmol) of metallic sodium and 60 ml of ethanol]. was added, at 25°, 0.78 g (3 mmol) of AICA-riboside (**1**). Twenty minutes later 9,10-dihydro-9,10-(11-carboxy-ethano) anthracene (4.76 g, 18 mmol) was added, and the mixture was heated to reflux for 23 h. The ethanolic solution was evaporated to dryness and the residue redissolved in water. The pH was adjusted to 3.0 with I N HCl, the solution stirred at 25° for 5 h and the pH readjusted to pH=7 with 1 N NaOH. The mixture was concentrated to dryness in vacuo, and the crude product was purified by column chromatography (SiO_2, EtOAc/MeOH = 8:1) to give 1.28 g of **3** as a mixture of diasterisomers. Yield: 91%, m.p. 175-182°. The ^1H NMR (CD_3OD) is complex, indicating diastereomers: ∂, 8.19 and 8.06 (2s, 1H,H-8), 7.30-6.88 (8H, m, H_{arom}), 5.71 and 5.59 (1H, 2d, H-1'), 4.61-3.56 (7H, m, H-5',H-4', H-3',H-2', H-9", H-10"), 2.46(1H, m, H-11'), 2.40-1.96 (2H,m, H-12") ppm.

The TBDMS-ether **4** was prepared with TDBMS chloride and imidazole in DMF. Purification on silica gel gave 79% of pure product. ^1H NMR ($CDCl_3$) ∂, 8.31 and 8.30 (1H, 2s, H-8), 6.28 and 5.98 (1H, 2d, H-1'). Anal. Calcd.: for $C_{44}H_{66}N_4O_5$: C, 64.82; H, 8.16; N, 6.87. Found: C, 65.00; H, 8.29; N, 6.91.

2-Vinyl-2',3',5'-tri-O-(tert-butyldimethyl-silyl)inosine (5).

The nucleoside silyl ether **4**, (156 mg, 0.19 mmol) was placed in a glass tube connected to a 1 Torr vacuum, and the

tube was immersed into a bath maintained at 265°C (Dow Corning 555). Anthracene crystals and a colorless oil appeared above the level of the bath and 30 min later, the reaction was terminated. The total sublimate was purified by TLC (EtOH/benzene 1:2) to give 62 mg (51%) of pure **5**. ^{1}H NMR($CDCl_3$): ∂ 12.72 (1H, s, NH), 8.20 (1H, s, H-8), 6.73 [1H, dd, $J_{3,2}$=17.5 Hz, $J_{1,3}$=10.4 Hz, (CH_1=$CH_2\underline{H}_3$)], 6.64 [1H, d, $J_{2,3}$=17.3 Hz, (CH_1=$C\underline{H}_2H_3$)], 6.02 (1H, d, J=4.31 Hz, H'), 5.82 [1H, d, J=10.6 Hz,($C\underline{H}_1$=CH_2H_3)], 4.48 (1H, m, H-4'), 4.32 (1H, m, H-3'), 4.14 (1H, m, H-2'), 4.02(1H, dd, J_{gem}=11.36 Hz, J=3.48, H-5'), 3.82 (1H, dd, J_{gem}=11.56 Hz, H-5'), 0.99-0.90 (27H, 3s, t-Bu), 0.18-0.10 (18H, m, $6CH_3$). Anal. Calcd. for C_{30} $H_{56}N_4O_5Si_3$: C, 56.56; H 8.86; N, 8.79; Found: C, 56.45; H, 8.87, N, 8.66.

2-VINYLINOSINE (6)

1 N tetrabutylammonium fluoride in THF (0.4 ml) was added to 22 mg of the nucleoside **5** and the solution was stirred at 25°. for 1/2 h. Removal of the solvent produced a residue, which after TLC purification (EtOAc/MeOH = 2:1), gave 6.5 mg of a pure sample of 2-vinylinosine **6**, 67% yield, m.p. 223-228°C rep.[3] 225-230°C. ^{1}H NMR (CD_3OD): 8.25 (1H, s, H-8), 6.54 [1H, dd, $J_{2,3}$=17.1 Hz, $J_{1,3}$=10.85 Hz (CH_1=$CH_2\underline{H}_3$)], 6.41 [1H, dd, $J_{3,2}$=17.31 Hz, $J_{1,2}$=1.3 Hz (CH_1=$C\underline{H}_2H_3$)], 6.00 (1H, d, H-1', J=5.63 Hz), 5.79 [1H, dd, $J_{1,3}$=10.37 Hz, $J_{1,2}$=1.20 Hz, ($C\underline{H}_1$=CH_2H_3)], 4.67 (1H, m, H-4'), 4.34 (1H, m, H-3') 4.15 (1H, m, H-2'), 3.91 (1H, dd, J_{gem}=12.2 Hz, J=3.4 Hz, H-5'), 3.79 (1H. dd, J_{gem}=12.3 Hz, J=3.3 Hz, H-5').

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REFERENCES

1. Yamasaki, A., Kumashiro, I., and Takenishi, T.: *J. Organic Chem.* **1967**, *32*, 3258.

2. Imai, K., Marumoto, R., Kobayashi, K., Yoshioka, Y., and Toda, J.: *J. Chem. Pharm. Bull.* **1971**, *19*, 576.

3. Nair, V., Turner, G.A., Buenger, G.S., and Chamberlain, S.D.: *J. Org. Chem.* **1988**, *53*, 3051.

4. Bartlett, P.D. and Tate, F.A.: *J. Am. Chem. Soc* **1953**, *75*, 91.

5. Wawzonek, S. and Hallum, J.V.: *J. Org. Chem.* **1953**, *18*, 288.

6. Lasne, M-C., Ripoll, J-L.: *Synthesis* **1985**, 121

7. Ichihara, A.: *Synthesis* **1987**, 207.

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