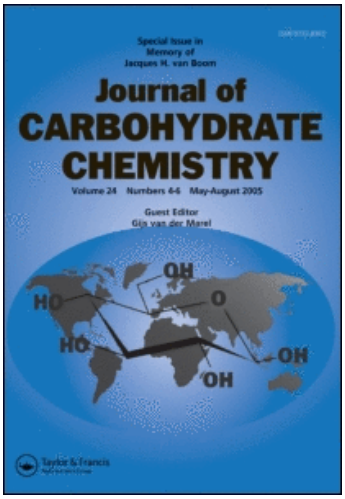


Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Comments on Conformational Studies of Monoglycosylated 3-*N*-Alkylcatechols

Glen D. Rockwell; T. Bruce Grindley; Jean-Pierre Lepoittevin

To cite this Article Rockwell, Glen D. , Grindley, T. Bruce and Lepoittevin, Jean-Pierre(1999) 'Comments on Conformational Studies of Monoglycosylated 3-*N*-Alkylcatechols', Journal of Carbohydrate Chemistry, 18: 1, 51 — 56
To link to this Article: DOI: 10.1080/07328309908543978
URL: http://dx.doi.org/10.1080/07328309908543978

J. CARBOHYDRATE CHEMISTRY, 18(1), 51–56 (1999)

COMMENTS ON CONFORMATIONAL STUDIES OF MONO-GLYCOSYLATED 3-*N*-ALKYLCATECHOLS

Glen D. Rockwell,[#] T. Bruce Grindley,[#,*] and Jean-Pierre Lepoittevin[+]

[#]Department of Chemistry, Dalhousie University, Halifax, N.S., Canada B3H 4J3
[+]Laboratoire de Dermatochimie, Université Louis Pasteur, Clinique Dermatologique, CHU, F-67091 Strasbourg, France

Received June 22, 1998 - Final Form October 5, 1998

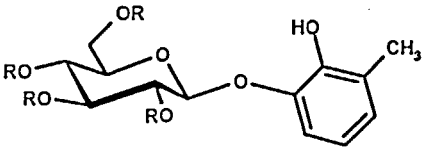
ABSTRACT

The variable temperature ^{1}H NMR spectra of the signals of the C-6 protons of 2-hydroxy-3-methylphenyl β-D-glucopyranoside (**9a**) and its 2,3,4,6-tetra-*O*-acetyl derivative (**2a**) had previously been interpreted as indicating that there was slow rotation around the C5-C6 bond in **2a** and for **9a**, that the *tg* rotamer was significantly populated while the *gt* rotamer had a negligible population. The data was reanalysed to demonstrate that neither conclusion was valid.

INTRODUCTION

The conformational analysis of rotation about the C5-C6 bond in hexopyranosides has been the subject of a number of recent reports because of its importance for oligosaccharides linked through O-6 and its relation to anomeric equilibria.[1-6] We have become interested in this problem because the various factors determining the position of the equilibria between the three rotamers were not well understood.[7] As a result, we were very interested in a paper by Mabic and Lepoittevin which described the synthesis, NMR spectra and conformational analysis of catechol β-glucosides in which the conformational

analysis of the rotamers about the C5-C6 bond was a major topic.[8] From their analysis of the variable temperature NMR spectra of **9a**, these authors concluded that rotation around the C5-C6 bond was slow on the NMR time scale, a highly significant observation, if valid. We disagree strongly with this and other conclusions drawn in the paper and present the basis for our disagreements here.

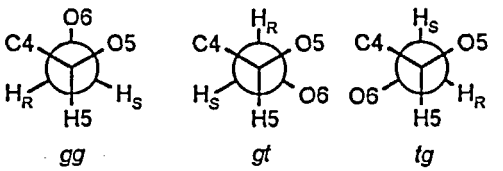


2a R = Ac
9a R = H

RESULTS AND DISCUSSION

Mabic and Lepoittevin reported the relative stabilities of the three C5-C6 rotamers of 2-hydroxy-3-methylphenyl β-D-glucopyranoside (**9a**) and its 2,3,4,6-tetra-*O*-acetyl derivative (**2a**) as calculated by the molecular mechanics program MacMimic 2.0[8] and used these to interpret NMR experiments. The three rotamers are shown in the Scheme.

We disagree with two areas of interpretation of the NMR experiments. These authors state that, on heating a $C_2D_2Cl_4$ solution of **2a**, the AB pattern for the H-6*R* and H-6*S* protons that arises on decoupling H-5 is transformed into an X_2 pattern. In fact, this transformation should never happen at any temperature[9] and was not observed there. The authors suggest that only two of the three possible rotamers are populated. H-6*R* and H-6*S* are diastereotopic in each rotamer. Therefore, under slow exchange conditions, each of the two populated conformers would give rise to an AB quartet if decoupling was successful. An eight line pattern like that shown for the 410 K spectrum in Figure 2[8] (see Figure) could be observed under slow exchange conditions, but *only* if the populations of the two rotamers were identical. More importantly, coalesence would then produce a single AB pattern because these two protons remain diastereotopic when the rotamers are interconverting rapidly on the NMR timescale;[9] coalescense to a single AB quartet was not observed nor was the X_2 pattern predicted[8] observed. Fortunately, the region of the NMR spectrum containing these signals was shown in Figure 2 of the author's paper at temperatures from 410 to 455 K[8] and the coalescence point was deemed to be 450 ±5 K. At 410 K, the part



Scheme. Newman Projections Outlining the Nomenclature Used for C5-C6 Rotamers

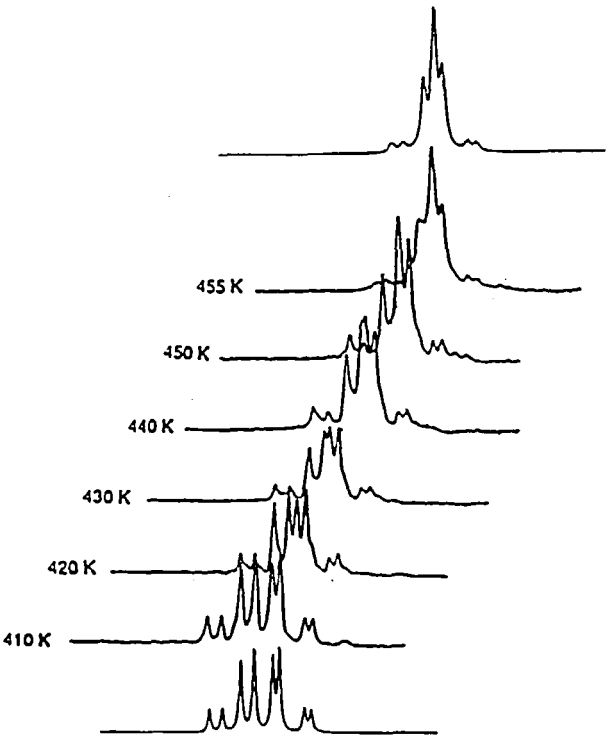


Figure. The part of the 200 MHz ^{1}H NMR spectra of 2-hydroxy-3-methylphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**2a**) in $C_2D_2Cl_4$ containing the signals of H-6S and H-6R: top, a simulated spectra; centre, the experimental spectra;[8] bottom, a simulated spectrum. See text for the parameters used for the simulations.

of the spectrum shown that contains the 8 lines, numbered 1-8 here, can be best interpreted as the AB part of an ABX pattern expected for the signals of H-6*R* and H-6*S* when no decoupling is performed. As the temperature is raised, the signals broaden somewhat and the chemical shift difference between H-6*R* and H-6*S* decreases sufficiently that the two central lines, lines 4 and 5, are coincident but no coalescence takes place.

The Figure reproduces the spectra in the previous[8] Figure 2, recorded at 200 MHz in $C_2D_2Cl_4$ and also contains two simulations. Below the experimental spectra is a simulation of an AB segment of an ABX pattern for *H*-6R and *H*-6S calculated with the coupling constants given[8] for a $CDCl_3$ solution, and with chemical shifts of 3.83, 4.19 and 4.29 ppm for H-5, H-6*S*, and H-6*R*, respectively and with a line width of 1.5 Hz. A slightly smaller chemical shift difference than reported[8] for the $CDCl_3$ solution was used to match the observed intensities of the 1, 2, 7 and 8 lines versus the 3, 4, 5, and 6 lines. Above the experimental spectrum, is a spectrum calculated with chemical shifts of 3.83, 4.215 and 4.265 ppm for H-5, H-6*S*, and H-6*R*, respectively and with $J_{5,6S}$ 3.3 Hz, $J_{5,6R}$ 4.5 Hz, $J_{6R,6S}$ -12.4 Hz and a line width of 2.5 Hz. As can be seen, the reported pattern at the temperature of "coalescence" was reproduced well with this set of many possible sets of parameters that would reproduce the experimental spectrum shown.

It should also be noted that an observation of separate patterns for individual rotamers is extremely unlikely in this system. The three rotamers (*tg*, *gg*, *gt*) are separated by three saddlepoints on the potential energy surface named[7] using the number of the atom eclipsed with O-6 in the saddlepoint, i.e., *syn*-O5, *syn*-H5, and *syn*-C4. Two pathways exist for interconversion of any two of the rotamers, e.g., for the *gg* rotamer to be converted to the *gt* rotamer, it could proceed directly over the *syn*-O5 saddlepoint, but it could also change into the *tg* rotamer via the *syn*-C4 saddlepoint, then to the *gt* rotamer over the *syn*-H5 saddlepoint. In order for the populated rotamers for **2a**, *gg* and *gt*, to undergo slow interconversion on the NMR timescale, both processes would have to be slow. It was recently calculated from the results obtained by ultrasonic relaxation on glucose and methyl β-D-glucopyranoside[10] that this barrier was about 19 kJ-mol^{-1},[7] too small to be observed by NMR spectroscopy.

In addition, Mabic and Lepoittevin[8] concluded that the two rotamers that were populated were different for the acetylated derivative **2a** and the non-esterified compound

9a, even though the $^3J_{5,6}$ values were similar for both compounds, 5.7 and 2.5 Hz for **2a** and 4.8 and 2.0 Hz for **9a**. For **2a**, the *gg* and *gt* rotamers were calculated to have populations of 66% and 34%, respectively, whereas for **9a**, it was considered that the populated conformers were the *gg* and *tg* conformers at 74% and 26%, respectively.

The assignments of the H-6*R* and H-6*S* protons cause the difference in the assessment of which two of the three rotamers had significant populations. The assignments were based[8] on literature reports in which it was concluded that the signal of H-6*R* appeared at a larger frequency than that of H-6*S* in various pyranoside derivatives.[2,11,12] However, Rao and Perlin have demonstrated that the above pattern of chemical shifts is reversed for glucopyranose and mannopyranose derivatives when both O-4 and O-6 are acetylated.[13] We have shown that the same is true if O-4 and O-6 are methylated and that the relative chemical shifts of these two protons is influenced by the rotamer populations, by the anisotropy of the group,[13] and by solvent effects.[7] Thus, in the paper by Mabic and Lepoittevin, the populated rotamers for **9a** should be the *gg* and the *gt* rotamers.

ACKNOWLEDGEMENT

TBG and GDR thank NSERC for a research grant and scholarships, respectively and Dr. A. D. French for a preprint.

REFERENCES

1. K. Bock and J. Ø. Duus, *J. Carbohydr. Chem.*, **13**, 513 (1994).
2. H. Ohrui, Y. Nishida, H. Itoh and H. Meguro, *J. Org. Chem.*, **56**, 1726 (1991).
3. J. W. Brown and B. D. Wladkowski, *J. Am. Chem. Soc.*, **118**, 1190 (1996).
4. Y. Nishida, H. Hori, H. Ohrui, H. Meguro, S. Zushi, J. Uzawa and T. Ogawa, *Agric. Biol. Chem.*, **52**, 1003 (1988).
5. K. Jansson, L. Kenne and I. Kolare, *Carbohydr. Res.*, **257**, 163 (1994).
6. I. Tvaroška and J. P. Carver, *J. Phys. Chem. B.*, **101**, 2992 (1997); S. E. Barrows, F. J. Dulles, C. J. Cramer, A. D. French, and D. G. Truhlar, *Carbohydr. Res.*, **276**, 219, 1995; S. E. Barrows, J. W. Storer, C. J. Cramer, A. D. French, and D. G. Truhlar, *J. Comp. Chem.*, in press, 1998.
7. G. D. Rockwell and T. B. Grindley, *J. Am. Chem. Soc.*, **120**, in press.
8. S. Mabic and J. P. Lepoittevin, *J. Carbohydr. Chem.*, **15**, 1051 (1996).
9. E. L. Eliel, S. H. Wilen and L. N. Mander, *Stereochemistry of Organic Compounds*, Wiley: New York, 1994, pp 492-502.

10. R. Behrends, M. K. Cowman, F. Eggers, E. M. Eyring, U. Kaatze, J. Majewski, S. Petrucci, K. H. Richmann and M. Riech, *J. Am. Chem. Soc.*, **119**, 2182, 1997.
11. M. M. Midland, G. Asirwatham, J. C. Cheng, J. A. Miller, and L. A. Morell, *J. Org. Chem.*, **59**, 4438 (1994).
12. D. Gagnaire, D. Horton, and F. R. Taravel, *Carbohydr. Res.*, **27**, 363 (1973).
13. V. S. Rao and A. S. Perlin, *Can. J. Chem.*, **61**, 2688 (1983).