This article was downloaded by:

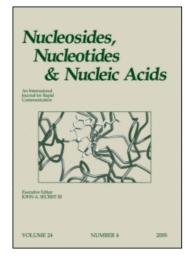
On: 26 January 2011

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

# *Ex-Novo* and *Revisum* Procedures for the Preparation of C-1' Branched Nucleosides

C. Chatgilialoglu<sup>a</sup>; C. Costantino<sup>a</sup>; C. Ferreri<sup>ab</sup>; T. Gimisis<sup>a</sup>; A. Romagnoli<sup>a</sup>; R. Romeo<sup>ac</sup>
<sup>a</sup> I. Co. C. E. A.- C. N. R., Bologna, Italy <sup>b</sup> Dipartimento di Chimica Organica e Biologica, Universita di Napoli "Federico IT", Napoli, Italy <sup>c</sup> Dipartimento Farmaco Chimico, Universita di Messina, Messina, Italy

To cite this Article Chatgilialoglu, C., Costantino, C., Ferreri, C., Gimisis, T., Romagnoli, A. and Romeo, R.(1999) 'Ex-Novo and Revisum Procedures for the Preparation of C-1' Branched Nucleosides', Nucleosides, Nucleotides and Nucleic Acids, 18: 4, 637 - 639

To link to this Article: DOI: 10.1080/15257779908041524 URL: http://dx.doi.org/10.1080/15257779908041524

#### 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.

## EX-NOVO AND REVISUM PROCEDURES FOR THE PREPARATION OF C-1' BRANCHED NUCLEOSIDES

C. Chatgilialoglu, C. Costantino, C. Ferreri, \*,1a T. Gimisis, A. Romagnoli and R. Romeo<sup>1 b</sup>

I.Co.C.E.A.- C.N.R., Via P. Gobetti 101, 40129 Bologna (Italy)

**ABSTRACT**: C-1' acylated derivatives of 2'-deoxyuridine were obtained either by revising the existing procedures or by introducing a new methodology.

C-1' branched nucleosides have attracted attention for their pharmacological and biological applications. In particular, the *tert*-butyl ketone at the C-1' position of 2'-deoxyuridine (7 R = t-Bu) has recently been applied to model studies of DNA damage.  $^{2,3}$  In connection with these studies, we wish to briefly report the *revisum* and *ex novo* procedures for the synthesis of 7, via derivatives  $3^4$  and 6, respectively.

Scheme 1 summarizes our innovations to the published strategies<sup>5,6</sup> for the preparation of 3. The steps i and vi were carried out by using (TMS)<sub>3</sub>SiH as the radical based reducing agent.<sup>7</sup> The reaction products precipitated from the reaction mixture by the addition of n-pentane, thus overcoming tedious purification procedures and contamination problems due to toxic tin compounds. In the coupling step between the sugar and base moieties, only the furanose form of the sugar is able to react. Therefore, by steps vii and viii, we obtained tribenzoylated 3-deoxyfructose 5 in good yield exclusively in the furanose form. It is worth noting that the coupling between the sugar and uracil (step x) gave an anomeric  $\alpha/\beta$  ratio of 5/1, which was recognized by comparison with the <sup>1</sup>H NMR spectrum of the pure  $\beta$ -anomer. This result is in conflict with the previous report.<sup>6</sup> The protection of 3a has been accomplished by a novel PdCl<sub>2</sub>-catalyzed procedure (step iii), which utilizes the less expensive TIPDS hydride.

SCHEME 1 Reagents and conditions: i) (TMS)<sub>3</sub>SiH, AlBN, benzene, 80°C, 3 hrs (92% yield); ii) MeONa, MeOH, r.t.; iii) TIPDS-H<sub>2</sub>, CCl<sub>4</sub>, 2% PdCl<sub>2</sub> then 0.15M of **3a** in Py, -35°C to r.t./overnight (33% yield of **3b** + 52% of other separable regioisomers); iv) 0.25% H<sub>2</sub>SO<sub>4</sub>, acetone; v) PhOC(S)Cl, DMAP, CH<sub>3</sub>CN; vi) (TMS)<sub>3</sub>SiH, AlBN, benzene, 80°C, 3 hrs (97% yield); vii) 1N HCl, THF, r.t.; viii) BzCN, Py, 67°C, 3 hrs; ix) 0.25% (v/v) H<sub>2</sub>SO<sub>4</sub>, MeOH, 24 hrs; x) uracil, NH(TMS)<sub>2</sub>, TMSCl, SnCl<sub>4</sub>, ClCH<sub>2</sub>Cl, -20°C; xi) MeONa, MeOH, r.t.

SCHEME 2 Reagents and conditions: i) (TMS) $_3$ SiH, AlBN, benzene, 80°C, 3 hrs (92% yield); ii) RLi, THF, -78°C, then work up and silica gel chromat.; iii) NH $_4$ F, MeOH, 60°C.

A new synthesis of C-1' acylated derivatives is reported in Scheme 2. The precursor 6, readily available from 1',2'-didehydro-2'-deoxyuridine by literature procedures, 10 was reduced using again (TMS)<sub>3</sub>SiH and then treated with organolithium reagents, to the desired products after deprotection.

#### REFERENCES

- Visiting scientists from: a) Dipartimento di Chimica Organica e Biologica, Università di Napoli "Federico II", Via Mezzocannone 16, 80134 Napoli (Italy); b) Dipartimento Farmaco Chimico, Università di Messina, 98168 Messina (Italy).
- Chatgilialoglu, C.; Gimisis, T.; Guerra, M.; Ferreri, C.; Emanuel, C. J.; Horner, J. H.; Newcomb, M.; Lucarini, M.; Pedulli, G. F. *Tetrahedron Lett.* 1998,39, 3947-3950. Chatgilialoglu, C.; Gimisis. T. *Chem. Commun.*, 1998, 1249-1250.

Downloaded At: 13:56 26 January 2011

- Tallmann, K. A.; Tronche, C.; Yoo, D. J.; Greenberg, M. M. J. Am. Chem. Soc., 1998, 120, 4903-4909. Tronche, C.; Goodman, B. K.; Greenberg, M. M. Chemistry & Biology, 1998, 5, 263-271.
- 4. For the preparation of 7 from 3, see: Goodman, B. K.; Greenberg, M. M. Nucleosides & Nucleotides, 1997, 16, 33-40.
- 5. Holy, A. Nucleic Acid Res., 1974, 1, 289-298.
- 6. Azhayev, A.; Guzaev, A.; Hovinen, J.; Mattinen, J.; Sillanpaa, R.; Lonnberg, H. Synthesis, 1994, 396-400.
- Chatgilialoglu, C. Acc. Chem. Res., 1992, 25, 118-194; Chatgilialoglu, C.; Ferreri, C.; Gimisis, T. in The chemistry of organic silicon compounds, Vol. 2; Rappoport, Z.; Apeloig, Y., Eds.; Wiley: Chichester, 1998; pp. 1539-1579.
- 8. For an analogous benzoylation of D-fructose, see: Lichtenthaler, F. W.; Klotz, J.; Flath, F.-J. *Liebigs Ann.*, 1995, 2069-2080.
- 9. Ferreri, C.; Costantino, C.; Romeo, R.; Chatgilialoglu, C. Tetrahedron Lett. in press.
- 10. Itoh, Y.; Haraguchi, K.; Tanaka, H.; Gen, E.; Miyasaka, T. J. Org. Chem. 1995, 60, 656-662.