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On the Possibility of Determining Stereochemistry in Acyclic Polyhydroxylated Compounds by the Combined Vicinal Coupling Constant/Molecular Mechanics Method. A Test with Alditol Peracetates[1]

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Abstract: Vicinal ^1H-^1H coupling constants on the backbone carbon chain of several alditol and deoxyalditol peracetates were calculated with a multiparametric extension of Karplus equation, using conformer distributions and structural information obtained by energy-minimizing all of the rotamers along the backbone chain MM2(85). The population-weighted coupling constants agreed moderately well with the observed: the standard deviation of errors in reproducing 160 experimental coupling constants was 0.74 Hz. A root-mean-square test indicates that, if a gross structure of an alditol or related compound is known, the combined NMR analysis and MM calculations can predict relative configurations for all stereogenic centres of the molecule with a success rate of 92%.

INTRODUCTION

In view of the rapid developments in the chemistry of acyclic polyhydroxylated compounds,[2-4] it is highly desirable to improve the spectroscopic method of determining the relative configuration of asymmetric carbon atoms along the backbone skeleton of these compounds. The current method relies on the vicinal ^1H-^1H coupling along the backbone chain.[3,4] The major problem lies in the estimation of conformer distribution: too much emphasis has been given to the preference of coplanar and fully extended conformation and the avoidance

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of 1,3-parallel nonbonded oxygen-oxygen interaction. This emphasis must have arisen from the survey of X-ray observations in the solid state, wherein the planar and extended conformation is inherently favored because of its packing properties.

In solution, however, acyclic polyhydroxylated compounds generally are expected to exist as an equilibrium mixture of a number of conformers. Hence the observed vicinal coupling constant (^3J) is population-weighted among conformers and should be given by $n_1J_1 + n_2J_2 + \cdots + n_NJ_N$, where $J_1, J_2 \cdots J_N$ are the coupling constants of the first, second....Nth conformer having molar fractions $n_1, n_2 \cdots n_N$, respectively, while N is the total number of conformers. A meaningful correlation of these values with stereochemistry requires accurate estimates of conformer distribution (n_i) as well as J_i ($i = 1, 2 \cdots N$).

We describe below our attempts at reproducing the observed vicinal ^1H-^1H coupling constants for the peracetates of tetra- to hexaalditol and related compounds with the aid of molecular mechanics[5] (for n_i) and a modified Karplus equation[6] (for J_i). This correlation discloses the degree of our ability to predict the conformer distribution. The methodology used here has been successfully applied to smaller, less flexible systems,[7] and to peracetylated cyanoalditols.[8] This work represents the first systematic effort to examine its validity as applied to moderate-sized polyhydroxylated acyclic molecules.

EXPERIMENTAL SECTION

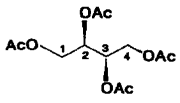
Material

A total of 25 peracetates of tetritol (**1**), 2-deoxypentitol (**2**), 3-deoxypentitol (**3**), pentitol (**4**), 2-deoxyhexitol (**5**), 3-deoxyhexitol (**6**), 2,4-bisdeoxy-2-methylhexitol (**7**), and hexitol (**8**) are prepared.[9] Proton NMR spectra of these compounds have been measured in $CDCl_3$ or C_6D_6 solution and the vicinal proton-proton coupling constants are obtained as described in the literature.[3]

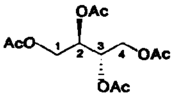
Molecular Mechanics

Allinger's 1985 version of MM2[10] was used.[11] Effective dielectric constants of 4.6 and 7.5 were used for $CDCl_3$ and C_6D_6, respectively.[12] Exhaustive geometry optimization of all possible rotamers of **1** to **8** is economically unfeasible, hence several conformational constraints had to be imposed in the rotamer search. The carbonyl group and the O-alkyl bond in the ester group are known to favor eclipsed conformation as shown in **A** and **B**.[13] The conformation about the acetoxy-alkyl bond (marked with an arrow) is dominated in the solid state by *antiperiplanar* (**A**) for the esters of primary alcohols and by *anticlinal* (**B**) for those of secondary alcohols, according to the analysis of Cambridge Structure Database.[14] Following these observations, we fixed the terminal and internal acetoxyl groups to conformations **A** and **B**, respectively. Note, however, that the whole molecule is always optimized and hence acetoxyl groups adjust themselves to the most favorable geometry in these conformations.

Only the rotation about the backbone C-C bonds are considered for **1**-**8**. High-energy conformers like those containing a succession of *synclinal* bonds with alternating signs or those involving too close substituents failed to reach the energy minimum. The total number (N) of successfully geometry-optimized rotamers for each stereoisomer is given in Table 1. Rotamers are generated by using highly automated routine implemented in the program.



1a



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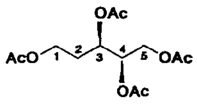

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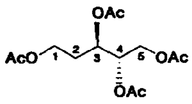

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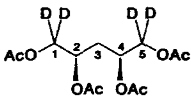

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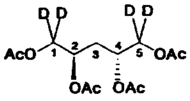

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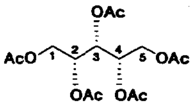

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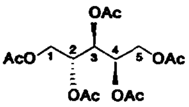

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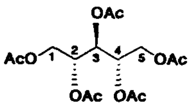

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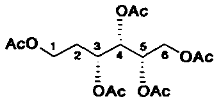

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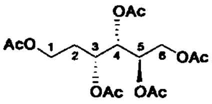

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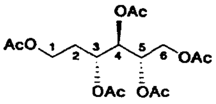

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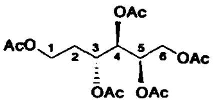

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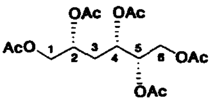

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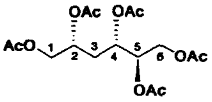

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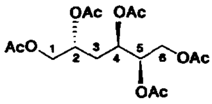

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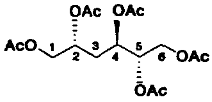

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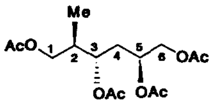

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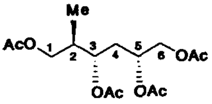

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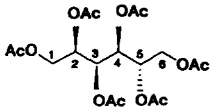

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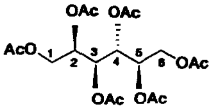

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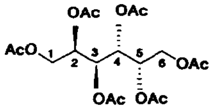

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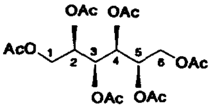

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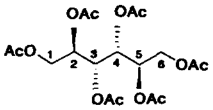

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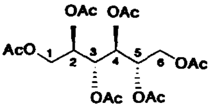
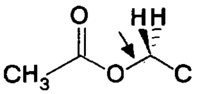
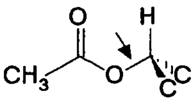


8f



A



B

Modified Karplus Equation

The new multiparametric extension of Karplus equation which we described recently[6,16] was used:

$$^{3}J_{HH} = A\cos\theta + B\cos2\theta + C\cos3\theta + D\cos^{2}2\theta + W(E\cos\theta\Sigma\Delta\chi_{i}\cos\phi_{i} + F\Sigma\Delta\chi_{i}\cos2\phi_{i} + G\Sigma\Delta\chi_{i})$$
$$+ H\{(\omega_1 + \omega_2)/2 - 110\} + I(r_{CC} - 1.5) + K\Sigma\Delta\chi^{\beta}{}_{j}\cos2\psi_{j} + Lr^{-4} + M \qquad (1)$$

where θ is the dihedral angle between the vicinal protons in question, ϕ_i is the dihedral angle between α-substituent R_i and one of the coupling protons, $\Delta\chi_i$ is Mullay's group electronegativity[15] of R_i, $\Delta\chi^{\beta}{}_{j}$ is that of j-th β-substituent R' forming a dihedral angle ψ with a coupling proton, ω_1 and ω_2 are the two H-C-C valence angles involving a coupling proton, r_{CC} is the distance of the C-C bond, r is the intramolecular nonbonded distance (less than 3.3 Å) involving a coupling proton and oxygen or carbon atom, and A to I, K to M and W are adjustable parameters.

RESULTS

Conformer Distribution

According to the MM-type force field, conformers of these flexible molecules distribute rather evenly. Populations of the most abundant conformers for **1a** to **8f** are given in Table 1. We note that the global energy-

Table 1. The Most Stable Conformers of 1 to 8 with Populations Calculated with MM2(85)

Compound	N[a]	Most stable conformer[b]	Population (%)
1a	27	*sc(+)-ap-ap*	16.3
1b	27	*sc(+)-ap-ap*	12.7
2a	81	*sc(-)-ap-ap-sc(+)*	11.8
2b	81	*sc(-)-ap-sc(-)-sc(-)*	7.6
3a	80	*ap-ap-ap-ap*	10.0
3b	81	*ap-ap-ap-ap*	14.2
4a	81	*sc(+)-ap-ap-sc(-)*	17.8
4b	80	*sc(+)-ap-sc(+)-sc(+)*	13.6
4c	81	*sc(+)-sc(+)-sc(+)-ap*	9.4
5a	227	*sc(-)-ap-ap-ap-sc(-)*	9.2
5b	227	*sc(+)-sc(+)-ap-sc(+)-sc(+)*	6.2
5c	232	*sc(-)-ap-sc(-)-sc(-)-sc(-)*	13.5
5d	232	*sc(+)-ap-sc(+)-ap-ap*	5.8
6a	223	*sc(-)-ap-ap-ap-sc(-)*	7.8
6b	231	*sc(-)-ap-ap-sc(+)-sc(+)*	5.3
6c	227	*ap-ap-ap-ap-sc(+)*	11.1
6d	229	*ap-ap-ap-sc(-)-sc(-)*	5.1
7a	206	*ap-ap-ap-ap-sc(+)*	9.1
7b	211	*sc(-)-ap-ap-sc(+)-sc(+)*	8.9
8a	236	*sc(+)-ap-ap-ap-sc(-)*	7.1
8b	228	*ap-ap-sc(-)-sc(-)-ap*	4.8
8c	237	*ap-ap-ap-ap-sc(-)*	6.1
8d	235	*sc(+)-ap-ap-ap-sc(+)*	13.8
8e	224	*sc(+)-ap-ap-ap-sc(+)*	6.3
8f	227	*sc(+)-ap-sc(-)-sc(-)-sc(-)*	6.9

[a] Total number of conformers geometry-optimized. [b] The underlined portion (three-atom system) of backbone chain contains 1,3-parallel orientation of a pair of acetoxy groups.

minimum conformer never exceeds 18% of the whole population. Two other features are worth commenting here. In only two instances, the global energy-minimum conformer has all the C-C bonds in *ap* conformation (**3a** and **3b**) and *sc* bonds appears very frequently in the global energy-minimum conformers. Furthermore, most of these conformers contain 1,3-parallel orientation of substituents. The underlined part of the backbone chain carries a pair of acetoxy groups in 1,3-parallel relation. Actually, it is recognized[7] that this interaction is less severe than that between 1,3-diaxial alkyl substituents on the chair six-membered ring in the case of 1,3-diaxial-dimethoxycyclohexanes. These observations on the flexibility of **1** to **8** are not in line with the previously held trends based on the x-ray analysis.[4] Our results are, however, force field dependent and should be taken with care.

Vicinal Coupling Constants

Table 2 summarizes the results of population-weighted calculations for **1** to **8**. In this Table, letter A in parentheses means that the solvent used is C_6D_6, and letter B means $CDCl_3$. The differences in the coupling constants between the two solvents are small. When our original parameters set of eq 1 was used, the standard deviation of errors in the calculated values from the observed values of the 160 coupling constants was 0.81 Hz for the combined performance of 'Calc(A)' and 'Calc(B)'. Upon re-optimization of the parameters set of eq 1 to best reproduce the observed coupling constants in Table 2, the standard deviation decreased to 0.74 Hz. Table 2 lists those calculated by the revised parameters set.[17]

Table 2. Observed and Calculated Vicinal ^1H-^1H Coupling Constants of Alditol Peracetates **1** to **8**

	Bond											
	1-2	1-2	1-2	1-2	2-3	2-3	3-4	3-4	4-5	4-5	5-6	5-6
2R,3R-Tetritol tetraacetate **1a**												
Obs(A)[a]	5.5	2.8	---	---	4.4	---	b	b	---	---	---	---
Cal(A)	7.1	3.8	---	---	4.5	---	b	b	---	---	---	---
2R,3S-Tetritol tetraacetate **1b**												
Obs(A)	5.8	4.0	---	---	6.7	---	b	b	---	---	---	---
Cal(A)	6.6	3.1	---	---	6.8	---	b	b	---	---	---	---
3R,4R-2-Deoxypentitol tetraacetate **2a**												
Obs(A)	6.9	6.9	5.7	5.7	c	c	4.0	---	6.7	4.4	---	---
Cal(A)	8.0	7.0	5.6	4.8			3.3	---	6.8	4.3	---	---
3R,4S-2-Deoxypentitol tetraacetate **2b**												
Obs(A)	8.2	5.9	5.9	5.6	8.8	3.9	4.8	---	6.3	3.5	---	---
Cal(A)	7.6	7.3	5.6	4.8	8.8	3.7	5.6	---	6.7	3.2	---	---
2R,4S-3-Deoxypentitol tetraacetate **3a**												
Obs(A)	---	---	---	---	7.5	5.7	b	b	---	---	---	---
Cal(A)	---	---	---	---	8.5	4.8	b	b	---	---	---	---
2R,4R-3-Deoxypentitol tetraacetate **3b**												
Obs(A)	---	---	---	---	11.0	3.2	b	b	---	---	---	---
Cal(A)	---	---	---	---	9.6	3.7	b	b	---	---	---	---
2R,3r,4S-Pentitol pentaacetate **4a**												
Obs(B)	6.0	4.3	---	---	5.3	---	b	---	b	b	---	---
Cal(B)	6.4	4.6	---	---	5.0	---	b	---	b	b	---	---
2R,4R-Pentitol pentaacetate **4b**												
Obs(A)	4.9	2.7	---	---	9.0	---	2.6	---	7.1	5.3	---	---
Obs(B)	4.8	2.7	---	---	8.4	---	2.4	---	7.1	4.8	---	---
Cal(B)	5.8	3.5	---	---	7.1	---	3.5	---	7.0	4.2	---	---

2R,3s,4S-Pentitol pentaacetate 4c												
Obs(A)	6.1	3.4	---	---	5.5	---	b	---	b	b	---	---
Obs(B)	6.0	3.4	---	---	5.8	---	b	---	b	b	---	---
Cal(B)	5.7	4.0	---	---	6.0	---	b	---	b	b	---	---
3R,4S,5S-2-Deoxyhexitol pentaacetate 5a												
Obs(A)	7.8	5.8	5.8	5.2	7.7	4.1	4.4	---	5.7	---	6.0	4.1
Obs(B)	6.2	6.2	6.2	6.2	c	c	c	---	6.0	---	5.8	3.9
Cal(A)	7.7	6.4	5.7	4.8	9.0	4.7	4.0	---	5.9	---	5.9	4.0
3R,4S,5R-2-Deoxyhexitol pentaacetate 5b												
Obs(A)	6.7	6.7	5.9	5.9	c	c	c	---	c	---	4.6	2.5
Obs(B)	c	c	c	c	8.9	4.6	2.6	---	8.5	---	4.9	2.7
Cal(A)	7.8	7.0	5.4	4.6				---		---	5.4	3.8
Cal(B)					9.1	5.8	3.4	---	8.0	---	---	---
3R,4R,5S-2-Deoxyhexitol pentaacetate 5c												
Obs(A)	7.5	7.0	5.0	5.0	9.7	3.4	4.1	---	6.5	---	6.1	2.8
Obs(B)	8.4	6.0	5.6	5.2	9.2	3.9	3.9	---	6.4	---	6.0	2.8
Cal(A)	7.6	6.8	5.6	5.1	8.8	3.8	3.8	---	6.4	---	5.4	3.5
3R,4R,5R-2-Deoxyhexitol pentaacetate 5d												
Obs(A)	8.4	6.2	5.6	5.2	8.8	3.2	7.4	---	3.4	---	6.8	5.1
Obs(B)	c	c	c	c	10.0	3.4	6.7	---	3.8	---	6.8	5.1
Cal(A)	7.9	7.2	5.4	4.7	8.9	3.6	5.8	---	4.3	---	6.7	4.2
2R,4S,5S-3-Deoxyhexitol pentaacetate 6a												
Obs(A)	5.7	3.5	---	---	7.3	5.7	7.3	5.7	4.0	---	6.4	4.4
Cal(A)	5.4	3.0	---	---	8.3	5.2	8.5	6.4	3.4	---	6.4	4.6
2R,4S,5R-3-Deoxyhexitol pentaacetate 6b												
Obs(A)	5.9	3.5	---	---	6.8	6.5	7.9	4.7	4.9	---	6.4	3.6
Cal(A)	5.4	3.0	---	---	8.8	5.0	8.2	4.2	4.7	---	6.2	3.6
2R,4R,5R-3-Deoxyhexitol pentaacetate 6c												
Obs(A)	6.2	3.5	---	---	11.0	3.3	10.6	3.7	4.1	---	7.0	4.1
Cal(A)	5.6	3.0	---	---	10.1	3.3	10.6	4.2	4.0	---	6.5	4.1
2R,4R,5S-3-Deoxyhexitol pentaacetate 6d												
Obs(A)	6.3	3.4	---	---	10.5	3.5	10.4	3.8	4.0	---	6.9	3.7
Cal(A)	4.9	3.4	---	---	9.6	3.8	9.7	3.1	5.1	---	6.2	3.3
2R,3S,5S-2,4-Bisdeoxy-2-methylhexitol tetraacetate 7a												
Obs(A)	6.2	5.9	---	---	5.9	---	10.9	3.0	10.7	3.3	6.3	3.5
Cal(A)	6.4	5.2	---	---	6.6	---	10.4	2.7	10.0	3.7	5.9	2.9
2R,3S,5R-2,4-Bisdeoxy-2-methylhexitol tetraacetate 7b												
Obs(A)	5.9	5.9	---	---	6.1	---	(6.1)[d]		(6.9)[d]		6.0	3.2
Cal(A)	6.7	5.7	---	---	4.2	---	(5.9)[d]		(7.0)[d]		5.6	2.8
2R,3S,4S,5S-Hexitol hexaacetate 8a												
Obs(B)	6.1	4.0	---	---	6.3	---	4.8	---	6.7	---	5.3	3.6
Cal(B)	5.8	4.4	---	---	6.5	---	4.3	---	7.0	---	5.3	3.8
2R,3S,4R,5R-Hexitol hexaacetate 8b												
Obs(B)	6.7	4.9	---	---	3.3	---	7.9	---	3.7	---	7.2	3.4
Cal(B)	6.5	5.0	---	---	4.7	---	6.8	---	5.8	---	6.5	4.0
2R,3S,4R,5S-Hexitol hexaacetate 8c												
Obs(B)	7.5	4.8	---	---	2.2	---	10.0	---	b	---	b	b
Cal(B)	6.4	4.7	---	---	3.6	---	8.9	---	b	---	b	b
2R,3S,4S,5R-Hexitol hexaacetate 8d												
Obs(B)	5.8	4.4	---	---	5.0	---	6.0	---	b	---	b	b
Cal(B)	6.0	5.3	---	---	4.9	---	5.5	---	b	---	b	b
2R,3R,4R,5R-Hexitol hexaacetate 8e												
Obs(B)	5.1	2.8	---	---	9.2	---	2.4	---	b	---	b	b
Cal(B)	5.0	3.9	---	---	8.2	---	3.6	---	b	---	b	b
2R,3R,4S,5S-Hexitol hexaacetate 8f												
Obs(B)	6.3	3.1	---	---	5.9	---	5.0	---	b	---	b	b
Cal(B)	5.4	4.1	---	---	6.9	---	4.0	---	b	---	b	b

[a] Obs = experimental coupling constant measure in C_6D_6 (A) or in $CDCl_3$ (B). Cal = coupling constant calculated according to equation 1 for C_6D_6 solution (A) or $CDCl_3$ solution (B). [b] Equivalent to other value due to symmetry. [c] Not observed. [d] C4 methylene protons appear as a triplet. In order to compare with the observed values, the two calculated constants are averaged.

DISCUSSION

Errors in the calculation of vicinal coupling constants in the flexible molecules **1**-**8** are still too large for this method to be applied directly to the assignment of the relative stereochemistry of asymmetric centres along the backbone chain in alditols. Yet, the agreements between the observed and calculated coupling constants can be considered gratifying, in view of the imposed constraints in the MM-calculation, especially the freezing of substituent rotation. A close look at Table 2 reveals that one half of the coupling constants are reproduced within 0.5 Hz of the observed values, and only 10% of the computed data deviate by more than 1.3 Hz from the observed. Clearly, our methodology can be regarded as qualitatively sound.

The Root-mean Square Criterion

Even if the precision of our computation does not warrant straightforward identification of a stereoisomer, it is still possible to use the present method as a tool in diagnosing the pattern of a set of coupling constants. Suppose we obtain a stereoisomer of tetritol peracetate **1** and its vicinal coupling constants are measured. Of the four stereoisomers (2*R*,3*R*; 2*S*,3*S*; 2*R*,3*S*; 2*S*,3*R*), the enantiomeric pair should show identical pattern of coupling constants, but the pattern should be basically different between diastereomers, e.g. between 2*R*,3*R* (**1a**) and 2*R*,3*S* (**1b**). The objective here is to see if the observed pattern of coupling constants in this particular stereoisomer of **1** can be matched with either of the calculated patterns for **1a** and **1b**.

The fit of coupling constant pattern is conveniently judged by the root-mean-squares (rms) criterion σ:[18]

$$\sigma = \{ [\sum_{k=1}^{M} (J_k^{obs} - J_k^{calc})^2] / M \}^{1/2} \qquad (2)$$

where M is the number of observed coupling constants for this stereoisomer, J_k^{obs} and J_k^{calc} are respectively the k-th observed and calculated coupling constants.

Table 3 summarizes the results of the rms test. If the unknown stereoisomer in the above example were **1a** (or its enantiomer 2*S*,3*S*), then we should have the observed coupling constant values listed as Obs(A) of this stereoisomer in Table 2. The σ criteria are computed by equation 2 using these values for J^{obs} and using 'Cal(A)' values of **1a** and **1b** for J^{calc} to give the rms values of 1.091 and 1.534, respectively. The observed coupling constant pattern fits better with **1a** than with **1b**, hence it is possible to identify this molecule to have either 2*R*,3*R* or 2*S*,3*S* configurations. **4b** is an exception, since the pattern of its six coupling constants can be readily differentiated from those of **4a** and **4c**, which give only three coupling constants due to molecular symmetry. Similarly, **8a** and **8b** can be distinguished from **8c** to **8f**, by simply counting the number of coupling constants (seven vs. four).

Twenty-four tests have been performed for the remaining cases (Table 3). Test failed only in two cases: **6d** and **7b**. Since the pairs, **6c**/**6d** and **7a**/**7b**, show very close patterns of coupling constants, these may be regarded as accidental coincidence. Simply put, if one uses the present methodology of identifying magnetically unique stereoisomers based only on the gross structure, the rate of success is 92%, even though there are marginal cases like **2b** and **5b**. These results imply that, even at the present level of precision, the combined MM/Karplus-type equation method can be used advantageously to narrow down, e.g. the load of structure determination of natural products having alditol-like fragments. If a gross structure is known, the application of

σ-criteria will provide an enantiomeric pair of complete three-dimensional structures as the potential candidates for the answer. For example, if the σ-criteria points to **1a**, then the correct structure should be either *2R,3R* or *2S,3S*.

The rate of success by the rms test decreased to 88% when the vicinal coupling constants were calculated by using the original parameters set for eq 1.[6] Since the decrease is only moderate, it does not seem absolutely necessary to use the re-optimization routine for the parameters of eq 1 attached to the 3JHHM program package.[16] The use of original parameters set should give qualitatively the same conclusion.

Table 3. The Root-Mean-Square Test for Identification of a Stereoisomer from among Magnetically Unique Set of Candidate Structures (Hz)

Target	Candidates				Result
	1a	**1b**			
1a	1.091	1.534			+
1b	1.480	0.698			+
	2a	**2b**			
2a	0.604	0.884			+
2b	0.855	0.750			+
	3a	**3b**			
3a	0.951	2.051			+
3b	2.099	1.051			+
	4a	**4c**			
4a	0.337	0.473			+
4b	0.864	0.404			+
	5a	**5b**	**5c**	**5d**	
5a	0.530	1.129	0.629	0.921	+
5b	1.226	0.891	0.984	1.989	+
5c	0.704	1.001	0.497	1.057	+
5d	1.511	2.180	1.669	0.768	+
	6a	**6b**	**6c**	**6d**	
6a	0.660	0.901	1.735	1.651	+
6b	1.103	0.893	1.828	1.567	+
6c	1.653	1.328	0.463	0.904	+
6d	1.509	1.160	*0.390*	0.796	–
	7a	**7b**			
7a	0.555	0.912			+
7b	*0.467*	0.960			–
	8a	**8b**			
8a	0.309	1.165			+
8b	2.358	1.133			+
	8c	**8d**	**8e**	**8f**	
8c	1.048	2.740	4.583	3.968	+
8d	1.645	0.527	2.055	1.402	+
8e	4.442	2.965	0.957	1.552	+
8f	2.402	1.243	1.548	0.976	+

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16. Program 3JHHM is available in public domain: QCPE No 591 (QCPE, Department of Chemistry, Indiana University, Bloomington, IN 47405, USA); JCPE No.12 (Japan Chemistry Program Exchange, c/o Japan Association for International Chemical Information, Gakkai Centre Building, 2-4-16 Yayoi, Bunkyo-ku, Tokyo 113, Japan).

17. The optimized set is as follows: A = -1.199, B = 6.621, C = -0.218, D = 0.368, E = 0.060, F = 0.424, G = 0.011, H = 0.148, I = 61.475, K = 1.071, L = -0.889 (oxygen atom), -1.200 (carbon atom), M = 7.921 (1,2-disubstituted), 7.394 (trisubstituted), 7.268 (tetrasubstituted), W = 1.000 (1,2-di), 2.152 (tri), 0.855 (tetra).
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APPENDIX

The compounds **1** to **8** were prepared as outlined below.

Tetritol Tetreacetates **1a** and **1b**.

Racemic and meso diethyl tartarates were reduced with LAH and the resulting tetraols acetylated, respectively.

2-Deoxypentitol Tetraacetates **2a** and **2b**.

See (a) Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Viti, S. M. *J. Org. Chem.* **1982**, *47*, 1378-1380.

3-Deoxypentitol Tetraacetates **3a** and **3b**.

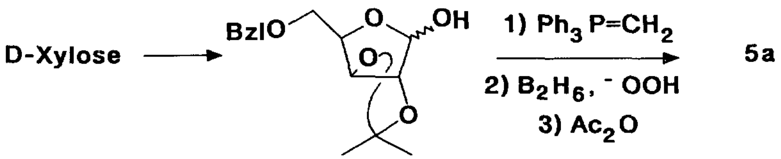
Meso and racemic diethyl α,α'-dihydroxyglutarates [Ingold, C. K. *J. Chem. Soc.* **1921**, 305, also see Darby, N. *Ph. D. Dissertation*, **1972**, University of Alberta, Canada] were reduced and then the tetraols were acetylated.

Pentitol Pentaacetates **4a-4c**.

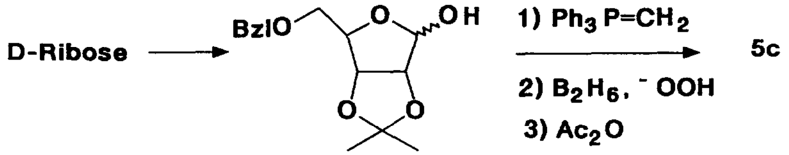
See (b) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373-1378.

2-Deoxyhexitol Pentaacetates **5a-5d**.

The schemes shown below were followed:

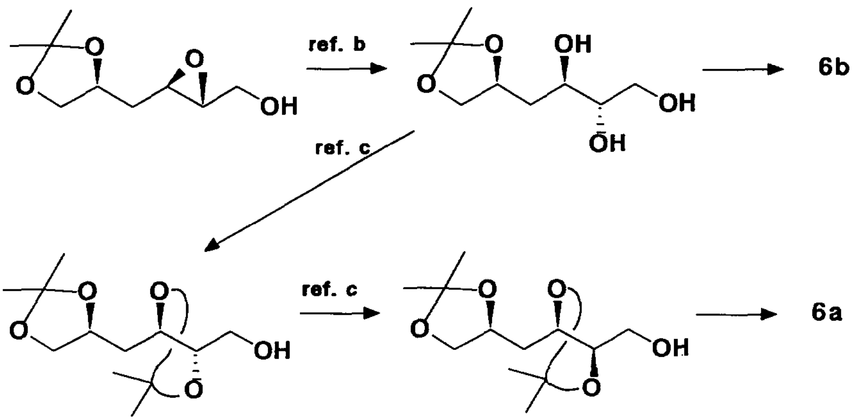


$$\text{D-2-Deoxygalactose} \xrightarrow[2)\ Ac_2O]{1)\ NaBH_4} \textbf{5b}$$

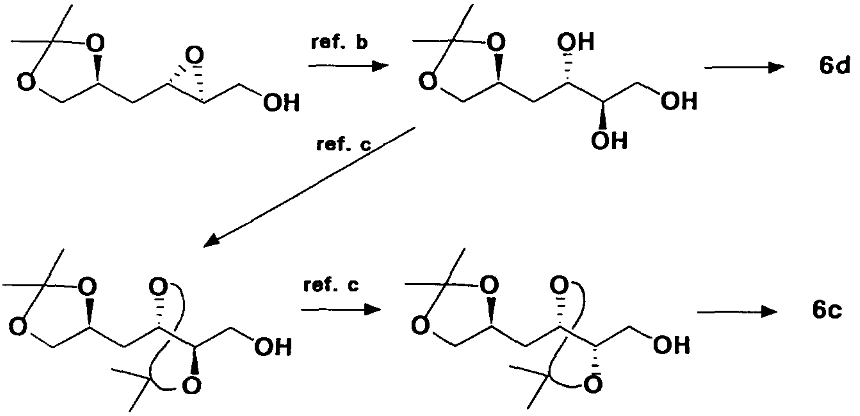


$$\text{D-2-Deoxyglucose} \xrightarrow[\text{2) Ac}_2\text{O}]{\text{1) NaBH}_4} \textbf{5d}$$

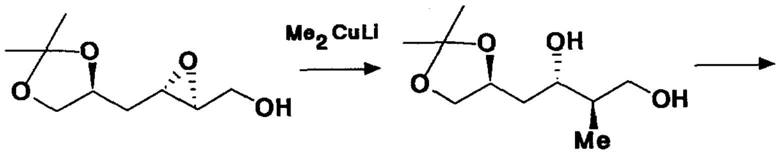
<u>3-Deoxyhexitol Pentaacetates</u> **6a-6d.**



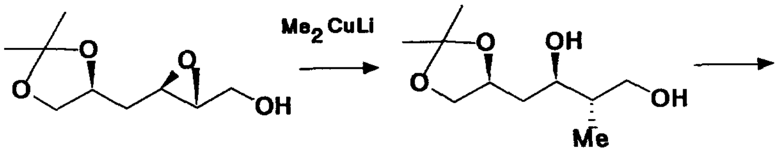
(c) Lee, A. W. M.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Walker, F. J. *J. Am. Chem. Soc.* 1982, *104*, 3515-3516.



2,4-Bisdeoxy-2-methylhexitol tetraacetates **7a** and **7b**.



7a



7b

Hexitol Hexaacetates **8a**-**8f**.

All these compounds were prepared from commercially obtained samples of the D- or L-hexoses. See ref. 2.