Tetrahedron Letters,Vol.23,No.9,pp 1013-1014,1982 0040-4039/82/091013-02$03.00/0
Printed in Great Britain

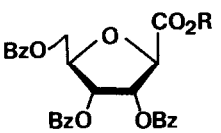
A NOVEL ELIMINATION REACTION OF 3,4,6-TRI-O-BENZOYL-2,5-ANHYDRO-D-ALLONIC ACID RIBOSYL → 2'-DEOXYRIBOSYL CONVERSION

L J S Knutsen, B D. Judkins, R F. Newton and D.I C Scopes*
Chemical Research Department, Glaxo Group Research Ltd ,
Ware, Hertfordshire, SG12 ODJ, England

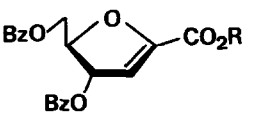
SUMMARY 3,4,6-Tri-O-benzoyl-2,5-anhydro-D-allonic acid (1a) has been converted into 2'-deoxy-C-nucleoside precursors *via* the novel dihydrofurans (2b) and (2c).

Although 2'-Deoxyribo-C-nucleosides represent an important class of potential antiviral and antitumour agents, relatively few examples of this structural type have been reported[1]. During the course of our studies on the synthesis of C-nucleosides from 3,4,6-tri-O-benzoyl-2,5-anhydro-D-allonic acid[2] (1a) we have discovered a useful elimination reaction which allows easy access *inter alia* to 2'-deoxyribo-C-nucleoside precursors.

Treatment of (1a) with 2-chloro-N-methylpyridinium iodide[3] (2 equiv) in the presence of triethylamine (3 5 equiv) and benzyl alcohol (1.5 equiv.) afforded the novel α,β-unsaturated ester[4] (2b) in 84% yield None of the straightforward coupled product (1b) was formed. However, (1b) was the product when only one equivalent of each of triethylamine, benzyl alcohol and the coupling agent was used Attempts to generate (2b) directly from (1b) were unsuccessful



(1a) R = H
(1b) R = CH_2Ph

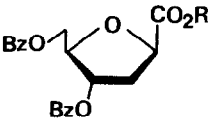


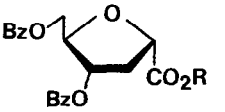
(2a) R = H
(2b) R = CH_2Ph
(2c) R = $CH_2CH_2SiMe_3$

By using 2-trimethylsilylethanol[5] in place of benzyl alcohol, the corresponding α,β-unsaturated ester (2c) ($[\alpha]_D^{21}$+179 3° ($CHCl_3$)) was obtained (73%) Attempts to prepare the acid (2a) *via* treatment of (2c) with n-Bu_4NF/THF gave instead 5-benzoyloxymethylfuran-2-carboxylic acid (93%)

Catalytic hydrogenation of (2b) (Pd/C, ethanol/THF) afforded an anomeric mixture of the acids (3β) and (3α) (4 1, 97%) Similar hydrogenation of (2c) gave a mixture of the esters (4β) and (4α) in 90% yield This mixture could be separated by chromatography on silica gel and each anomer deprotected (n-Bu_4NF/THF) to provide the pure acids (3β)[1d]

($[\alpha]_D^{21}$+29 6° ($CHCl_3$)) and (3α) ($[\alpha]_D^{21}$+39 9° ($CHCl_3$))





(3β) R = H (3α)

(4β) R = $CH_2CH_2SiMe_3$ (4α)

The sequence (1a) → (2b) → (3) thus provides a high yielding direct conversion of a ribose to 2-deoxyribose system[6] suitable for application to the syntnesis of 1'- and 2'-modified C-nucleosides[7]

A typical procedure is as follows 3,4,6-Tri-O-benzoyl-2,5-anhydro-D-allonic acid (15 0g, 30 6mmol) was dissolved in acetonitrile (600ml) and 2-chloro-N-methylpyridinium iodide (15 5g, 60 6mmol) was added with stirring Triethylamine (10 8g, 107 1mmol) was introduced and stirring continued for 1 5h before benzyl alcohol (5 0g, 46 0mmol) was added After standing overnight, the solution was evaporated to a gum which was taken up in ethyl acetate (400ml) and washed with 0 02N hydrochloric acid (300ml). The organic layer was separated, dried ($MgSO_4$), treated with activated charcoal, and then evaporated to a gum which was subjected to flash chromatography on silica gel Elution with benzene gave the [4S,5R]-4-benzoyloxy-5-benzoyloxy-methyl-4,5-dihydro-2-furancarboxylic acid, benzyl ester (2b) 11.7g (84%) m p 112 - 114°C (Cyclohexane) ($[\alpha]_D^{22}$+196 2° ($CHCl_3$))

ACKNOWLEDGEMENTS

We thank Dr J H Hunt and Dr G Klinkert for n m r spectra and optical rotations and Mr S Krolik for mass spectra

REFERENCES AND NOTES

1 See for example a) A Matsuda, C K. Chu, U Reichman, K. Pankiewicz, K A. Watanabe, and J J Fox, J. Org Chem , 46, 3603 (1981), b) T. Huynh-Dinh, A Kolb, C Gouyette, J Igolen and S Tran-Dinh, J. Org Chem , 40, 2825 (1975), c) T Huynh-Dinh, R.S Sarfati, C. Gouyette, J. Igolen, E Bisagni, J M Lhoste and A Civier, J Org Chem , 44, 1028 (1979), d) A M Mubarak and D M Brown, Tetrahedron Lett , 22, 683 (1981)

2. M Bobek and J Farkas, Coll. Czech Chem Commun , 34, 247 (1969).

3. T. Mukaiyama, M Usui, E Shimada, and K Saigo, Chem Lett , 10, 1045 (1975)

4 ^1H NMR ($CDCl_3$) δ4 64 (d, H_6), 5 07 (dt, H_5), 5 30 (AB, CH_2Ph), 6 12 (t, H_4), 6 20 (d, H_3) ^{13}C NMR ($CDCl_3$) δ63 8 (C_6), 67 3 (CH_2Ph), 78 8 (C_4), 84 8 (C_5), 107 5 (C_3), 152.7 (C_2), 159 2 (C_1)

5 P. Sieber, Helv Chim Acta, 60, 2711 (1977).

6. M J. Robins and J S Wilson, J. Am. Chem Soc , 103, 932 (1981), R A Lessor and N. J Leonard, J Org Chem., 46, 4300 (1981) have recently reported conversions of ribo- into 2'-deoxyribonucleosides

7 All new compounds have analytical/m s and n m r spectral data consistent with the assigned structures

(Received in UK 21 Decemb er 1981)