Notes

Conformational Instability of Polysubstituted Carbon Chains: Temperature Dependence of the Conformation of Tetra-*O*-acetyl-D-ribose Diisobutyl Dithioacetal[1,2]

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Systematic conformational studies on polysubstituted tetrahydropyran ring systems as a function of stereochemical substitution mode, through use of complete configurational series of pyranose sugar derivatives in solution, have revealed in the majority of instances a high degree of conformational homogeneity;[3,4] variable-temperature ^{1}H NMR studies have shown certain examples where two chair conformers coexist to the extent that signals for both conformers in slow equilibrium (on the NMR time scale) may be observed at low temperature. The ease of ring inversion has been found to be not substantially different from that of unsubstituted tetrahydropyran.[5,6] Steric factors, and to a greater extent the anomeric effect,[4] dominate the favored conformational disposition of the substituted derivatives.

In acyclic systems, as constituted by related configurational families of acyclic sugar derivatives, it is well established[1,4,6-8] that the favored conformation is perturbed from the extended zigzag arrangement of a polymethylene chain, as a consequence of unfavorable interaction of parallel β-disposed polar substituents. By rotation about one or more C–C bonds in the extended conformation, gauche ("sickle") conformations are generated wherein such interactions may be alleviated. A single such conformer is frequently[1] encountered as the principal form in solution. The observation with certain compounds of vicinal proton–proton NMR couplings having values intermediate between those (~9 Hz) of antiparallel and those (~3 Hz or less) of gauche-disposed protons in such derivatives is indicative of conformational mixtures implicating more than one acyclic conformer. Although quantitative treatments have been attempted, detailed attribution of individual contributors and their proportions in such mixtures in thermal equilibrium, on the basis of observed ^{1}H couplings, is at best only speculative.[1] The possibility of using low-temperature "conformational freeze-out" [5] as a basis for secure assignments is complicated by the lack of suitable examples for study, by problems of insufficient spectral resolution, by problems in selection of suitable solvents, and above all, by the low energy barrier for conformational inversion in such acyclic systems. This last factor is a major limitation because of the necessity for operation at low temperatures with use of a high-field spectrometer.

From the basis of detailed comparative studies on acyclic sugar derivatives,[1,9] especially dithioacetals, this report describes the ^{1}H NMR spectral behavior at 250 MHz of tetra-*O*-acetyl-D-ribose diisobutyl dithioacetal (1) in acetone-d_6 over the temperature range +20 to −120 °C. The compound was obtained by acetylating the known[10] D-ribose diisobutyl dithioacetal. This example is significant because: (a) compound 1 in acetone-d_6 shows vicinal proton–proton couplings at ~20 °C (Table I) whose intermediate magnitudes indicate substantial population of at least two conformational states, neither of which is the planar, extended, zigzag form (**1a**); and (b) the compound remains in solution and gives an essentially first-order NMR spectrum at 250 MHz over the temperature range of the experiment (see Figure 1).

Table I. Proton–Proton Spin-Coupling Values[a] for Tetra-*O*-acetyl-D-ribose Diisobutyl Dithioacetal (1) in Acetone-d_6 over the Temperature Range +20 to −105 °C

Temp, °C	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$[b]	$J_{4,5'}$[b]	$J_{5,5'}$[b]
+19	6.0	6.4	4.0	3.5	7.6	12.4
−40	5.5	7.0	3.5	3.0	8.5	12.2
−60	5.5	7.2	3.5	2.5	8.5	12.0
−70	5.2	7.5	3.2	2.3	8.9	12
−80	5.0	7.8	3.0	2.0	9.0	12
−85	4.7	8.0	3.0	2.0	9.0	12
−90	4.5	8.0	3.0	2.0	9.0	12
−95	4.5	8.0	3.0		9.0	12
−100	4.0	8.3	3.0			
−105	3.5					

[a] Measured directly from line spacings of spectra recorded at 250 MHz; all multiplets showed fully first-order characteristics. [b] The proton at C-5 resonating at higher field is designated H-5′.

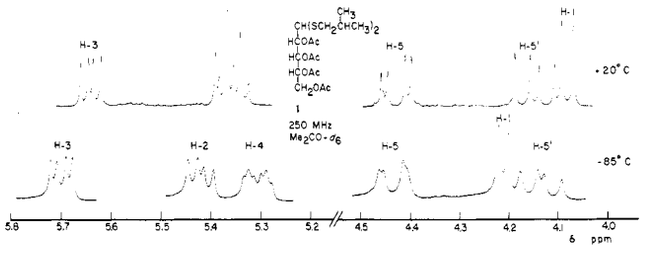
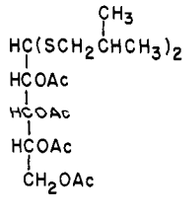


Figure 1. The 250-MHz NMR spectrum of tetra-*O*-acetyl-D-ribose diisobutyl dithioacetal (1) in acetone-d_6, showing the resonances of H-1, 2, 3, 4, 5 and 5′ at +20 °C (upper trace) and at −85 °C (lower trace).



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The planar, zigzag conformation (**1a**, see Figure 2) of **1**, corresponding to maximal staggering of small–medium–large groups along each carbon–carbon bond, would be considered unfavorable because it has two sets of parallel interactions between β-disposed substituents (2-OAc–4-OAc and 3-OAc–1-S-*i*-Bu); rotation about C-1–C-2 to generate conformer **1b** would alleviate one of these interactions. Both interactions could be relieved by rotation about C-2–C-3 to generate conformer **1c**; alternatively, rotation about C-3–C-4 to generate conformer **1d** would remove one but not both β interactions. Further C-1–C-2 rotation starting from conformer **1d** would generate conformer **1e** free of β interactions.

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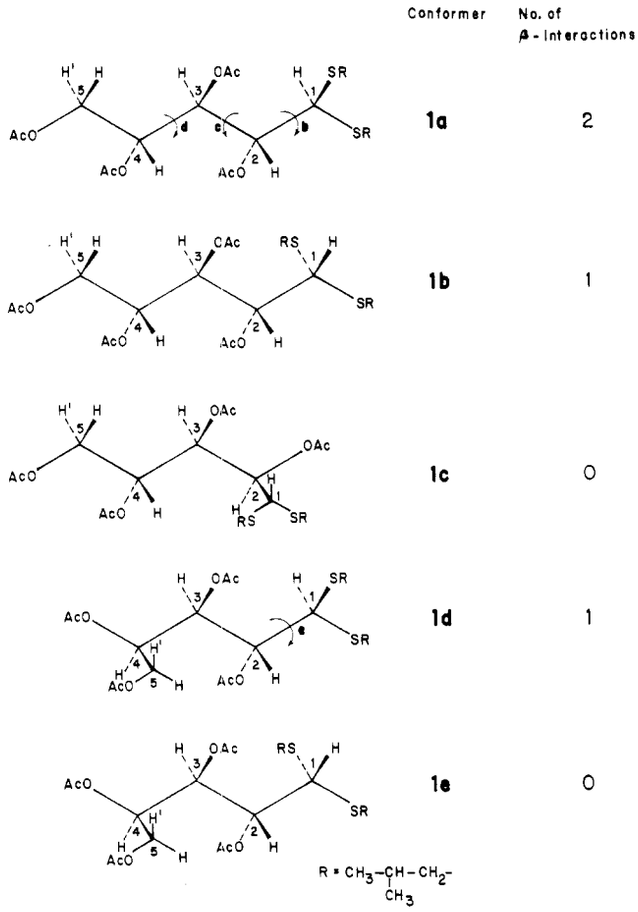

Figure 2. The extended, planar zigzag conformation (**1a**) of tetra-*O*-acetyl-D-ribose diisobutyl dithioacetal (1) and alternative conformations derived by rotation through 120° as indicated in **1a** about C-1–C-2 (b) to give **1b**, about C-2–C-3 (c) to give **1c**, about C-3–C-4 (d) to give **1d**, and about C-1–C-2 (e) in **1d** to give **1e**. The number of parallel, β interactions of nonhydrogen substituents is indicated.

The spin couplings observed (Table I) for **1** in acetone-d_6 at ~20 °C of particular relevance are $J_{1,2}$ = 6.0, $J_{2,3}$ = 6.4, $J_{3,4}$ = 3.2, $J_{4,5}$ = 7.1, and $J_{4,5'}$ = 3.5 Hz. Assuming the model values indicated for antiparallel and gauche-disposed vicinal protons, compound **1** clearly exists as a conformational mixture at 20 °C in solution. The relatively large value of $J_{1,2}$ is noteworthy, indicating significant, but far from exclusive, population by conformers having H-1 and H-2 antiparallel. Substantial, but not exclusive, population of conformers having H-2 and H-3, and H-4 and H-5, antiparallel is indicated by the $J_{2,3}$ and $J_{4,5}$ values; the small value of $J_{3,4}$ demonstrates major, but not exclusive, population of the C-3–C-4 rotamer having H-3 and H-4 gauche disposed. The data are best accommodated by postulating a conformational mixture populated mainly by conformers **1c**, **1d**, and **1e**, with little contribution, if any, by conformers **1a** and **1b**; no single conformer preponderates overwhelmingly.

As the temperature of the solution of **1** is lowered, substantial changes are observed (Table I) in the spin couplings and also in the chemical shifts of the protons along the chain (Figure 3). Such variations are not noted in the spectra of related aldose dithioacetal peracetates that display, from their spin couplings, apparent conformational homogeneity at room temperature; variations of the type observed with **1** may be considered indicative of conformational mobility. The changes in chemical shift for the proton signals are approximately linear with temperature (Figure 3); it is noteworthy that the H-1 signal, at highest field at 20 °C, moves progressively to

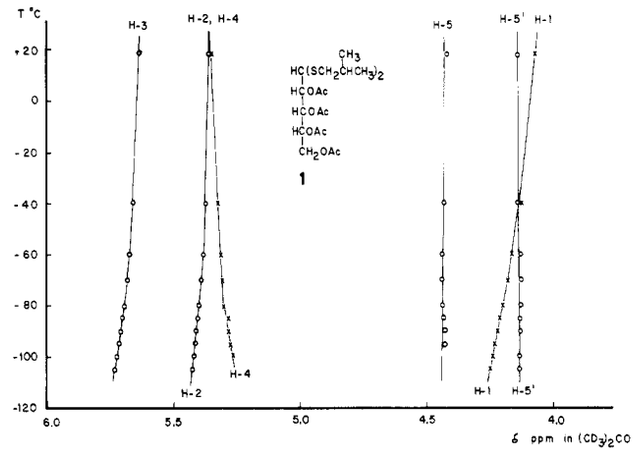

Figure 3. Chemical shifts (δ values) of H-1, 2, 3, 4, 5, and 5′ for solutions of **1** in acetone-d_6 over the temperature range +20 to −105 °C, determined from spectra at 250 MHz.

lower field with decrease in temperature and falls below the resonance of H-5 at the lower temperatures. The H-4 signal, practically superimposed on the H-2 signal at 20 °C, moves progressively upfield as the temperature decreases. The line shapes remained generally sharp until the very lowest temperature employed, although broadening of the H-5 and H-5′ signals took place before the other resonances displayed such broadening.

The acetate-group resonances also showed substantial temperature dependence (Figure 4), again indicative of conformational mobility in **1** as a function of temperature, but as these signals have not been individually assigned, it is difficult to draw specific conclusions concerning changing orientations of acetoxyl groups.

The changes in spin couplings with decrease in temperature are remarkable; the $J_{1,2}$ value diminishes from an initial 6.0 Hz to a value of 3.5 Hz at −110 °C, whereas the $J_{2,3}$ value rises from 6.4 to 8.5 Hz. The $J_{3,4}$ and $J_{4,5}$ values also proceed from equilibrated mixture values at 20 °C (4.0 and 7.6 Hz, respectively) to extreme values (2.6 and 8.7 Hz, respectively) at −110 °C. The solution froze at about −120 °C, precluding further observations, but studies at still lower temperatures in $D_3CClC{=}CD_2$ indicated no evidence of further change in these values. Although the temperature of "conformational freeze-out" was probably not reached (and there was no evidence for appearance of a second set of signals for an additional conformer in slow equilibrium with the principal conformer), it is evident that the data at −110 °C correspond to the spin couplings of a single conformer; the values observed accord with this being conformer **1e**.

The overall picture that emerges is of conformational flexibility in solutions of **1** at room temperature, dominated by the principle of avoidance of parallel β interactions but allowing mobility especially toward the ends of the chains; the involvement of one of the conformers (**1e** in this instance) is only as a minor contributor at room temperature, but it assumes progressively greater significance as the temperature is lowered, eventually becoming essentially the exclusive contributor. Instances observed[3] in cyclic systems have shown progression from a weakly favored conformer to its exclusive population as the solution temperature is lowered, but have not demonstrated such an extreme of conformational variance as the present acyclic example.

It may be postulated as a general principle, at least for compounds that do not display strong intermolecular interactions, that the conformation favored in solution at low temperature will be the same as that existing when the compound is in the solid state. Although compound **1** has not been

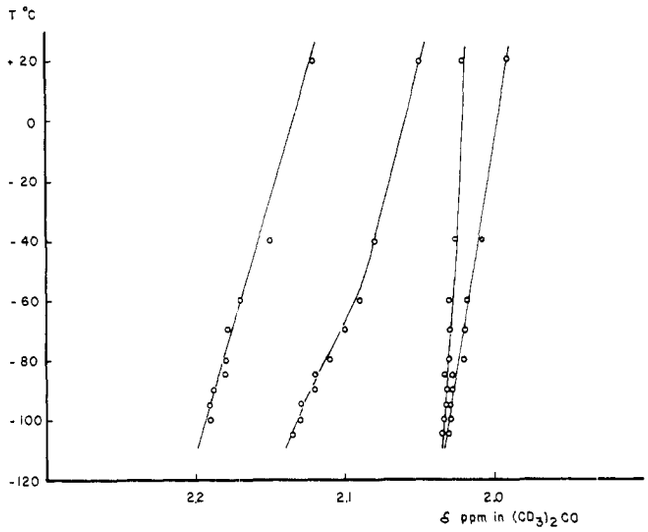

Figure 4. Changes in chemical shifts of acetoxyl group signals of 1 in acetone-d_6 over the temperature range +20 to −105 °C, determined from 250-MHz spectra.

crystallized, there are related instances, for example D-ribose diethyl (and diphenyl) dithioacetals[1] and their tetraacetates,[9] for which NMR studies in solution at room temperature indicate population by mixtures of conformers,[1] whereas comparative X-ray crystallographic studies[11] have revealed a single conformer present in the same compound in the crystalline state.

For molecules that display evidence of conformational flexibility, it is thus understandable, and maybe to be expected, that the conformation adopted in the solid state will correspond most closely to that present in solution at low temperature and will not necessarily be one that is preponderant at room temperature. The present example provides a particularly favorable molecule for observing this conformational mobility over a wide temperature range. This type of experiment would not be feasible for most water-soluble acyclic carbohydrates and their derivatives because of strong conformational bias, poor spectral resolution, and the limited temperature range available with suitable solvents in the liquid state.

Experimental Section

NMR Spectra. Spectra were recorded at 250 MHz with a CAMECA-250 spectrometer (Thomson CSF, Paris) with solutions (~13%) of 1 in acetone-d_6 containing ~5% of tetramethylsilane as internal reference (δ 0.00) and lock signal. At each of the temperatures indicated, the spectrum was recorded initially at 3000-Hz sweep width; detailed examination of the spectrum was then performed at 300-Hz sweep width for measurement of exact chemical shifts and line spacings. Values were recorded as indicated at progressively lower temperatures, allowing time for thermal equilibration at each temperature; some line broadening occurred at the lower temperatures and the signals collapsed abruptly into featureless broad humps at −120 °C as the solution froze. Spectra were again recorded at selected temperatures as the temperature was raised progressively to +20 °C; no significant differences were observed at corresponding temperatures with spectra recorded at successively lower temperatures. Temperature calibration was achieved by reference to signals of *o*-dichlorobenzene for temperatures >0 °C and by use of isopentane for temperatures <0 °C; a thermocouple was inserted directly in the sample tube. The temperatures indicated are considered correct to ±2 °C.

The experiments were repeated with 2-chloro-1-propene-d_5 as the solvent; the results were essentially similar to those recorded for solutions in acetone-d_6 except for minor differences in chemical shifts and spin coupling values; the solution froze at approximately −140 °C.

Tetra-*O*-acetyl-D-ribose Diisobutyl Dithioacetal (1). A solution of D-ribose diisobutyl dithioacetal[10] (6 g) in pyridine (18 mL) and acetic anhydride (24 mL) was kept for 18 h at ~20 °C and then poured into water. The product (1) was then isolated by conventional extraction with chloroform and obtained as an oil; yield 9.193 g (quantitative). The sample (928 mg) used for spectral analysis was purified by placing it on a column containing silica gel (Merck No. 60, 70–230 mesh) which was eluted with 3:1 dichloromethane–ether to afford 871 mg of pure product; it was dried in vacuo for 12 h at 50 °C: $[\alpha]^{24}_D$ +21.5° (*c* 1.1, chloroform); NMR data see Figures 1, 3, and 4 and Table I; signals observed in acetone-d_6 (~20 °C) at δ 0.97 (12 H, 4 closely spaced singlets, CMe_2) and 1.79 (2 H, multiplet, $CCHC_2$) were attributed to the two isobutyl groups in slightly different magnetic environments; the signals for the CH_2 portion of the isobutyl group were overlapped by the solvent resonance.

Anal. Calcd for $C_{21}H_{36}O_8S_2$: C, 52.47; H, 7.56; S, 13.34. Found: C 52.29; H, 7.60; S, 13.45.

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Registry No.—1, 35304-00-8; D-ribose diisobutyl dithioacetal, 66290-78-6.

References and Notes

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A New Preparation of Triarylsulfonium and -selenonium Salts via the Copper(II)-Catalyzed Arylation of Sulfides and Selenides with Diaryliodonium Salts

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In support of our recent work involving the development of photoinitiators for cationic polymerization, we required a general method for the preparation of pure triarylsulfonium salts. Although the literature contains a number of synthetic procedures for the preparation of these compounds,[1-8] these routes were deemed unsatisfactory for our purposes due to their poor yields, high degree of complexity, long reaction times, or general lack of applicability to a wide variety of substituted symmetrical and unsymmetrical triarylsulfonium salts.

In 1957, Nesmeyanov and his co-workers[9,10] reported that diphenyl sulfide could be directly arylated using diphenyliodonium fluoroborate at 220–230 °C to give triphenylsulfonium fluoroborate (eq 1).

$$(C_6H_5)_2S + (C_6H_5)_2I^+BF_4^- \xrightarrow{220\text{–}230\ °C} (C_6H_5)_3S^+BF_4^- + C_6H_5I \quad (1)$$

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