Tetrahedron Letters No. 17, pp 1525 - 1528, 1973. Pergamon Press. Printed in Great Britain.

III. C-Nucleosides and related compounds.

The synthesis of D,L-3-(2α,3α-dihydroxy-4β-hydroxymethylcyclopent-1β-yl)-5-amino-1,2,4-triazole

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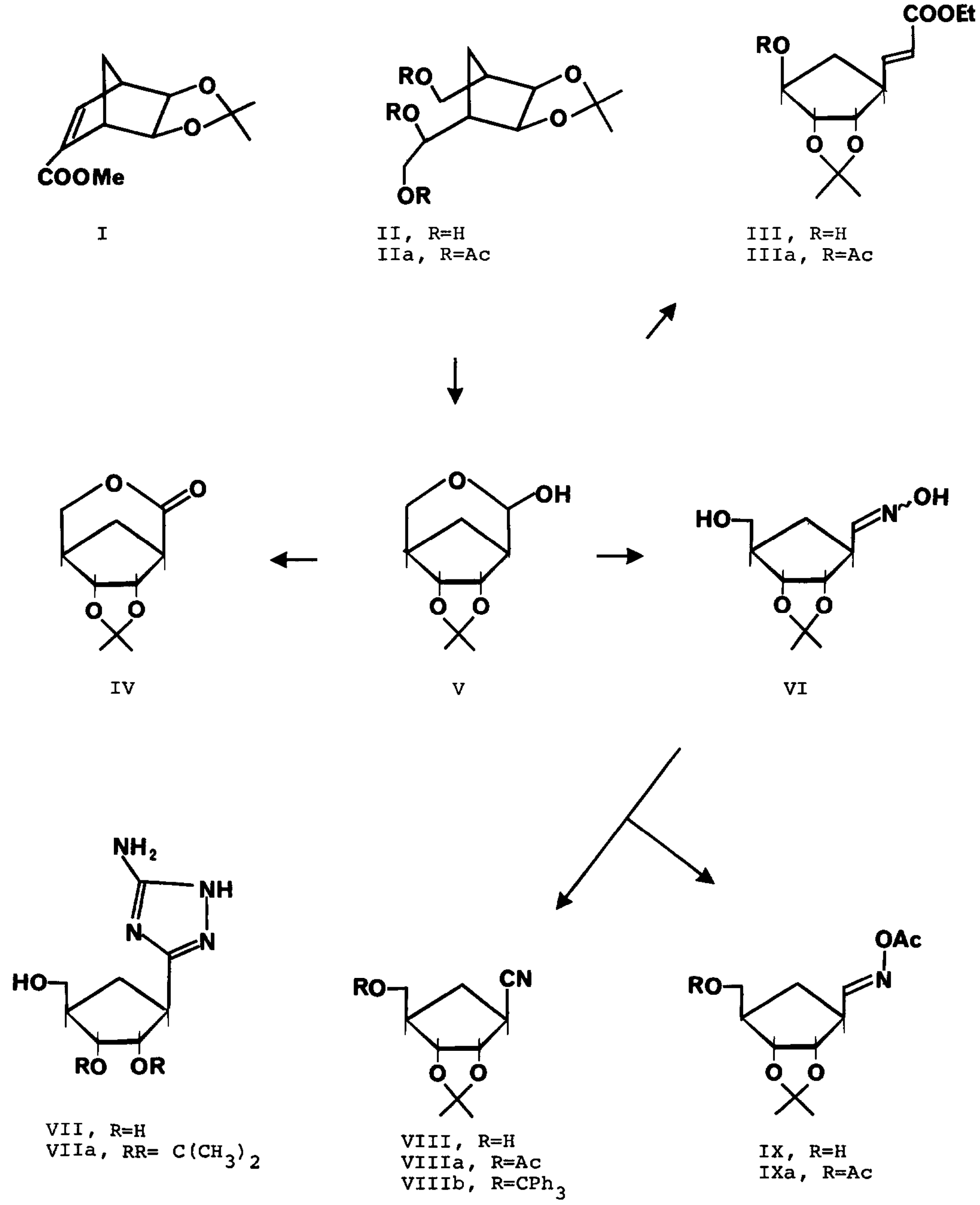
(Received in USA 2 January 1973; received in UK for publication 19 March 1973)

In the preceding paper, we described the synthesis of the norbornene derivative I, which is obtained in approximately 35% yield from cyclopentadiene and bromoacrylic acid. Ozonolysis, reduction of the ozonide with dimethyl sulphide, and further reduction of the intermediate keto aldehyde with sodium borohydride in iso-propanol gave triol II, characterized as its triacetate[1]. Periodate cleavage of triol II gave V[1], m.p. 109-112°, as a mixture of isomers. V was obtained in 75% from I when the intermediates were not purified.

The suitability of the hemiacetal V as a precursor to a range of modified C-nucleosides was explored. Hemiacetal V does not react cleanly with highly reactive Wittig reagents under standard conditions[2]. However, reaction with carbethoxymethylenetriphenylphosphorane in dimethylformamide[3] gave the oily trans-acrylic ester derivative III[1] in high yield. Reaction of V with derivatives of hydrazine under conditions which did not hydrolyze the isopropylidene group were not successful. With hydroxylamine, a 3:2 mixture of syn- and anti-oximes VI[1] was obtained in 60% yield after one hour reaction time. After 24 hours, the syn to anti ratio was 4:1 (determined by n.m.r.). Uncatalysed acetylation with acetic anhydride at room temperature for



I

II, R=H
IIa, R=Ac

III, R=H
IIIa, R=Ac

IV

V

VI

VII, R=H
VIIa, RR= $C(CH_3)_2$

VIII, R=H
VIIIa, R=Ac
VIIIb, R=CPh_3

IX, R=H
IXa, R=Ac

8 minutes[4] gave a mixture of oily syn-oxime acetate IX and nitrile VIII which were separated by t.l.c. Nitrile VIII formed an oily acetate VIIIa[1], and a trityl derivative VIIIb[1], m.p. 139-140°. The syn-oxime acetate IX was characterized as the oily diacetate IXa[1].

Oxidation of hemiacetal V with Collins reagent[5] or Fetizon's reagent[6] gave lactone IV[1], m.p. 128-129°. Treatment of IV with one equivalent of aminoguanidine bicarbonate in refluxing pyridine[7] for 10 hours gave upon evaporation in good yield (n.m.r.) oily VIIa. Purification on t.l.c. gave crystalline VIIa, which upon recrystallization from hot acetone melted at 206-207°[1]. Hydrolysis in 4% aqueous trifluoroacetic acid gave oily VII[1].

The spectral and chemical properties of VII and VIIa were similar to those of a model compound derived from butyrolactone[7]. The mass spectrum of VIIa showed strong peaks at 254 (M^+), M^+-CH_3, M^+-CH_2O and M^+-CH_3-CH_2O. The mass spectrum of VII showed M^+ at 214, and a strong peak at 111, which was common to VII, VIIa and the model compound derived from butyrolactone. This peak possibly corresponds to protonated 3-amino-5-vinyl-1,2,4-triazole.

We wish to thank the National Research Council of Canada for financial support. Grant Reader gratefully acknowledges receipt of National Research Council of Canada Scholarship, 1971-73.

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