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Characterization of D-glucaric acid using NMR, X-ray crystal structure, and MM3 molecular modeling analyses

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ABSTRACT

D-Glucaric acid was characterized in solution by comparing NMR spectra from the isotopically unlabeled molecule with those from D-glucaric acid labeled with deuterium or carbon-13 atoms. The NMR studies provided unequivocal assignments for all carbon atoms and non-hydroxyl protons of the molecule. The crystal structure of D-glucaric acid was obtained by X-ray diffraction techniques and the structure was a close match to the low energy conformation generated from a Monte-Carlo-based searching protocol employing the MM3 molecular mechanics program. The molecule adopts a bent structure in both the crystalline and computationally generated lowest-energy structure, a conformation that is devoid of destabilizing eclipsed 1,3-hydroxyl interactions.

1. Introduction

D-Glucaric acid (**2**) is a naturally occurring aldaric acid that is found in small amounts in a variety of vegetables and fruits[1,2] and is touted for its dietary value, particularly as a cancer preventative agent.[1] D-Glucaric acid was first reported by Sohst and Tollens in 1888[3] by the nitric acid oxidation of D-glucose (**1**) and isolated as its monopotassium salt (**3**, Fig. 1). Although nitric acid has been widely employed over the past century as a general agent for the oxidation of aldoses to their corresponding aldaric acids, other oxidative processes have also been used for these conversions.[4–6] A crystalline form of D-glucaric acid was generated by Rehorst by treating the silver salt with hydrochloric acid,[7] whereas Hirasaka et al. converted the monopotassium salt (**3**) to **2** using a cation exchange resin.[8]

D-Glucaric acid has been of particular interest to us as a diacid monomer for condensation polymerizations with diamines to give the corresponding poly(D-glucaramides).[9–12] Poly(D-glucaramides) are conformationally complex structures given that the repeating asymmetric D-glucaryl unit has four chiral carbons. To gain additional insight into possible conformations the D-glucaryl group might adopt in these polyamides, we undertook a study designed to provide us with some conformational information on D-glucaric acid in aqueous solution employing ^{1}H NMR, in the solid state via an X-ray crystal structure analysis and computationally, employing a new MM3 molecular mechanics protocol.[13] An added incentive for this study stemmed from a forecast in a US Department of Energy publication pointing to the significant potential commercial value of D-glucaric acid as an important renewable chemical building block derived from widely available D-glucose.[14]

2. Results and discussion

2.1. NMR studies on D-glucaric acid (2)

The NMR studies on D-glucaric acid were carried out in order to unequivocally assign the proton and carbon chemical shifts of the molecule and compare the results with those from earlier reports.[15–17] The NMR studies described here differ from the previously reported studies in that NMR data were obtained directly from samples of crystalline D-glucaric acid dissolved in D_2O rather than in salt form or where acyclic **2** was in equilibrium with its acid/lactone and dilactone forms. In addition, results from three different isotopically labeled samples of **2** were used for verification of specific chemical shift assignments. ^{1}H NMR and ^{13}C NMR chemical shifts and coupling constants for **2** (D_2O, Table 1) were obtained from spectra recorded at 600 MHz and 150 MHz, respectively. Spectral assignments for **2** were made from detailed analyses of HOMO and HETERO nuclear, two dimensional NMR spectra (COSY and HSQC, respectively—Supplementary data).

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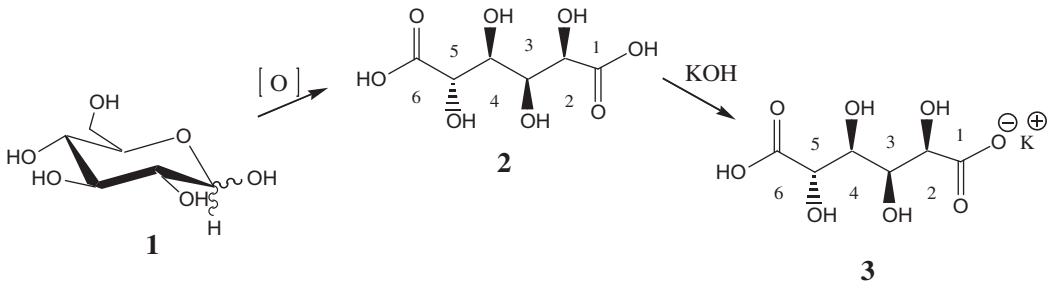

Figure 1. General oxidative conversion of D-glucose (**1**) to D-glucaric acid (**2**), isolated as monopotassium D-glucarate (**3**).

Table 1
NMR assignments for **2**

Hydrogen No.	2	3	4	5
Chemical shift (ppm)	4.48	4.14	3.96	4.36
Vicinal ^{1}H–^{1}H coupling	$J_{2,3}$	$J_{3,4}$		$J_{4,5}$
J value (Hz)	3.00	5.87		5.14

Carbon No.	1	2	3	4	5	6
Chemical shift (ppm)	176.74	72.47	72.43	74.12	72.26	176.43

Supporting ^{1}H and ^{13}C NMR spectral information was garnered from spectra of 2-^{2}H, 1-^{13}C and 6-^{13}C isotopically labeled samples of **2** (**2a**, **2b,** and **2c**, respectively, Fig. 3) generated by the nitric acid oxidation of correspondingly labeled D-glucose.

The ^{1}H NMR spectra of unlabeled D-glucaric acid (**2**) and labeled D-[2-^{2}H]- (**2a**), D-[1-^{13}C]- (**2b**), and D-[6-^{13}C]-glucaric acid (**2c**) are shown in Figure 2. The spectrum of D-[2-^{2}H]-glucaric acid (**2a**) is missing the doublet at δ 4.48 ppm (H2) seen in that of unlabeled **2** and shows the signal at δ 4.14 ppm (H3) as a doublet in place of the quartet of unlabeled **2**. These spectral changes confirm the assignment of the H-2 proton chemical shift (4.48 ppm) and clearly show the $J_{3,4}$ coupling (5.87 Hz) from the H3 doublet at 4.14 ppm. The^{1}H NMR spectra of D-[1-^{13}C]- and [6-^{13}C]-glucaric acid, **2b** and **2c**, in addition to supporting the proton chemical shift assignments for **2**, also have some notable spectral differences. The spectrum of **2b** displays the H2 signal (4.48 ppm) as a doublet of doublets, consistent with the added ^{13}C1–C2–^{1}H2 two bond coupling (J = 5.03 Hz), and the H-3 signal (4.14 ppm) as a complex multiplet, resulting from the additional ^{13}C1–C2–C3–^{1}H3 vicinal coupling (J = 1.76 Hz). The H4 and H5 signals of **2c** are also more complex than those of **2** due to the additional ^{13}C6–C5–C4–H4 vicinal coupling (J = 4.11 Hz) and ^{13}C6–C5–H5 two bond coupling (J = 4.12 Hz), respectively. The ^{13}C spectra of **2b** and **2c** were particularly valuable in that each was distinguished by a single enhanced downfield signal, allowing for direct chemical shift assignment of C1 and C6 in **2** at 176.74 ppm and 176.43 ppm, respectively.

The chemical shifts and ^{1}H–^{1}H coupling constant values reported here update those values previously reported.[15–17] The assignments for **2** given in Ref. 16 were also aided from spectral data acquired with D-[2-^{2}H]-glucaric acid, but details were not reported. A recent report[17] gives comparable but slightly different ^{1}H chemical and ^{13}C shift values for **2**. However, in that report, spectra were recorded of an equilibrium mixture of **2** as its open chain diacid, lactone/acid and dilactone forms in DCl/D_2O and not as a single component in D_2O, as reported here.

2.2. Comparison of the X-ray crystal structure and computationally generated structures of D-glucaric acid

The structure of D-glucaric acid in the crystal state was determined to have a sickle-like (bent) $_2G^+{}_3G^+$ conformation (Fig. 4), applying conformational nomenclature previously established[18] to the inner three C2–C3, C3–C4, and C4–C5 backbone bonds. The crystal structures of a number of D-glucaric acid derivatives have been reported, some of which adopt varying bent conformations with others being extended. Included among the former derivatives are potassium sodium D-glucarate hydrate,[19] monopotassium D-glucarate,[20] and diammonium D-glucarate,[21] whereas *N,N′*-dimethyl D-glucaramide[19] and dipotassium D-glucarate[19] are conformationally extended. A conformational characteristic found with crystalline D-glucaric acid is the absence of hydroxyl groups eclipsed in 1,3-parallel interactions, which is in contrast to what was observed with extended structures noted above. Extended *N,N′*-dimethyl D-glucaramide[19] represents a previously reported conformational model for the glucaryl repeating unit in poly-D-glucaramides that includes the diamido functionality of typical glucaric acid-based polyamides.

Crystalline D-glucaric acid (**2**) is extensively hydrogen bonded as shown in Figure 5. All six hydroxyl groups donate to intermolecular hydrogen bonds with the O4 and O7 hydroxyl groups each donating into two interactions. Except for the terminal hydroxyl oxygen atoms (i.e., O2 and O7), all the molecule's oxygen atoms accept hydrogen bonds. Two oxygen atoms, the O1 carbonyl oxygen atom and the O3 hydroxyl oxygen atom accept hydrogen bonds from two donating hydroxyl groups. The hydrogen bonds form a single cooperative network, but do not form either closed rings or infinite chain structures. No intramolecular hydrogen bonds exist.

Employing the method of Dowd et al.,[13] a Metropolis Monte-Carlo search routine was coupled to the MM3 molecular mechanics program[22–24] and a 20,000-step search of the D-glucaric acid conformational space was run. The search was conducted at a dielectric constant of 3.5 to reduce the strength of intra-molecular hydrogen bonds, and a shaking routine was used to keep the search from becoming trapped in a single low-energy region.[13]

The conformational search found 3310 distinct conformers. Twenty-one conformers were found within 1 kcal/mol of the global energy minimum (Table 2), the group falling into four conformational families, $_3G^+{}_4G^+$, $_2G^-{}_4G^+$, $_2G^-{}_4G^-$, and $_4G^+$. No fully extended conformations were observed among the lowest-energy structures. The lowest energy conformer had backbone torsion angles of 178.5° (C1–C2–C3–C4), 61.3° (C2–C3–C4–C5), and 58.5° (C3–C4–C5–C6), comparable to those in crystalline D-glucaric acid of 169.17° (C1–C2–C3–C4), 57.84° (C2–C3–C4–C5), and 67.93° (C3–C4–C5–C6), respectively. This backbone shape, $_3G^+{}_4G^+$, accounted for 57% of the conformers found with 1 kcal/mol of the computed structures (Table 2). These angles produce a 'bent' shape that avoids sterically unfavorable 1,3-oxygen–oxygen interactions.[25]

Although the backbone conformation of the global MM3 minimum (Fig. 6) closely matched that of the D-glucaric acid crystal structure (Fig. 4), differences in the structures were apparent. In the modeled structure, the terminal C1–C2 and C5–C6 carboxyl moieties and the hydroxyl groups had torsional orientations that

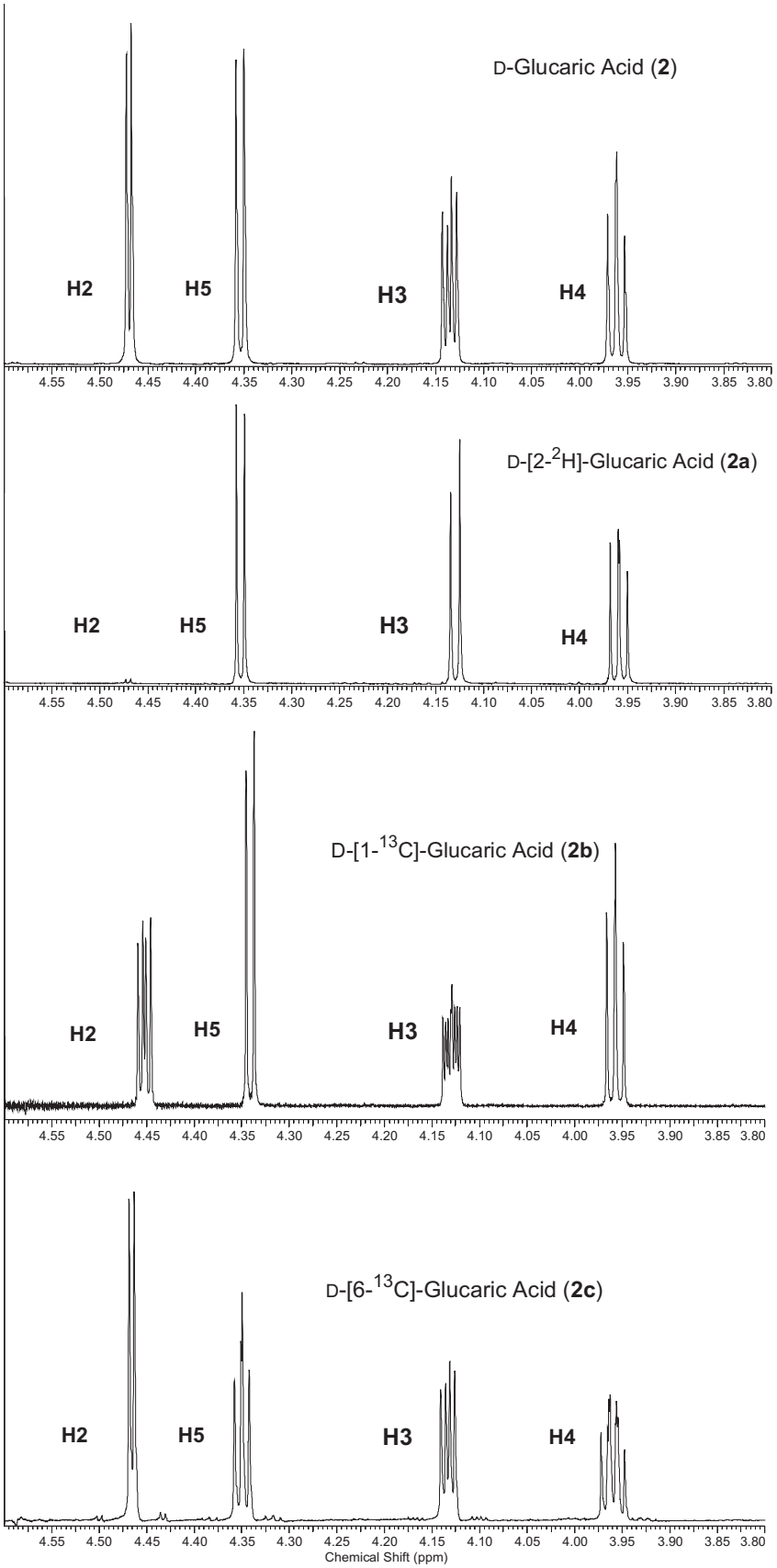

Figure 2. ^{1}H NMR spectra (600 MHz) of D-glucaric acid (**2**) and isotopically labeled D-glucaric acids (**2a**–**2c**).

differed from the crystal form. As an elevated dielectric constant was the only consideration applied to mimic the condensed phase during the modeling, the hydroxyl and carboxyl groups would not be influenced by intramolecular and environmental effects while the crystal structure would be sensitive to intermolecular hydrogen bonding and packing effects. Hence, differences in hydroxyl

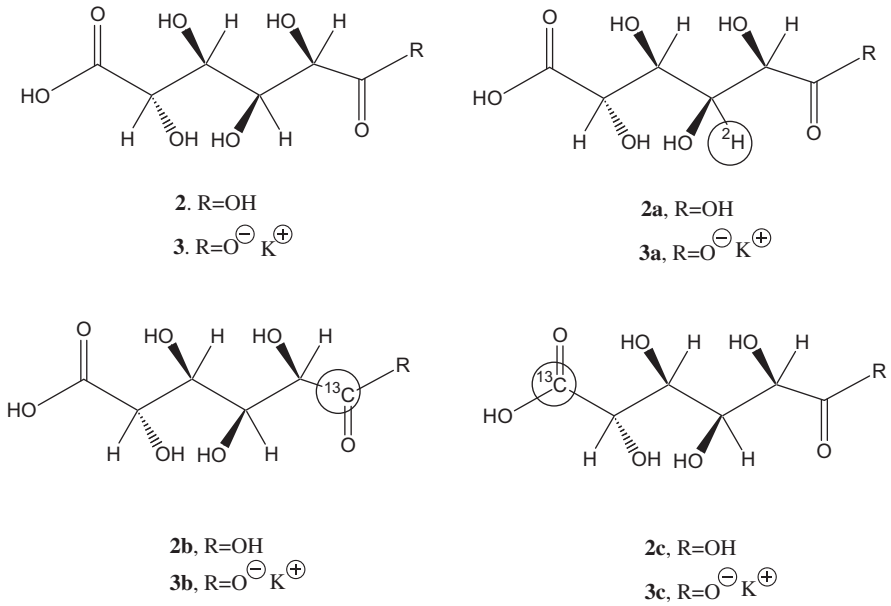

Figure 3. D-Glucaric acid (**2**), isotopically labeled D-glucaric acid (**2a–2c**), monopotassium D-glucarate (**3**) and monopotassium salts (**3a–3c**) of **2a–2c**.

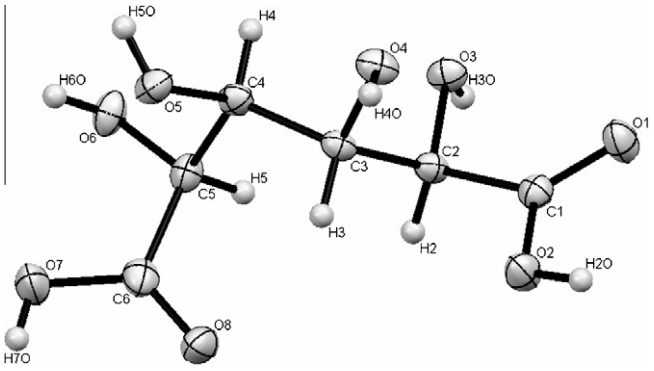

Figure 4. X-ray crystal structure of D-glucaric acid (**2**).

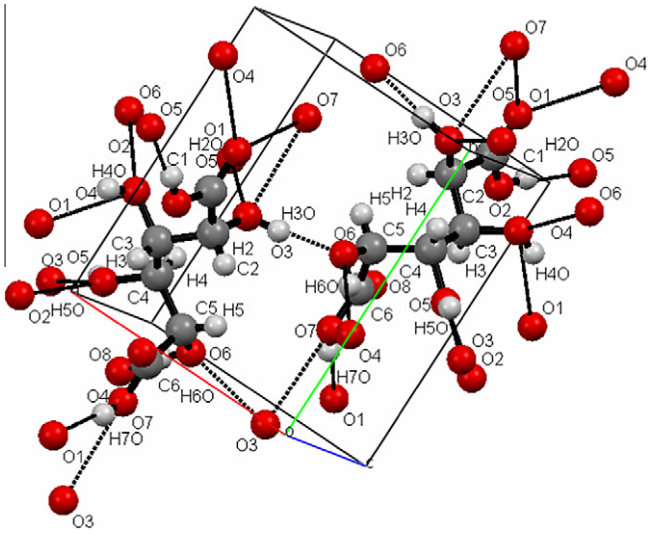

Figure 5. The unit cell of crystalline D-glucaric acid (**2**) showing the hydrogen bonding system associated with the crystal structure.

and carboxyl orientations between the solid-state and modeled conformers were not surprising.

Hydrogen–hydrogen coupling constants were calculated for each MM3 conformer with the Karplus equations of Haasnoot et al.[26] Population-averaged coupling constants for the three internal backbone bonds were in the 3.4–4.6 Hz range and were within range of the experimental values (Table 1). Calculated coupling constants averaged over the whole population were: $J_{2,3}$ =

Table 2
Distribution of MM3 generated conformers within 1 kcal/mol of the lowest-energy structure

C-1···C-4 angle	C2···C5 angle	C3···C6 angle	Conformer designation	Number found
180	60	60	$_3G^+{}_4G^+$	12
−60	180	−60	$_2G^-{}_4G^-$	5
−60	180	60	$_2G^-{}_4G^+$	3
180	180	60	$_4G^+$	1

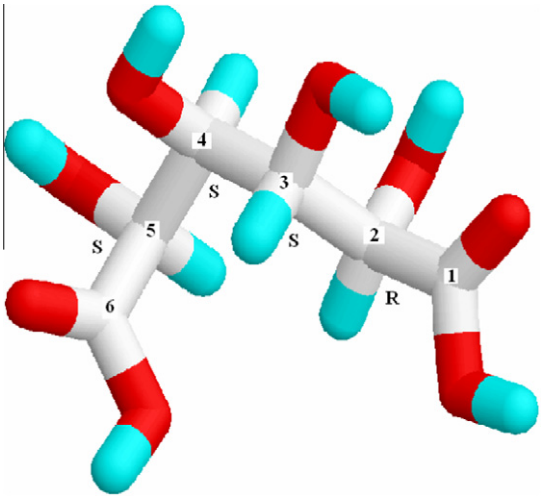

Figure 6. The lowest-energy MM3 conformer ($_3G^+{}_4G^+$) of D-glucaric acid (**2**).

4.63 Hz (3.00 Hz), $J_{3,4}$ = 3.69 Hz (5.87 Hz), $J_{4,5}$ = 3.4 Hz (5.14 Hz). The experimental values are in parenthesis. Because many conformers had relatively low energies, the calculated values resulted from the contribution of several forms and not from a single dominant backbone orientation. Hence, the modeling does not support the existence of an 'average' solution structure but rather a mixture of many structures. In addition, calculated coupling constants for the lowest-energy conformer, which had a backbone structure in good agreement with that of crystalline D-glucaric acid, were markedly different ($J_{2,3}$ = 0.56 Hz, $J_{3,4}$ = 9.87 Hz, and $J_{4,5}$ = 2.65 Hz) from the experimental results. This indicates that the aqueous and crystalline conformations of D-glucaric acid must be quite different. Jeffrey has made a similar observation regarding alditols.[27]

3. Experimental

3.1. General methods

All solvents and ion exchange resins were purchased from commercial sources and used without further purification. D-[1-^{13}C]-glucose and D-[6-^{13}C]-glucose were purchased from Cambridge Isotope laboratories, Inc., Andover, MA and D-[2-^{2}H]-glucose was purchased from Omicron Biochemicals, Inc., South Bend, IN. Solutions were concentrated in vacuo using a rotary evaporator with a vacuum of 15–20 mbar and bath temperature of 40 °C. Melting points were determined using a differential scanning calorimeter (Jade DSC, Perkin–Elmer, Shelton, CT) scanning from 5 °C to 250 °C at 10 °C/min and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature and 600 MHz and 150 MHz, respectively, on a Varian Unity spectrometer. Chemical shifts were reported in parts per million (ppm, δ) using *tert*-butyl alcohol [1.203 ppm (^{1}H), 30.695 ppm (^{13}C)] in D_2O as an internal standard. Two-dimensional HOMO and HETERO nuclear spectra were obtained using standard macros in the Varian Unity software. All NMR spectra were transformed and processed with ACD/SpecManager software using the standard 1D NMR and 2D NMR macros. Infrared spectra were recorded on a Thermo Nicolet 633 FT-IR spectrophotometer as KBr pellets. Optical rotations were measured at room temperature at the sodium D-line using a Perkin–Elmer 241 polarimeter and 1-dm tubes.

3.1.1. D-Glucaric acid (2)

To a slurry of Dowex 50WX8-100 H^+ form ion-exchange resin (20.8 mL, 43.7 mmol H^+) in deionized water (40 mL) was added solid monopotassium D-glucarate (**1**, 10 g, 40.3 mmol) and the resultant slurry was stirred at room temperature for exactly 10 min. The resin was removed by gravity filtration and washed with water (10 mL). The combined filtrate was frozen (dry ice/2-propanol) and the water was removed by lyophilization to afford a mixture of small crystals and an amorphous, off-white solid. Approximately 2 mL of the amorphous solid was removed from the flask, dissolved in a minimum amount of boiling water. The solution was cooled to room temperature, seeded with a few crystals from the flask, cooled to 4 °C and held overnight. The crystals formed were removed from the vial and triturated with acetone (10 mL). The acetone was carefully removed with a pipette and the crystalline solid was again washed with acetone (2 × 10 mL). The D-glucaric acid crystals obtained (398 mg) were not suitable for X-ray structure determination, as they appeared fractured and slightly opaque, but were useful as seed crystals.

3.1.2. X-ray quality, crystalline D-glucaric acid (2)

Monopotassium D-glucarate (**1**) was treated with Dowex 50WX8-100 H^+ form ion-exchange resin as above and following removal of the resin by filtration, the combined filtrate was concentrated. The syrupy residue was seeded with a crystal from above and stored at 4 °C for 12 h. The crystals were removed from the flask, washed, quickly, with 97% ethanol and the fine solid and ethanol were removed with a pipette to afford X-ray quality, crystalline D-glucaric acid: mp 119.3 °C (lit.[8] 117–118 °C, lit.[7] 125–126 °C); $[\alpha]_D^{20}$ +5.7 (*c* 0.064, D_2O, 5 min.) [lit.[8] +6.1 (*c* 1.0, H_2O, 5 min), lit.[7] +6.9 (*c* 1.0, H_2O); ^{1}H NMR (D_2O): δ 4.48 (d, 1H, H2, $J_{2,3}$ = 3.00 Hz), 4.36 (d, 1H, H5, $J_{4,5}$ = 5.14 Hz), 4.14 (dd, 1H, H3, $J_{2,3}$ = 3.00 Hz, $J_{3,4}$ = 5.87 Hz), 4.00 (m, 1H, H4). ^{13}C NMR (150 MHz, D_2O): δ 176.74 (C1), 176.43 (C6), 74.12 (C4), 72.47 (C2), 72.43 (C3), 72.26 (C5); IR (KBr): $\tilde{\nu}$ 3492–2917 (s, O–H stretch), 1729 (s, C=O stretch), 1692 (s, C=O stretch) cm^{-1}.

3.1.3. Conformational modeling

The 1996 version of MM3[22–24] was used for modeling preferred D-glucaric acid conformations. Default parameters were used with the full-matrix optimization method. A dielectric constant of 3.5 was chosen for this work, as dielectric constants between 3.0 and 4.0 have been used in prior MM3 studies of carbohydrates and have been generally found to yield preferable results.[19,28] Because D-glucaric acid has 11 torsion angles that define its conformation, a full staggered search of the confomational space would require 3^{11} or greater than 177,000 optimizations. To reduce the computer cost, the MM3 program was embedded within a Unix-based Metropolis-Monte-Carlo search routine to allow for a quicker more focused search of the low-energy regions of the molecule.[13] A 'shaking' routine was included in the search to prevent the search from being trapped within a region of low energy. A 20,000-step search found essentially all of the low-energy MM3 forms, as repeated searches produced essentially the same set of lowest energy forms. In addition, a routine was written to calculate the Karplus hydrogen–hydrogen coupling constants from the Haasnoot et al. model.[26] Transition-state structures were excluded from the conformer population by checking for imaginary vibrational frequency for each structure as it was found.

3.1.4. Monopotassium D-[2-^{2}H]-glucarate (3a)

To a mixture of D-[2-^{2}H]-glucose (536 mg, 2.96 mmol) and sodium nitrite (ca. 5 mg) at room temperature was added concentrated nitric acid (1 mL) and the solution was stirred for 5 min when an exothermic, brown/green gas generating reaction occurred. After an additional 5 min, when gas evolution had subsided, the solution was warmed to 60 °C, stirred for 2 h, and then concentrated under reduced pressure. The residue was dissolved in water, the solution cooled to 0 °C, the pH of the solution adjusted to 11 with aqueous potassium hydroxide solution (45%) and maintained above pH 10 for 1 h by addition of potassium hydroxide solution as needed. The solution was acidified to a pH of about 3.5 with concentrated hydrochloric acid to precipitate monopotassium D-[2-^{2}H]-glucarate (**3a**). The slurry was cooled to 0 °C, stirred for 30 min and the solid formed was isolated by filtration. The solid was then washed with a minimal amount of ice water to remove colored material, washed with acetone, and then dried at room temperature under vacuum to give monopotassium D-[2-^{2}H]-glucarate (**3a**, 239 mg, 23% yield) as a white powder. The powder was used in the next step without further purification.

3.1.5. D-[2-^{2}H]-Glucaric acid (2a)

A solution of **3a** (40 mg) in D_2O (2 mL) was treated with Dowex 50WX8-100 H^+ form ion-exchange resin (ca. 2 mL, previously washed three times with D_2O) for 5 min, the solid materials were removed by filtration and the ^{1}H NMR spectra of resulting D-[2-^{2}H]-glucaric acid (**2a**) was recorded: ^{1}H NMR (D_2O): δ 4.35 (d, 1H, H5, $J_{4,5}$ = 4.99 Hz), 4.13 (d, 1H, H3, $J_{3,4}$ = 5.87 Hz), 3.96 (dd, 1H, H4, $J_{4,5}$ = 4.99 Hz, $J_{3,4}$ = 5.87 Hz). ^{13}C NMR (150 MHz, D_2O): δ 176.72 (C1), 176.42 (C6), 74.07 (C4), 72.36 (C3), 72.27 (C5).

3.1.6. Monopotassium D-[1-^{13}C]-glucarate (3b)

D-[1-^{13}C]-Glucose (250 mg, 1.38 mmol) was oxidized according to the procedure for **3a** to afford **3b** as a white powder (143 mg, 42% yield). The powder was used in the next step without further purification.

3.1.7. D-[1-^{13}C]-Glucaric acid (2b)

A solution of **3b** (143 mg) in D_2O (1 mL) was protonated according to the procedure for **3a** and the NMR spectra of **2b** was recorded: ^{1}H NMR (D_2O): δ 4.45 (d, 1H, H2, $J_{2,3}$ = 3.0 Hz, $J_{C1,H2}$ = 5.03 Hz), 4.34 (d, 1H, H5, $J_{4,5}$ = 4.96 Hz), 4.14 (ddd, 1H, H3, $J_{2,3}$ = 3.23 Hz, $J_{3,4}$ = 5.00 Hz, $J_{C1,H3}$ = 1.76 Hz), 4.96 (d, 1H, H-4, $J_{4,5}$ = 4.99 Hz, $J_{3,4}$ = 5.59 Hz). ^{13}C NMR (150 MHz, D_2O): δ 176.83 (C1), 176.54 (C6), 74.12 (C4), 72.75 and 72.36 (C2, d, $J_{C1,C2}$ = 58.34 Hz), 72.41 (C3), 72.36 (C5).

3.1.8. Monopotassium D-[6-^{13}C]-glucarate (3c)

D-[6-^{13}C]-glucose (250, 1.38 mmol) was oxidized following the procedure for D-[2-^{2}H]-glucose to afford **3c** as a white powder (153 mg, 42% yield). The powder was used in the next step without further purification.

3.1.9. D-[6-^{13}C]-Glucaric acid (2c)

A solution of **3c** (20 mg) in D_2O (2 mL) was protonated according to the procedure for **3a** and the NMR spectra of **2c** recorded: ^{1}H NMR (D_2O): δ 4.47 (d, 1H, H2, $J_{2,3}$ = 3.27 Hz), 4.35 (dd, 1H, H5, $J_{4,5}$ = 4.90 Hz, $J_{H5,C6}$ = 4.12 Hz), 4.13 (dd, 1H, H3, $J_{2,3}$ = 3.33 Hz, $J_{3,4}$ = 5.87 Hz), 3.96 (ddd, 1H, H4, $J_{4,5}$ = 4.99 Hz, $J_{3,4}$ = 5.59 Hz, H4, $J_{H4,C6}$ = 4.11 Hz). ^{13}C NMR (150 MHz, D_2O): δ 176.74 (C1), 176.45 (C6), 74.09 (C4), 72.50 (C2), 72.47 and 72.08 (C5, d, $J_{C5,C6}$ = 59.47 Hz), 72.49 (C3).

Table 3
Crystal data and structure refinement for D-glucaric acid (**2**)

Identification code	D-Glucaric acid	
Empirical formula	$C_6H_{10}O_8$	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 6.7589(4) Å	α = 90°
	b = 8.6385(6) Å	β = 93.832(2)°
	c = 7.2420(4) Å	γ = 90°
Volume	421.89(5) Å^3	
Z	2	
Density (calculated)	1.654 Mg/m^3	
Absorption coefficient	1.412 mm^{-1}	
F(000)	220	
Crystal size	0.36 mm × 0.33 mm × 0.21 mm	
θ range for data collection	6.12–66.11°	
Index ranges	$-7 \leqslant h \leqslant 7$, $-8 \leqslant k \leqslant 8$, $-8 \leqslant l \leqslant 7$	
Reflections collected	2541	
Independent reflections	1261 [R(int) = 0.0148]	
Completeness to θ_{max}	92.0%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7559 and 0.6304	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	1261/1/168	
Goodness-of-fit on F^2	1.091	
Final R indices [$I > 2\sigma(I)$]	$R1$ = 0.0190, $wR2$ = 0.0495	
R indices (all data)	$R1$ = 0.0190, $wR2$ = 0.0495	
Flack parameter	0.12(16)	
Extinction coefficient	0.0387(19)	
Largest diff. peak and hole	0.131 and −0.119 e Å^{-3}	

3.1.10. Collection of X-ray diffraction data and solution of the crystal structure for D-glucaric acid, 2

A suitable crystal of **2** was coated with Paratone N oil, suspended in a small fiber loop and placed in a cooled nitrogen gas stream at 100 K on a Bruker D8 SMART 1000 CCD sealed tube diffractometer with graphic monochromated Cu Kα (1.54178 Å) radiation. Data were measured by means of a combination of φ and ω scans with 10-s frame exposures and 0.3° frame widths. Data collection, indexing and initial cell refinements were carried out with SMART[29] software. Frame integration and final cell refinements were done with SAINT[30] software. The final cell parameters were determined from least-squares refinement of 4070 reflections. The structure was solved by direct methods and difference Fourier techniques (SHELXTL, V5.10).[31] Hydrogen atoms were found in difference maps and were refined isotropically. Scattering factors and anomalous dispersion corrections are taken from the International Tables for X-ray Crystallography.[32] Structure solution, refinement, graphics, and publication materials were generated with SHELXTL, V5.10 software. Crystal data and structure refinement for D-glucaric acid (**2**) are shown in Table 3.

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Supplementary data

Details of X-ray crystallographic data for compound **2** are included as supplementary data. Tables of atomic coordinates and equivalent isotropic displacement parameters, bond lengths and angles, anisotropic displacement parameters, hydrogen coordinates, torsion angles, and$_5$ hydrogen bonds of **2** have been included as supplementary data.

Complete crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 798054. Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 336033, email: deposit@ccdc.cam.ac.uk or via: http://www.ccdc.cam.ac.uk.

COSY and HSQC spectra of **2** are also included.

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2011.08.016.

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