

This article was downloaded by:

On: 27 January 2011

Access details: *Access Details: Free Access*

Publisher *Taylor & Francis*

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



## Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

## Synthetic Approach to D-Psicofuranosyl Nucleosides and Their 1-Deoxy Analogues

Annie Brouiller<sup>a</sup>; Anne-Dominique Lespinasse<sup>a</sup>; Jean-Marc Ricca<sup>a</sup>

<sup>a</sup> Université Lyon I, ESCIL, Laboratoire de Chimie Organique II, Villeurbanne, France

**To cite this Article** Brouiller, Annie, Lespinasse, Anne-Dominique and Ricca, Jean-Marc(1988) 'Synthetic Approach to D-Psicofuranosyl Nucleosides and Their 1-Deoxy Analogues', *Nucleosides, Nucleotides and Nucleic Acids*, 7: 5, 675 — 678

**To link to this Article:** DOI: 10.1080/07328318808056307

**URL:** <http://dx.doi.org/10.1080/07328318808056307>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

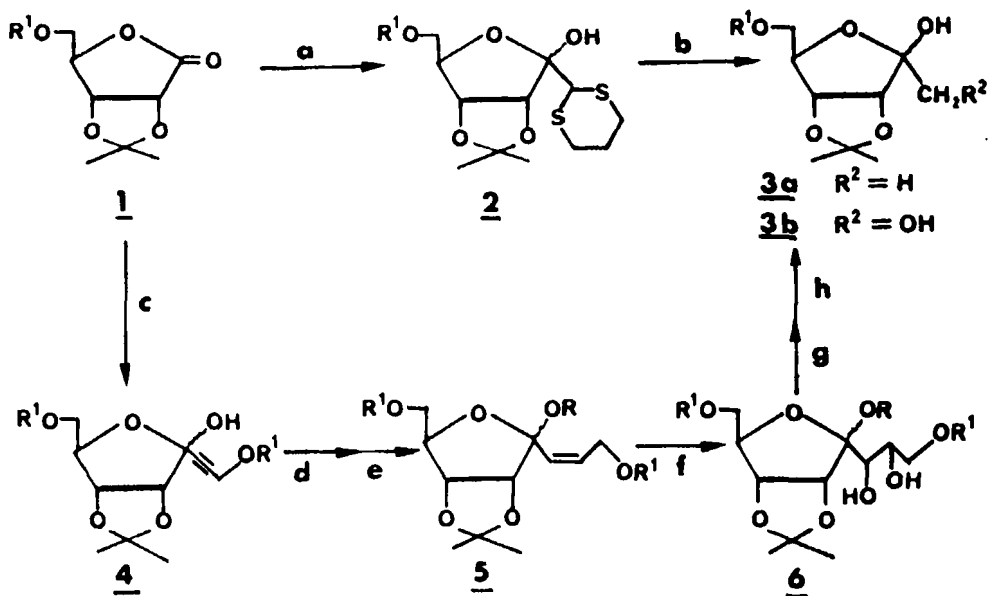
**SYNTHETIC APPROACH TO D-PSICOFURANOSYL  
NUCLEOSIDES AND THEIR 1-DEOXY ANALOGUES.**

Annie Grouiller\*, Anne-Dominique Lespinasse and Jean-Marc Ricca  
Université Lyon I, ESCIL, Laboratoire de Chimie Organique II  
43 Boulevard du 11 Novembre 1918 - 69622 Villeurbanne (France)

**Abstract:** The sugar moiety of ketofuranosyl nucleosides derived from D-psicofuranose and 1-deoxy-D-psicofuranose are readily available through nucleophilic addition of D-ribo-1,4-lactone with lithiated reagents.

As a part of our work on the synthesis of ketofuranosyl nucleosides, conveniently substituted D-psicofuranose and 1-deoxy-D-psicofuranose were required. Their 1-halo<sup>1</sup> and 2,6-anhydro derivatives<sup>2,3</sup> have been previously reported. The corresponding halogenoses were also prepared in many steps for their use in conventional nucleoside synthesis<sup>4-8</sup>. We now describe a new synthesis route for the target compounds 3a and 3b from inexpensive commercially available D-ribo-1,4-lactone.

Nucleophilic addition of 2,3-O-isopropylidene-5-O-tetrahydropyranyl-D-ribonolactone (1) with the carbanion generated from 2-lithio-1,3-dithiane afforded the dithioacetal 2 in 90 % yield. Any standard method<sup>9-11</sup> for conversion of a dithianyl group such as that in 2 into an aldehyde group was unsuccessful. In contrast, 2 readily underwent desulfurization by hydrogen-saturated Raney nickel in boiling ethanol to give the protected 1-deoxy-D-psicofuranose 3a in 60 % yield. Reaction of 1 with methyllithium in tetrahydrofuran initially at -78°C and later at 0 °C gave in 93 % yield a chromatographically homogeneous oil identical with 3a.



a. 2-lithio-1,3 dithiane, THF, -78°C. b. Raney nickel, EtOH,  $\Delta$ .  
 c. Li-C $\equiv$ C-CH<sub>2</sub>OTHP, THF, -78 °C. d. MeI, Ag<sub>2</sub>O. e. Pd/SO<sub>4</sub>Ba, NEt<sub>3</sub>,  
 H<sub>2</sub>, AcOEt. f. OsO<sub>4</sub> (catalytic), Me<sub>3</sub>N-O-*tert*- BuOH,  $\Delta$ . g. NaIO<sub>4</sub>, aq.  
 MeOH. h. NaBH<sub>4</sub>, MeOH.

Similar nucleophilic addition of **1** with the carbanion generated from lithium 1-O-tetrahydropyranyl-2-propynide afforded the pentofuranosyl-propyne **4** in quantitative yield. Hydrogenation of **4** using palladium on barium sulfate was performed at room temperature to afford the vinyl compound **5**. *Cis* dihydroxylation of **5** provided the diol **6** in 70 % yield. Periodate oxydation of **6**, followed by reduction of the intermediate aldehyde with sodium borohydride, produced substituted D-psicofuranose **3b** in 75 % overall yield.

The assignment of the structures to compounds **2** - **6** was based upon elemental analysis and magnetic resonance spectroscopy (proton and carbon 13).

a) Absolute configuration of the anomeric carbon in **3a** issued from reaction of **1** with methyllithium was determined to be  $\beta$  from <sup>13</sup>C-n.m.r. studies and comparison with similar D-psicofuranosyl derivatives<sup>12,13</sup>. This R chirality was in agreement with the stereoselectivity observed in the reaction of sugar lactone with lithiated heterocycles<sup>14</sup>.

b) The product from reaction of 1 with 2-lithio-1,3-dithiane was a mixture of the  $\alpha$  and  $\beta$ -anomers of 2. Its  $^{13}\text{C}$ -n.m.r. spectrum indicated a ratio of 56 %  $\alpha$  / 44 %  $\beta$ , based on the intensities of the signals relative to the anomeric and isopropylidene carbons. A similar behavior of  $\gamma$ -valerolactone had been previously observed by D. Horton et al.<sup>15</sup>.

c) The quantitation for the anomeric mixture of 4 was determined from the same criteria as for 2 and gave an identical result.

d) The analytical data of 3b are in agreement with those described by other authors for various substituted  $\alpha$  and  $\beta$ -D-psicofuranoses<sup>12,16,17</sup>.

In conclusion, this work provides versatile intermediates for the synthesis of various nucleosides which is actually under investigation. The 1-deoxy-  $\beta$  -D-psicofuranosyl nucleosides are particularly worthwhile on account of their resemblance with the biologically important 2'-deoxynucleosides.

## REFERENCES

1. J. Farkas, Collect. Czechoslov. Chem. Commun., **31**, 1535 [1966].
2. K. Heyns, H. R. Neste and J. Thiern, Chem. Ber., **11**, 891 [1981].
3. I. Izquierdo Cubero and D. Garcia Poza, Carbohydr. Res., **138**, 139 [1985].
4. E. J. Reist, P. A. Hart, B. R. Baker and L. Goodman, J. Org. Chem., **27**, 1722 [1962].
5. J. Farkas and F. Sorm, Collect. Czech. Chem. Commun., **32**, 2663 [1967].
6. H. Hrebabecky, J. Farkas and F. Sorm, Ibid., **39**, 2115 [1974].
7. E. J. Prisbe, J. Smejkal, J. P. H. Berheyden and J. G. Moffatt, J. Org. Chem., **41** [10], 1836 [1976].
8. A. Grouiller and J. Chattopadhyaya, Acta. Chem. Scand. B **38** (5), 367 [1984].
9. B. T. Grobel and D. Seebach, Synthesis, **6**, 357 [1977].
10. M. Balogh, A. Cornélis and P. Laszlo, Tetrahedron Lett., **31**, 3313 [1984].
11. W. A. Szarek, A. Zamojski, K. N. Tiwari and E. R. Ison, Tetrahedron Lett., **33**, 3827 [1986].
12. P. C. M. Herve du Penhoat and A. S. Perlin, Carbohydr. Res., **36**, 111 [1974]; Ibid. **71**, 149 [1979].
13. C. S. Wilcox, G. W. Long and H. Suh, Tetrahedron Lett., **4**, 395 [1984].
14. H. Ogura, K. Furuhashi and H. Takahashi, Nucleic Acids Res., Spec. Publ. n° 3, s23 [1977].
15. D. Horton and W. Priebe, Carbohydr. Res., **94**, 27 [1981].
16. K. Heyns and R. Reinhold, Liebigs Ann. Chem., 122 [1981].
17. B. Aebischer, J. H. Bieri, R. Prewé and A. Vasella, Helv. Chim. Acta., **65**, 2251 [1982].

## 18. Indicative structural data for compounds N°:

(Primed and second numbers are respectively used for atoms in the tetrahydropyranyl and 1,3-dithiane rings.  $^1\text{H}$  and  $^{13}\text{C}$  n.m.r. spectra were recorded at 300.13 and 75.47 MHz - Brucker).

**2:** oil;  $[\alpha]_D^{20}$  -10.3° (c 1, chloroform);  $\nu_{\text{max}}$  film 3400 (OH), 1380 and 1370 ( $\text{CMe}_2$ ) and  $750\text{ cm}^{-1}$  ( $\text{CH}_2\text{-S-CH}_2$ );  $^1\text{H-n.m.r.}$  ( $\text{CDCl}_3$ ):  $\delta$  5.06 (s, 1, OH), 4.92-4.53 (m, 1, H-2), 4.62 (s, 1, H-2'), 4.38-4.17 (m, 1, H-3), 3.98-3.20 (m, 6, H-4, 5, 1', 5'), 3.14-2.54 (m, 4, H-4'', 6''), 2.19-1.97 (m, 2, H-5''), 1.89-1.43 (m, 6, H-2', 3', 4'), 1.58 and 1.47 (2s, 6,  $\text{Me}_2$ );  $^{13}\text{C-n.m.r.}$ :  $\delta$  115.4 and 112.7 ( $\text{CMe}_2$  for  $\alpha$  and  $\beta$ ), 108.9 and 105.5 (C-1 for  $\alpha$  and  $\beta$ ), 98.9 (C-1'), 86.2, 85.2, 81.6 (C-2, 3, 4), 68.1 (C-5'), 62.7, 62.3, 62.1, 61.9 (C-5), 49.3, 48.9, 48.4, 47.6 (C-2''), 31.8, 25.6, 19.1 (C-2', 3', 4'), 29.8, 27.6, 25.4 (C-4'', 5'', 6''), 26.6 and 25.1 ( $\text{Me}_2$ ).

**3a**  $\beta$ , oil;  $[\alpha]_D^{20}$  -22.6° (c 0.012, chloroform);  $^1\text{H-n.m.r.}$  ( $\text{CDCl}_3$ ):  $\delta$  5.0-4.78 (m, 2, H-3, 4); 4.59-4.55 (m, 1, H-5), 4.09-4.03 (m, 2, H-6), 3.95-3.89 (t, 1, H-1'), 3.70-3.59 (m, 2, H-5'), 1.89-1.89 (m, 6, H-2', 3', 4'), 1.62 (s, 6,  $\text{ipCH}_3$ ), 1.44 (s, 3, H-1);  $^{13}\text{C-n.m.r.}$ :  $\delta$  112.4 ( $\text{CMe}_2$ ), 106.8 (C-2), 98.9 (C-1'), 87.6, 84.5, 82.6 (C-3, 4, 5), 88.7 (C-5'), 62.4, 61.9 (C6), 30.0, 25.0, 19.2 (C-2', 3', 4'), 26.6 and 25.1 ( $\text{Me}_2$ ), 21.7 (C-1).

**4:** oil;  $[\alpha]_D^{20}$  28.2° (c 1, chloroform);  $\nu_{\text{max}}$  film 3350 (OH), 2250 ( $\text{C}\equiv\text{C}$ ), 1380 and 1370  $\text{cm}^{-1}$  ( $\text{CMe}_2$ );  $^1\text{H-n.m.r.}$  ( $\text{CDCl}_3$ ):  $\delta$  5.11-4.72 (m, 3, H-2, 3, OH), 4.68-4.39 (m, 3, H-4,  $\text{C}\equiv\text{C-CH}_2\text{O}$ ), 4.27-3.86 and 3.80-3.53 (2m, 8, H-6, 1', 5'), 1.96-1.40 (m, 12, H-2', 3', 4'), 1.69 and 1.51 (2s, 6,  $\text{ipCH}_3$ );  $^{13}\text{C-n.m.r.}$ :  $\delta$  115.3 and 113.1 ( $\text{CMe}_2$  for  $\alpha$  and  $\beta$ ), 101.6 and 99.3 (C-1 for  $\alpha$  and  $\beta$ ), 98.9 (C-1'), 87.9, 84.9, 82.3 (C-2, 3, 4), 74.0 ( $\text{C}\equiv\text{C}$ ), 68.3 (C-5'), 61.9 (C-5), 30.1, 25.3, 18.9 (C-2', 3', 4'), 26.5 and 25.9 ( $\text{CMe}_2$ ).