

Number 18
1988

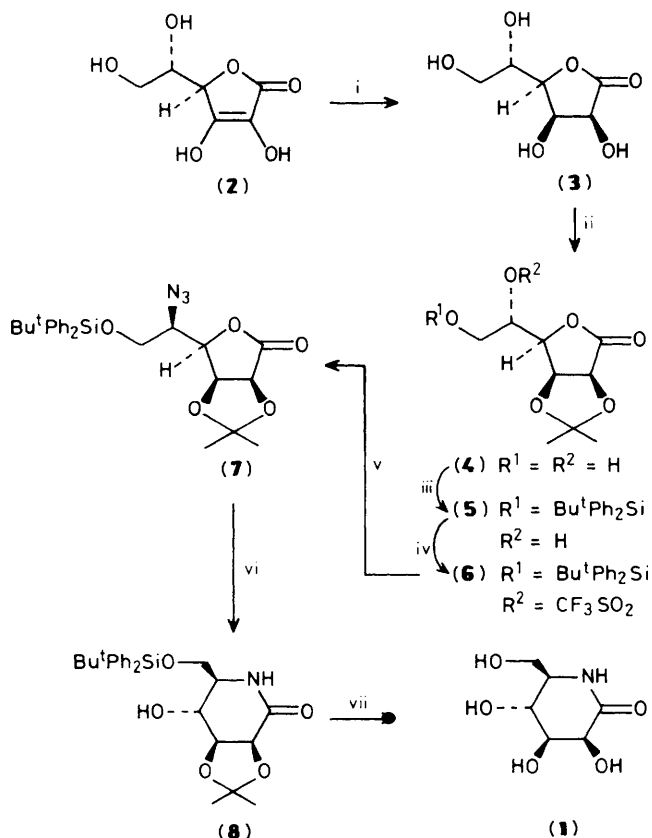
Enantiospecific Synthesis of D-Mannono- δ -lactam from Vitamin C

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An eight-step synthesis of the glycosidase inhibitor D-mannono- δ -lactam from vitamin C is described.

Very recently, the potential of polyhydroxylated δ -lactams as a new class of glycosidase inhibitors has been indicated.¹ D-Mannono- δ -lactam (**1**), previously formed by microbial



Scheme 1. Reagents: i, Pd, H₂, H₂O (100%); ii, Me₂CO/HCl then aq. AcOH (68%); iii, Bu^tPh₂SiCl, pyridine (95%); iv, (CF₃SO₂)₂O, CH₂Cl₂, pyridine (92%); v, Bu₄ⁿNN₃, tetrahydrofuran (76%); vi, H₂, Pd(OH)₂, EtOAc (88%); vii, aq. CF₃CO₂H (85%).

oxidation of nojirimycin B, is a potent inhibitor of rat epididymal α -mannosidase and of apricot β -glucosidase.² This communication reports the first enantiospecific synthesis of (**1**) from a non-carbohydrate precursor, vitamin C (**2**).

The strategy involves a stereoselective hydrogenation from the less hindered side of the enediol (**2**) to secure the chirality of the resultant C-2 and C-3 hydroxy groups and introduction of nitrogen with inversion of configuration at C-5. Thus hydrogenation of (**2**) gave stereospecifically the saturated lactone (**3**),³ which was bis-acetonated and then partially hydrolysed to the diol (**4**), † m.p. 130–132 °C (Scheme 1). The primary hydroxy group in (**4**) was protected by *O*-silylation to give (**5**), $[\alpha]_D^{20} + 61.1^\circ$ (c 1.4 in CHCl₃), which was subsequently esterified to give the trifluoromethanesulphonate (**6**). A nucleophilic displacement reaction of (**6**) with tetrabutylammonium azide afforded the azido lactone (**7**), m.p. 97–98 °C; $[\alpha]_D^{20} + 6.5^\circ$ (c 1.4 in CHCl₃), which was hydrogenolysed to form the protected lactam (**8**), $[\alpha]_D^{22} + 35.8^\circ$ (c 0.6 in CHCl₃). Hydrolysis then furnished D-mannono- δ -lactam (**1**), m.p. 170–172 °C; $[\alpha]_D^{22} + 2.0^\circ$ (c 0.8 in water) {lit.² m.p. 169–170 °C, $[\alpha]_D^{20} + 1.6^\circ$ (c 1.0 in water)}.

Synthetic applications of vitamin C, enhanced by its cheapness and availability, should attract more attention from organic chemists.

I thank Professor J. K. Sutherland for discussion.

Received, 24th May 1988; Com. 8/02078G

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† All new compounds gave satisfactory analytical and spectral data.