occuring on the surface of the target, converts T^+ to hot T atoms of essentially the same kinetic energy. T_2^+ is expected to yield hot T atoms of the same average velocity in a transition to the repulsive $^3\Sigma_u^+$ state and $T_2(^1\Sigma_g^+)$ molecules. Since a fraction of the latter species is likely to be in a high vibrational state, due to its formation by a Franck–Condon transition, it may undergo collision-induced dissociation upon further collision.[8] The tritium atoms thus formed should then react further to yield labeled products by normal hot abstraction and displacement mechanisms.[1]

These expectations are borne out by the following data. (1) Yields increase with energy, which is normal for hot-atom processes. (2) The yield of cyclohexane-*t* from a high-energy T^+ beam is within experimental error of that from hot atoms produced by nuclear recoil (Figure 3). As expected, the yield is somewhat lower for T_2^+ since not all of these ions are converted to hot atoms (Figure 2). (3) The shape of the yield function is, after appropriate normalization, similar for initial T_2^+ and T^+ beams.[8]

Some salient results of this study may be pointed out. The efficiency for hydrogen displacement to form cyclohexane-*t* rises steeply from a threshold at about 1 ev to the vicinity of 10 ev. (Excitation functions derived from these results will be discussed in the full report on the work.) Hexene-*t* and *n*-hexane-*t* production, which involve rupture of a C–C as well as a C–H bond, have a threshold of about 5 ev.[9] This appears to be the first measurement of the threshold of a reaction not occurring at thermal energies which involves only neutral species.

Acknowledgments. This work owes much to Professors R. Fink and R. Beringer, who helped develop a prototype of ADAM. (Details on this apparatus will be published separately.) Technical assistance by Mr. S. Y. Tang is greatly appreciated. We are grateful to Dr. J. Futrell for permission to cite his results prior to publication. The work was supported by the U. S. Atomic Energy Commission.

[8] The yield of cyclohexane-*t* production at low energies appears to be lower for T_2^+ than for T^+ beams. This may result from a decreased efficiency of hot-T-atom production when the energy is so low that collision-induced dissociation of excited $T_2(^1\Sigma_g^+)$ (as produced by neutralization) becomes ineffective.

[9] As is emphasized by the log–log plots of the data, there appear to be small but finite yields of *n*-hexane-*t* and cyclohexane-*t* as the energy approaches zero. This would be due to nonhot-atom processes having low or zero thresholds. Examples of such would be ionic or radical reactions on the surface of the target.

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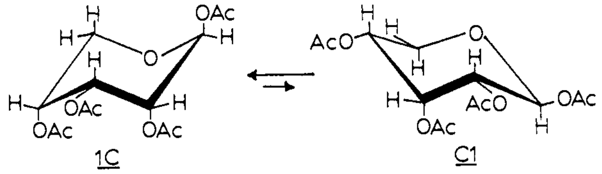
Conformational Inversion of Pyranoid Ring Sugars. The Conformational Equilibrium of β-D-Ribopyranose Tetraacetate[1]

Sir:

Pyranoid ring sugars and their derivatives may be formulated in two energetically nonequivalent chairlike conformations, interconversion between which involves an energy barrier, and in a "flexible cycle" of skew forms interconvertible through energy barriers corresponding to the boat forms.[2,3] Steric and electronic interactions between substituents on the tetrahydropyran ring usually cause one chair conformer to be favored strongly over the alternative chair form.[4–6] Nmr spectroscopic and other evidence indicates that most pyranoid sugars and their derivatives exhibit a high degree of conformational homogeneity in one of the two chairlike conformations;[4,5] convincing evidence for major contributions from nonchair conformers has been presented only in the case of systems having other rings fused to the pyranose ring.[7]

It has not been established directly whether the conformational homogeneity indicated for pyranoid sugar derivatives by nmr spectroscopy reflects a time-averaged spectrum of conformers in rapid interconversion, with a preponderant contribution from the favored chair conformation, or whether interconversion is slow, so that spectra of the separate conformers are obtained but the proportion of the minor conformer is so small that its signals are lost in the background noise of the spectrum. Available evidence[4,5,8] suggests that the energy barrier for chair–chair interconversion is small, so that interconversion is rapid and a time-averaged spectrum is seen, because, in a few examples where the energy difference between the two chair conformers is predictably small, the nmr spectral parameters appear to be intermediate between those predicted for each separate chair conformer. Such an example[5a] is β-D-ribopyranose tetraacetate (**1**). The present communication reports direct observation of separate conformers of **1** by low-temperature nmr spectroscopy, thereby establishing that **1**, and presumably other pyranoid sugar derivatives, indeed exists in rapid conformational equilibrium at room temperature. Such conformational equilibria have been observed with cyclohexane[9] and some of its derivatives.[10]



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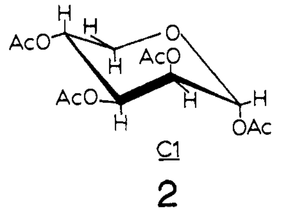

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[1] This paper is part of a series "Application of 220-MHz Nmr to the Solution of Stereochemical Problems." For previous, related papers, see (a) N. S. Bhacca and D. Horton, *Chem. Commun.*, 867 (1967); (b) C. V. Holland, D. Horton, M. J. Miller, and N. S. Bhacca, *J. Org. Chem.*, **32**, 3077 (1967); (c) C. V. Holland, D. Horton, and J. S. Jewell, *ibid.*, **32**, 1818 (1967).

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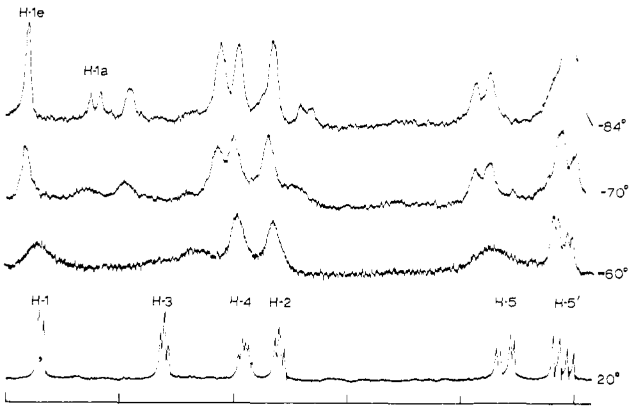

Figure 1. The low-field portion of the 220-MHz nmr spectrum of β-D-ribopyranose tetraacetate (**1**) in acetone-d_6, at 20, −60, −70, and −84°. Each scale division corresponds to 100 Hz.

The 220-MHz spectrum of **1** in acetone-d_6 at room temperature (Figure 1, lowest curve) was completely first order, and analysis[1b,11] gave the following first-order couplings: $J_{1,2} = 4.8$ Hz, $J_{2,3} = 3.0$ Hz, $J_{3,4} = 3.6$ Hz, $J_{4,5} = 3.2$ Hz, $J_{4,5'} = 5.6$ Hz, $J_{3,5} = \sim 0.5$ Hz, and $J_{5,5'} = 12.0$ Hz. These values are intermediate between those predicted[1b,5,11] for **1** in the *C1* conformation ($J_{1,2} = 8$–10 Hz) and those predicted for **1** in the *1C* conformation ($J_{1,2} = 1$–2 Hz). As the temperature was lowered the spectrum showed progressive changes; at −32° slight line-broadening was evident, and with decreasing temperature the H-1, H-3, and H-5 signals collapsed to broad humps, and the shapes of the other signals broadened, until at −60° the spectrum shown in Figure 1 (second curve) was observed. New signals began to appear as the temperature was lowered further, and the appearance of the spectrum at −70° is shown in Figure 1 (third curve). The signals became sharper at still lower temperatures, and the spectrum observed at −84° (Figure 1, top curve) was not substantially different from that observed at −78°. The signals for the acetyl groups also showed changes, from the simple four-line pattern observed at 20° to a more complex pattern at −84°.

The observed data indicate that substance **1** exists at room temperature as a mixture of conformers undergoing rapid interconversion, and that at −84° the interconversion is slow on the nmr time scale, so that spectra of the separate conformers are seen. Assuming that the H-1 proton of either conformer gives its signal at lower field than those of the other ring protons, the broadened singlet at lowest field and the wide doublet at next higher field can be assigned to H-1 of the two conformers. The former signal is assigned to H-1 of the *1C* conformation ($J_{1,2} = \sim 1$ Hz), and the latter is assigned to H-1 of the *C1* conformation ($J_{1,2} = 8.0$ Hz), and the relative magnitudes of the signals indicate that the *1C* and *C1* conformers are present in 2:1 proportion, corresponding to a free-energy difference of $\Delta G^\circ = 0.3$ kcal/mole. Upfield from the H-1 signals can be observed three signals of intensity similar to the H-1e signal; these are presumably those of the methine protons of the *1C* conformer. Two additional signals, of intensity equal to that of the H-1a signal, are observed and are presumably those of two of the methine protons of the *C1* conformer, and the signal of the remaining methine proton of the *C1* conformer appears as a broad resonance partially overlapped by one of the stronger signals.

The separation of the H-1e and H-1a signals at −84° is 58.5 Hz. From this it may be calculated[12] that at −60°, the approximate temperature at which the H-1e and H-1a signals coalesce to give a broad singlet, the rate of interconversion of the *C1* and *1C* chair conformers is approximately 130 times per second.

It was suggested in early investigations[13] that the conformers of α-D-lyxopyranose tetraacetate (**2**) have approximately the same energy. However, the 220-MHz spectrum of **2** in acetone-d_6 showed $J_{1,2} = 3.0$ Hz, $J_{2,3} = 3.2$ Hz, $J_{3,4} = 8.8$ Hz, $J_{4,5e} = 4.8$ Hz, and $J_{4,5a} = 9.2$ Hz, in a spectrum that was fully first order, these data support the *C1* form as the major or sole chair conformer. As the temperature was lowered to −76°, the H-3 signal moved upfield and the positions of the acetyl-group signals changed, but no new signals were detected in the anomeric-proton region,[14] indicating that any of the *1C* form present could not have comprised more than 2% of the total.

The greater stability of the *1C* form of **1**, having three of the four substituents axial, over the *C1* form, having only one axial substituent, and the failure to observe any detectable proportion of the *1C* form of **2** in equilibrium with the *C1* form, even though both forms have two axial and two equatorial substituents, further illustrate[1c,11] the strong influence of the "anomeric effect" in determining the favored conformation of tetrahydropyran derivatives.

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Removal of Protected Peptides by Hydrazinolysis after Solid-Phase Synthesis

Sir:

The effectiveness of the solid-phase synthesis of polypeptides[1] has been documented in the syntheses of the A and B chains of insulin,[2] bradykinin,[3] and angiotensin II.[4] The synthesis of longer peptides or proteins might be facilitated by the availability of methods for the preparation of fully protected α-N-blocked peptides suitable for successive coupling to a growing COOH-terminal fragment. We have recently described[5] a modified solid-phase procedure which has proved useful in the preparation of a number of protected peptide

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