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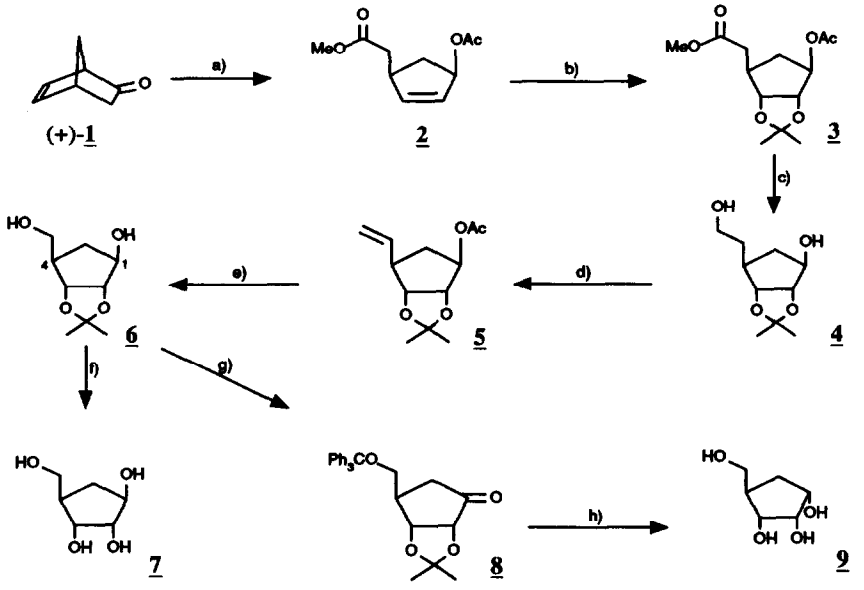
SYNTHESIS OF α- AND β-D-CARBARIBOFURANOSE FROM (+)-NORBORN-5-EN-2-ONE

Christoph Marschner, Gerhard Penn+, and Herfried Griengl*
Institute of Organic Chemistry, Graz University of Technology
Stremayrgasse 16, A-8010 Graz, Austria

Abstract: *α- and β-D-carbaribofuranose 7 and 9, resp., are prepared from (+)-norborn-5-en-2-one in a 6-step (8-step, resp.) synthetic sequence in 27% (13%, resp.) overall yield.*

Carbasugars, where the ring oxygen of the acetal moiety of carbohydrates is replaced by a CH_2-group, are an area of intense research due to their biological properties. Besides carbahexopyranoses[1], carbapentofuranoses[2,3] have been studied mainly in connection with carbocyclic nucleosides[4]. As part of a larger program for the synthesis of carbocyclic analogues of carbohydrates we report here a short access to α- and β-D-carbaribofuranose from (+)-norborn-5-en-2-one. α- and β-D-carbaribofuranose have been prepared recently from carbohydrates[2,3].



Reaction conditions: a) i: H_2O_2/NaOH/H_2O/ether; ii: MeI/DMF; iii: Ac_2O/pyridine/DMAP/CH_2Cl_2 b) i:OsO_4/NMNO/acetone; ii: 2,2-dimethoxypropane/ 4-TosOH c) $LiAlH_4$/ether/0°C d) i: $Ph_3P/Br_2/Et_3N$; ii: 2-nitrophenylselenocyanate/$NaBH_4$/EtOH; iii: H_2O_2/THF; iv: Ac_2O/pyridine/DMAP/CH_2Cl_2 e) i: OsO_4/$NaIO_4$/H_2O/ether; ii: $LiAlH_4$/ether f) BCl_3/CH_2Cl_2/-78°C g) i: triphenylchloromethane/pyridine/DMAP/CH_2Cl_2; ii: PDC h) i: $NaBH_4$/MeOH/-20°C; ii: BCl_3/CH_2Cl_2/-78°C.

+ Present adress: Sandoz Pharma AG, CH-4002 Basle, Switzerland

Starting with enantiomerically pure (+)-norborn-5-en-2-one 1[5] an alkaline *Baeyer-Villiger* reaction[6] was performed. After esterification with iodomethane and acetylation[7] the cyclopenteneester 2 was obtained (71% yield). Treatment of 2 with OsO_4/N-methylmorpholine-N-oxide[8] gave the corresponding diol, which was converted to the dioxolane derivative 3 in 77% yield. Diester 3 was reduced to the diol 4 with $LiAlH_4$ (97%). Bromination of 4 with $Ph_3P/Br_2/Et_3N$[9] in CH_2Cl_2, followed by treatment of the resulting bromide with 2-nitrophenylselenocyanate/$NaBH_4$ in ethanol and reaction with H_2O_2[10] in THF afforded an olefin, the hydroxy group of which was acetylated to give 5 (61%). Reaction of 5 with $OsO_4/NaIO_4$[11] in a biphasic ether/water system gave the corresponding aldehyde which was readily reduced to the key intermediate 6 using $LiAlH_4$ (88%). Deprotection of 6 with BCl_3[12] in CH_2Cl_2 yielded the desired β-D-carbaribofuranose 7[2a,13,14] (95%). In order to obtain the α-derivative, inversion of configuration at C-1 was required. Thus, the primary hydroxy group of 6 was protected selectively with triphenylchloromethane. After pyridinium dichromate oxidation the ketone 8 (77%) was reduced with $NaBH_4$ at -20°C to give the α-isomer exclusively. Finally, deprotection with BCl_3 in CH_2Cl_2 yielded the α-D-carbaribofuranose 9[2b,13,14] (58%). Choice of (-)-norborn-5-en-2-one[5] as starting material leads to the corresponding carbafuranoses of the L-series.

The approach described is versatile: all carbapentofuranoses can be correlated retrosynthetically to norborn-5-en-2-one. The synthetic strategy outlined is being pursued in this laboratory.

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13. All novel compounds are fully characterized using NMR, IR and elemental analysis.
14. Optical rotations and spectral data of the carbafuranoses are as follows 7: $[\alpha]_D^{23}$ 8.0 (c 2.9, CH_3OH); ^{1}H-NMR (CD_3OD) δ 1.23-1.32 (1H,m), 2.03-2.13 (1H,m), 2.22-2.28 (1H,m), 3.54 (1H,dd,J=6.5Hz,10.6Hz), 3.66-3.74 (2H,m), 3.87-3.90 (1H,dd,J=5.5Hz,5.5Hz) 3.90-4.05 (1H,dd,J=6.5Hz,11.4Hz); ^{13}C-NMR(CD_3OD) δ 33.94, 46.35, 65.59, 74.86, 77.04, 79.92. 9: $[\alpha]_D^{25}$ 33.3 (c 0.4, CH_3OH), ^{1}H-NMR (CD_3OD) δ 1.56-1.64 (1H,m), 1.96-2.04 (1H,ddd,J=2.6Hz,9.8Hz,14.1Hz), 2.35-2.40 (1H,m), 3.50-3.61 (2H,m), 3.96-4.02 (2H,m), 4.18-4.22 (1H,m); ^{13}C-NMR (CD_3OD) δ 34.02, 48.44, 64.92, 74.72, 75.55, 75.81.

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