Tetrahedron Letters, Vol.31, No.49, pp 7099-7100, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

^{13}C NMR Chemical Shift Correlations in 1,3-Diol Acetonides. Implications for the Stereochemical Assignment of Propionate-Derived Polyols

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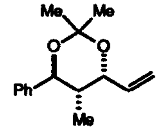
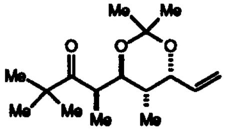
Abstract: Rychnovsky's recent correlation of the stereochemistry-dependent ^{13}C NMR chemical shifts of 4,6-disubstituted 1,3-diol acetonides with diol stereochemistry may be extended to more highly substituted dioxolanes bearing substituents in the 5-position. The ^{13}C resonances of the acetonide carbons follow a predictable, stereoregular pattern which depends solely on the diol stereochemical relationship.

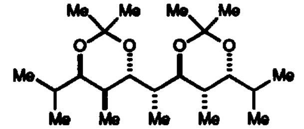
Recently, Rychnovsky and Skalitzky described a simple procedure for determining the relative stereochemistry of 1,3-diols from the chemical shift correlation of the ^{13}C NMR resonances of the three acetonide carbons.[1] The conformational differences between the *syn* (chair) and *anti* (twist boat) 1,3-diol acetonides result in significantly different ^{13}C spectra of the ketal carbon and associated methyl substituents. The generalization is that the *syn* isomers display carbon resonances for the acetonide methyl groups at 30 and 19 ppm, while the *anti* isomers have methyl resonances in the range of 24-25 ppm.

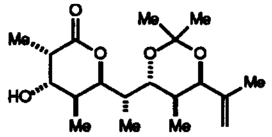
Our interest in the synthesis of polypropionate-derived natural products led us to explore whether this generalization might be logically extended to the analogous stereochemical assignments of the more heavily substituted 1,3-polyols carrying an intervening methyl-bearing stereocenter in either stereochemical orientation.[2] The incorporation of this additional stereocenter provides a good test for the Rychnovsky generalization since it doubles (to four) the number of acetonide diastereomers which now must adhere to the chemical shift constraints. In affirming the chemical shift correlations of these polyols we have studied over 40 different compounds and have found no exceptions to the above generalizations. Representative examples are collected in the accompanying Tables.

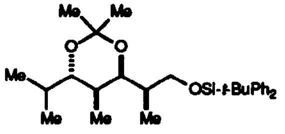
Table 1. ^{13}C NMR Acetonide Resonances of *Anti* Polypropionate Polyols (δ: ketal carbon; methyl carbons).

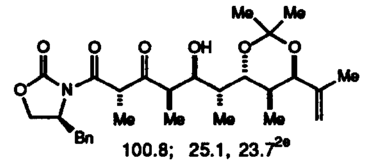

101.0; 25.2, 24.2

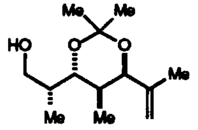

100.5; 25.6, 24.0

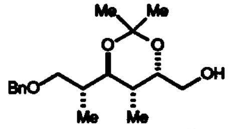

100.2, 100.2; 25.6, 24.8, 23.8, 23.7

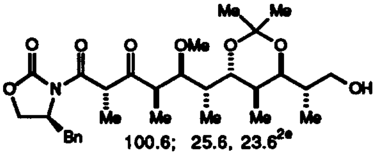

100.8; 25.0, 23.8[2e]


100.3; 25.3, 23.5[2a]


100.8; 25.1, 23.7[2e]

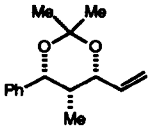

100.7; 25.5, 23.6[2e]


100.5; 25.4, 23.5[2b]

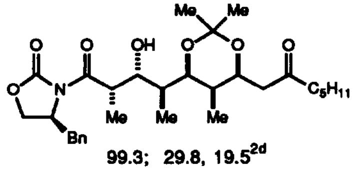

100.6; 25.6, 23.6[2e]

Also included in the Tables are the ^{13}C chemical shifts of the ketal carbons which, in accord with Rychnovsky's findings, follow a stereoregular pattern where the *anti* diol acetonides resonate above 100 ppm, while *syn* diol acetonides appear below 100 ppm. These resonances are often more useful for assigning stereochemistry than the acetonide methyl resonances in polypropionate-derived compounds due to the large number of methyl groups present in such structures. *It is noteworthy that the stereochemistry at the methyl-bearing center of the dioxolane ring has no effect upon these trends.*

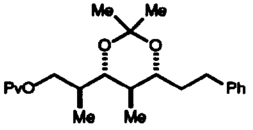
Table 2. ^{13}C NMR Acetonide Resonances of *Syn* Polypropionate Polyols (δ: ketal carbon; methyl carbons).



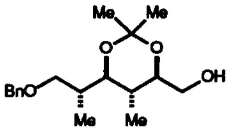
99.3; 29.9, 19.5



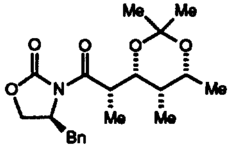
99.3; 29.8, 19.5[2d]



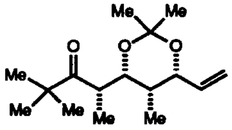
98.0; 30.1, 19.4



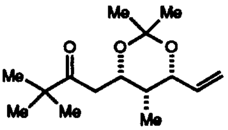
98.2; 30.0, 19.5[2b]



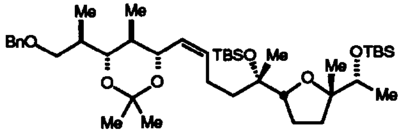
99.1; 29.9, 19.6[2c]



98.2; 30.0, 19.6



99.1; 29.8, 19.6



97.4; 30.0, 19.2[2b]

The results of our studies are summarized in the Figure below. The indicated ^{13}C chemical shifts represent averages for all of the compounds included in the data set (40) with their respective 95% confidence limits. In conclusion, with the added weight of the data provided by this study, the Rychnovsky generalizations may now be extended to the stereochemical assignments of polypropionate-derived polyols.

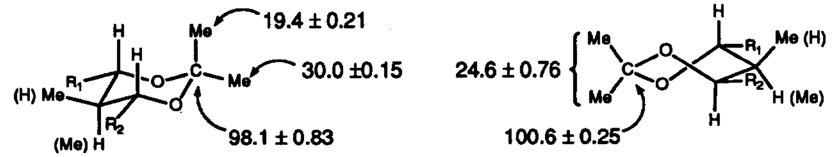


Figure. Average Values for ^{13}C NMR Resonances of *Syn* and *Anti* Polypropionate Polyols (ave ± σ).

Acknowledgment. Support has been provided by the National Institutes of Health, the National Science Foundation, and Merck. The NIH BRS Shared Instrumentation Grant Program 1 S10 RR01748-01A1 is acknowledged for providing NMR facilities. Fellowships for D. L. R. (American Cancer Society postdoctoral) and J. R. G. (NSF predoctoral) are appreciated.

References

(1) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945-948.

(2) (a) This compound was prepared by Dr. J. Stephen Clark. (b) Dow, R. L., Ph. D. Thesis, Harvard University, 1985. (c) This compound was prepared by Dr. Bret Huff. (d) DiMare, M. M., Ph. D. Thesis, Harvard University, 1988. (e) These compounds were prepared by Dr. George S. Sheppard.

(Received in USA 30 August 1990)