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Note

A convenient preparation of aldonohydroxamic acids in water and crystal structure of L-erythronohydroxamic acid

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Abstract

Hydroxamic acids derived from aldonic acids, namely aldonohydroxamic acids, have become an increasingly important class of inhibitors of enzymes involved in the metabolism of carbohydrates. We now report the straightforward preparation of various types of aldonohydroxamic acids by a new methodology involving the use of commercial 50% aqueous hydroxylamine as the source of the free base hydroxylamine that reacts directly with the corresponding aldonolactone dissolved in water. The reaction proceeds almost instantaneously in water at room temperature, yielding generally pure products in quantitative yield. To date, this methodology is probably the most facile and efficient way to synthesize aldonohydroxamic acids. We also determined by X-ray diffraction analysis the first crystal structure of a free aldonohydroxamic acid reported to date. Crystals of L-erythronohydroxamic acid belonged to the monoclinic system, space group $P2_1$, $a = 5.511(3)$, $b = 7.556(1)$, $c = 8.071(3)$ Å, $\beta = 109.10°$, and $Z = 2$.

Keywords: Hydroxamic acids; Hydroxylamine; Lactones; Water, reactions in; Monosaccharides; X-ray crystal structure

1. Introduction

Hydroxamic acids derived from aldonic acids, namely aldonohydroxamic acids, were first introduced by Mathis more than 50 years ago with the syntheses of D-glucono- (**1**, Scheme 1), L-ribono-, L-arabinono-, D-mannono- and D-galactonohydroxamic acids.[1] Aldonohydroxamic acids have become an increasingly important class of compounds. They have proven key compounds, as potent inhibitors, for the study of the mechanistic and structural aspects of several enzymes involved in the metabolism of simple carbohy-

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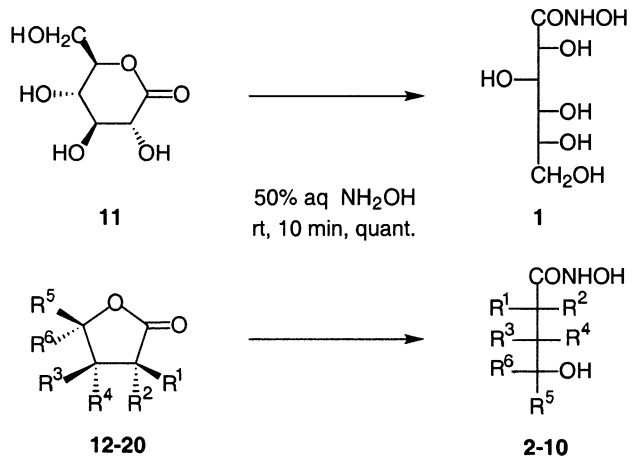

configuration	AL[a]	AHA[b]	R^1	R^2	R^3	R^4	R^5	R^6
5P-D-*arabino*[c]	**12**	**2**	OH	H	H	OH	CH_2OP	H
D-*lyxo*	**13**	**3**	OH	H	OH	H	CH_2OH	H
D-*arabino*	**14**	**4**	OH	H	H	OH	CH_2OH	H
L-*erythro*	**15**	**5**	OH	H	OH	H	H	H
L-*threo*	**16**	**6**	H	OH	OH	H	H	H
L-*lyxo*	**17**	**7**	H	OH	H	OH	H	CH_2OH
D-*erythro*	**18**	**8**	H	OH	H	OH	H	H
D-*ribo*	**19**	**9**	H	OH	H	OH	CH_2OH	H
5-deoxy-L-*lyxo*	**20**	**10**	H	OH	H	OH	H	CH_3

[a] AL = aldono-1,4-lactone. [b] AHA = aldonohydroxamic acid. [c] P = disodiumphosphate.

Scheme 1. Preparation of aldonohydroxamic acids **1**–**10** from the corresponding aldonolactones **11**–**20**.

drates, being used as mimetics of the postulated high-energy intermediates or transition states. The known examples are phosphoglycolohydroxamic acid,[2,3] D-threonohydroxamic acid,[4] D-arabinonohydroxamic acid 5-phosphate[5] (**2**, Scheme 1), D-lyxonohydroxamic acid[6] (**3**, Scheme 1), D,L-xylarohydroxamic acid[7] and D-arabinonohydroxamic acid[8] (**4**, Scheme 1). These compounds were commonly prepared by reaction of the free base hydroxylamine with the corresponding methyl or ethyl aldonates or aldonolactones. However, and as far as the experimental details were reported, the free base hydroxylamine was always obtained by neutralization of a hydroxylamine hydrochloride solution either: (i) in dry methanol using sodium methoxide, allowing removal of some of the precipitated sodium chloride; or (ii) in aqueous solution using lithium hydroxide or another base. In most cases, the aldonohydroxamic acids had to be further purified by size-exclusion chromatography, precipitation, or ion-exchange chromatography.

In a general project dealing with the study of aldonohydroxamic acids, we report here the syntheses of several aldonohydroxamic acids of various lengths and configurations from their corresponding aldonolactones: the known aldonohydroxamic acids **1**–**4** and new aldonohydroxamic acids **5**–**10** (Scheme 1). We had first prepared these products according to the classical methodology using hydroxylamine hydrochloride and sodium methoxide

in methanol. A large amount of sodium chloride was always present with the product, which proved very difficult to remove completely without hydrolysis of the aldonohydroxamic acid to the corresponding aldonate during the purification steps, such as during size-exclusion chromatography. We observed that most of the prepared aldonohydroxamic acids are more or less unstable in water at room temperature, even at neutral pH. Hence, we report in this paper, the synthesis of the pure analytical aldonohydroxamic acids **1**–**10** by a new methodology which does not involve any chromatographic purification step: the use of commercial 50% aqueous hydroxylamine as the source of the free base hydroxylamine that reacts directly with the corresponding aldonolactone dissolved in water. There are only a few examples in the literature that reported the use of 50% aqueous hydroxylamine, but as far as we know, only for the synthesis of hydroxamic acid derivatives of amino acids (in ethanol or THF).[9,10] For one of the prepared products, L-erythronohydroxamic acid **5**, we were able to obtain crystals suitable for X-ray diffraction analysis (attempts to crystallize the other analogs either failed or led to unsuitable crystals). Crystal structures for two aldonohydroxamic acids, D-threonohydroxamic acid and phosphoglycolohydroxamic acid, complexed at the active site of their target enzymes were reported.[4,11–13] We now report the first crystal structure of a free aldonohydroxamic acid. It will contribute to the better understanding of the solid-state structure of monosaccharides derivatives, and more particularly of aldonohydroxamic acid derivatives.

2. Results and discussion

Synthesis.—Aldonohydroxamic acids **1**–**10** were prepared from their corresponding aldonolactones, D-glucono-1,5-lactone (**11**), and the aldono-1,4-lactones of the following configurations: 5-phospho-D-*arabino*- (**12**), D-*lyxo*- (**13**), D-*arabino*- (**14**), L-*erythro*- (**15**), L-*threo*- (**16**), L-*lyxo*- (**17**), D-*erythro*- (**18**), D-*ribo*- (**19**) and 5-deoxy-L-*lyxo*- (**20**) (Scheme 1). D-Glucono-1,5-lactone (**11**), D-erythrono-1,4-lactone (**18**) and D-ribono-1,4-lactone (**19**) are commercially available (Aldrich, Acros). D-Arabinono-1,4-lactone 5-phosphate (**12**)[14] and L-lyxono-1,4-lactone (**17**)[15] were prepared as previously described. D-Lyxono-1,4-lactone (**13**),[16,17] D-arabinono-1,4-lactone (**14**),[18,19] L-erythrono-1,4-lactone (**15**)[20] and L-threono-1,4-lactone (**16**)[21] were obtained from barium D-lyxonate,[22] potassium D-arabinonate[23] (by hypoiodite oxidation[22] of D-arabinose), potassium L-erythronate[23] and calcium L-threonate (Aldrich), respectively, using the reported lactonization procedure[19] (except that P_2O_5 was used instead of magnesium perchlorate). 5-Deoxy-L-lyxono-1,4-lactone **20**[24,25] was obtained from L-fucose by oxidative alkaline degradation,[26] followed by lactonization.[19] New spectral data of the aldonolactones **15**, **16**, **17** and **20** are reported below.‡

As a general procedure, 50% aqueous hydroxylamine (Aldrich, 306 μL, 5 mmol) was added to a solution of the lactone (1 mmol) in water (1.7 mL). The reaction mixture was then stirred for 10 min at room temperature. The corresponding aldonohydroxamic acid was obtained by evaporation of water and hydroxylamine under diminished pressure ($T = 25$ °C, $P = 0.1$ torr). Complete removal of hydroxylamine was achieved by adding water (5–10 mL) to the residue, followed by evaporation; this procedure was repeated until a constant mass was reached. Generally, the final lyophilization step produced the pure product in quantitative yield. ^{13}C NMR analysis in deuterium oxide at neutral pH showed the C-1 chemical shift at approximately 171.0 ppm, a value characteristic of aldonohydroxamic acids. Possible hydrolysis of the product to the corresponding hydroxylammonium aldonate would give a typical C-1 resonance at 179–180 ppm. As a matter of fact, this was observed in the case of compounds **1**, **3**, **5** and **7**; while these compounds were at least 95% pure according to their NMR spectra, they had to be recrystallized to give pure analytical products. All aldonohydroxamic acids reported in this paper gave spectroscopic data

‡ ^{13}C NMR (D_2O, 50.3 MHz): **15**: δ 179.4 (C-1); 73.8 (C-4); 70.5 (C-2); 69.6 (C-3). **16**: δ 178.0 (C-1); 73.9 (C-2); 73.0 (C-3); 70.3 (C-4). **17**: δ 179.0 (C-1); 82.4 (C-4); 71.3 (C-2); 70.3 (C-3); 60.6 (C-5). **20**: δ 179.5 (C-1); 79.3 (C-4); 72.0, 71.8 (C-2, C-3); 13.8 (C-5).

and microanalyses in full agreement with the proposed structures (see Section 3).

Our methodology offers the obvious advantage that there is no salt to remove. The reaction proceeds almost instantaneously in water at room temperature, yielding, in most cases, pure products in quantitative yield. Except for a few of the prepared aldonohydroxamic acids, there are no side-products, no work-up and no purification step. There is no need to synthesize a hydroxylamine reagent, and no need for protective groups on the starting aldonolactones. To date, this methodology using 50% aqueous hydroxylamine is probably the easiest and most efficient way to synthesize aldonohydroxamic acids. There is no doubt that it will soon prove useful in the synthesis of other types of hydrophilic hydroxamic acid derivatives.

Table 1
Crystal parameters, data collection and structure refinement for L-erythronohydroxamic acid **5**

Crystal parameters	
Molecular formula	$C_4H_9NO_5$
Molecular weight	151.12
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions	
a (Å)	5.511(3)
b (Å)	7.556(1)
c (Å)	8.071(3)
β (°)	109.10
V (Å^3)	317.6(2)
Z	2
ρ_{calcd} (g cm^{-3})	1.58
μ (Mo K$_\alpha$) (cm^{-1})	0.14
$F(000)$	160.08
Crystal size (mm)	$0.25\times0.35\times0.45$
Crystal color and shape	colorless hexagonal rods
Data collection	
Diffractometer	Enraf–Nonius CAD4
Monochromator	graphite
Radiation	Mo K$_\alpha$ ($\lambda = 0.71069$ Å)
Scan mode	$\omega-2\theta$
Temperature (K)	291
θ Range for data collection (°)	2–30
Index range of h, k, l	$-8\le h\le 8$, $0\le k\le 12$, $0\le l\le 13$
Absorption correction	DIFABS
T_{min}	0.82
T_{max}	1.00
Reflections collected/unique	2945/1469
Reflections observed [$I>3\sigma(I)$]	853
Structure refinement	
Parameters	95
Final R	0.0388
Final R_w	0.0422
Weighting scheme	Chebyshev
Coefficient Ar	1.07, 1.18, −0.193
Goodness-of-fit on F^2	1.0339
$(\Delta/\sigma)_{max}$	0.011643
$\Delta\rho_{min}/\Delta\rho_{max}$ (e Å^{-3})	−0.215/0.224

Table 2
Fractional atomic coordinates and equivalent isotropic thermal parameter U_{eq} for non-hydrogen atoms of L-erythronohydroxamic acid **5** [a]

Atom [b]	x/a	y/b	z/c	U_{eq}
O-1	−0.0496(4)	0.0614(3)	0.4248(3)	0.0339
O-2	0.4719(4)	0.0663(3)	0.4396(2)	0.0294
O-3	0.0049(5)	0.1771(3)	0.0169(3)	0.0337
O-4	0.4894(5)	0.2294(3)	0.0182(3)	0.0292
O-5	0.7521(4)	0.4951(3)	0.2228(2)	0.0264
N-5	0.5265(4)	0.4240(3)	0.2372(3)	0.0235
C-1	0.0496(6)	−0.0514(4)	0.3191(4)	0.0315
C-2	0.2704(5)	0.0336(3)	0.2784(3)	0.0237
C-3	0.1901(5)	0.2090(3)	0.1796(3)	0.0222
C-4	0.4163(5)	0.2888(3)	0.1378(3)	0.0210

[a] E.s.d's in parentheses refer to the last significant digit. U_{eq} is defined as the cube root of the product of the principal axes.

[b] 100% occupancy.

Determination of the X-ray structure of L-*erythronohydroxamic acid* **5**.—Crystal structure of **5** contributes to the study of the solid-state structures of monosaccharides aimed at a better understanding of the factors that determine which structure type is formed, particularly in the case of aldonohydroxamic acids for which, to our knowledge, no crystal structure has been reported to date. The refined unit cell constants and other relevant crystal data for L-erythronohydroxamic acid **5** are presented in Table 1, together with details of the intensity measurements. Final fractional atomic coordinates and equivalent isotropic temperature factors for non-hydrogen atoms of compound **5** are reported in Table 2. Selected torsion angles and hydrogen-bond parameters are illustrated in Tables 3 and 4, respectively. The ORTEP view of the title compound is represented in Fig. 1, together with the labeling of the atoms and hydrogen bonds. The molecular packing scheme is represented in Fig. 2.

Table 3
Selected torsion angles for atoms of L-erythronohydroxamic acid **5**

Sequence	Angle (°)
O-1–C-1–C-2–C-3	−59.40
C-1–C-2–C-3–C-4	−178.89
O-2–C-2–C-3–C-4	61.18
O-3–C-3–C-4–N-5	136.68
C-2–C-3–C-4–N-5	−104.42
O-4–C-4–N-5–O-5	−6.82
C-3–C-4–N-5–O-5	173.16
C-4–N-5–O-5–H-5	90.05

Crystals of L-erythronohydroxamic acid **5** belonged to the monoclinic space group $P2_1$ with $a = 5.511(3)$, $b = 7.556(1)$, $c = 8.071(3)$ Å, $\beta = 109.10°$. The unit cell consists of two molecules of L-erythronohydroxamic acid **5** (Fig. 2). X-ray crystallography revealed that compound **5** crystallizes without solvent molecules, as observed in the case of formohydroxamic acid,[27] but contrarily to acetohydroxamic acid which was reported to crystallize as its hemihydrate.[28]

Although comparison with other aldonohydroxamic acids is not possible, bond lengths and angles for the polyhydroxylated chain of compound **5** all compare well with the corresponding average values found from X-ray studies of alditols, like D-glucitol for example.[29] The same holds for torsion angles (Table 3). The carbon chain adopts an extended planar zigzag conformation. As observed for tetritols and some other alditols,[29] no unfavorable 1,3-parallel O‖O or C‖O interactions (as well as no intramolecular hydrogen bonds) occur in the crystal structure of **5** as a result of the configuration of the stereogenic centers C-2 and C-3. However, the terminal hydroxyl group is not in the linear extension of the zigzag chain, but adopts a gauche orientation (Fig. 1), as observed in the crystal structure of various compounds like L-mannonic acid hydrazide.[30]

Figs. 1 and 2 show that the hydroxamic acid moiety of compound **5** is in the *Z* conformation. The O-4–C-4–N-5–O-5 torsion angle is −6.8°, showing that the hydroxamic acid moiety is not quite planar, probably because it forms an extensive hydrogen-bonding network with neighboring molecules. This type of conformation was observed in the solid state for several hydroxamic acids like cyclohexanecarbohydroxamic acid[31] and formohydroxamic acid.[27] Bond lengths and angles of the hydroxamic acid moiety of **5** are close to the mean values reported for a series of N-unsubstituted hydroxamic acids.[27] The H-5–O-5 bond is turned out of the plane of the hydroxamic acid group (C-4–N-5–O-5–H-5 torsion angle is 90°), in agreement with the reported crystal structures of various hydroxamic acids which show H–O–N–C torsion angles in the range ±(50–140)°.[27,28,31] This orientation of the N–OH hydroxyl group is obviously more appropriate for intermolecular hydrogen bonding, and appears as an important factor determining the conformation in crystals of hydroxamic acid derivatives. In contrast, ab initio studies on hydroxamic acids generally show the N–OH hydroxyl group intramolecularly hydrogen-bonded to the oxygen of the carbonyl group, which puts the N–OH hydroxyl group in the plane of the hydroxamic acid moiety.[32–34]

All heteroatoms are involved in a dense hydrogen-bonding network (Fig. 1). H-Bond parameters of Table 4 all compare well with

Table 4
Hydrogen bond parameters for L-erythronohydroxamic acid **5**

Donor	Acceptor	Distances (Å)		Angle (°)	Symmetry operation on acceptor
(D–H)	(A)	D···A	H···A	D–H···A	
O-5–H-5	$O4^{i}$	2.645(3)	1.701(3)	161.93	i = $-x+1$, $y+1/2$, $-z$
N-5–H-51	$O2^{ii}$	2.82(3)	1.876(4)	159.40	ii = $-x+1$, $y+1/2$, $-z+1$
O-1–H-1	$O5^{iii}$	2.825(4)	1.925(3)	172.43	iii = $-x+1$, $y-1/2$, $-z+1$
O-3–H-3	$O4^{iv}$	2.818(3)	2.064(3)	148.85	iv = $x-1$, y, z
O-2–H-2	$O1^{v}$	2.679(3)	1.793(3)	162.59	v = $x+1$, y, z,

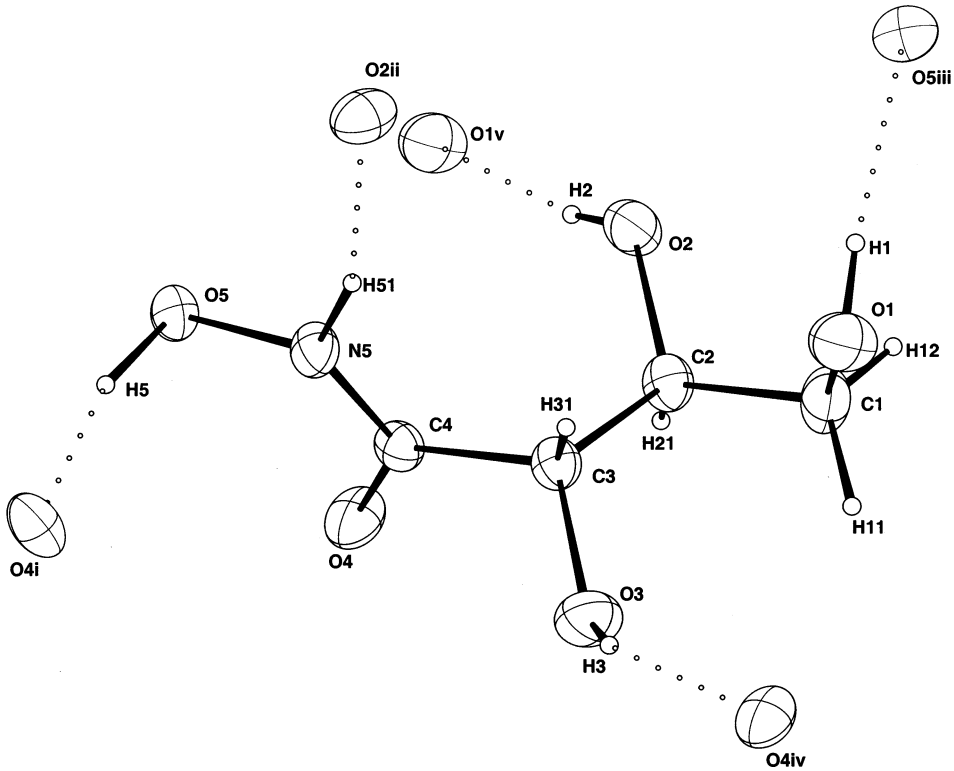

Fig. 1. ORTEP view of L-erythronohydroxamic acid **5** was generated by the CAMERON program. Atom labeling was generated by the CRYSTALS program (it does not correspond to the usual labeling of monosaccharides). Thermal ellipsoids are drawn at the 50% level. Dashed lines indicate hydrogen bonds.

the reported values for various monosaccharides derivatives.[35–38] The packing arrangement assumed by L-erythronohydroxamic acid **5** shows that one molecule interacts with six other molecules. Molecules of **5** are linked by 'head-to-tail' interactions in which the NH–O group of each molecule forms a hydrogen-bonded bridge across the C-1 and C-2 hydroxyl groups of a neighboring molecule, forming an eight-membered ring in which the N-5–H-51 and O-1–H-1 groups are H-bond donors and O-5 and O-2 are H-bond acceptors. A similar pattern was recently described for D-mannose oxime.[37] Molecules of **5** are also linked by 'head-to-head' interactions in which three hydroxamic acid groups are involved: the N–OH group of a given molecule is H-bond donor to the carbonyl oxygen of a first neighboring molecule, while the oxygen carbonyl is H-bond acceptor with the N–OH group of a second molecule. Finally, molecules of **5** are linked together through O-2–H-2···O-1 and O-3–H-3···O4 hydrogen bonds (Fig. 1).

Conclusions.—We have developed a novel, simple and efficient methodology for the synthesis of aldonohydroxamic acids, using commercial 50% aqueous hydroxylamine as the source of the free base that reacts directly with the corresponding aldonolactone in water. The reaction proceeds almost instantaneously in water at room temperature, yielding, in most cases, pure products in quantitative yield. In the case of L-erythronohydroxamic acid, we also report the first crystal structure of a free aldonohydroxamic acid.

3. Experimental

General methods.—Unless otherwise stated, chemicals (used at their commercial purity) were obtained from Acros and solvents from SDS. Melting points were measured on a Reichert apparatus and not corrected. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. ^{1}H NMR spectra were recorded at 200, 250 or 400 MHz, and were referenced to residual internal HOD (4.80

ppm). For CH_2 groups, H-4′, H-5′, and H-6′ resonances appear arbitrarily at higher field than H-4, H-5, and H-6 resonances, respectively. ^{13}C NMR spectra were recorded at 50.3 or 62.5 MHz and referenced to internal 1,4-dioxane (67.40 ppm). Chemical shifts are reported in ppm (δ). Infrared spectra were recorded with a FT-IR Bruker IFS-66 spectrometer. Low-resolution mass spectrometry (MS) and high-resolution mass spectrometry (HR-MS) analyses of the trimethylsilylated (TMS) derivatives[39] were performed by electrospray with positive ionization mode. Non-silylated derivatives were analyzed by low-resolution electrospray mass spectrometry with negative ionization mode. Evaporations were performed under diminished pressure below 25 °C. Final products were stored at − 18 °C. Elemental analyses were performed by the microanalytical laboratory at the ICSN, CNRS, Gif-sur-Yvette. With aq $FeCl_3$, all aldonohydroxamic acids had characteristic visible absorption peaks from λ 488 to 498 nm.

Crystal structure analysis.—Crystals of compound **5** were grown by slow cooling of a boiling saturated abs EtOH–water solution. Following filtration, the crystals were rinsed with abs EtOH and filtered by succion. The crystals were mounted, using glass fibers, on an Enraf–Nonius CAD4 diffractometer equipped with a graphite monochromator. The lattice parameters were refined using 25 reflections. The data were collected using the $\omega - 2\theta$ scan technique and with Mo K_α radiation ($\lambda = 0.71069$ Å). During the data collection, three intensity control reflections were monitored every 2 h, showing no loss of intensity. The data were corrected for Lorentz and polarization effects. The structure was solved by a combination of direct methods using SIR procedure[40] and heavy-atom techniques and refined by full-matrix least-squares method based on F^2, using the CRYSTALS software.[41] An empirical absorption correction with the program DIFABS[42] was used. Anisotropic displacement parameters were assigned to all non-hydrogen atoms. The hydrogen atoms were introduced in calculated idealized positions (d(C–H) = 0.98 Å) and their atomic coordinates were recalculated after each cycle. They were given isotropic thermal parameters 20% higher than those of the carbon to which they are attached. Least-squares refinements were performed by minimizing the function $\Sigma\, w(|F_o| - |F_c|)^2$, where F_o and F_c are the observed and calculated structure factors. The weighting scheme used in the last-refinement cycles was $w = w'[1 - (\Delta F/6\sigma(F_o)^2)]^2$ where $w' = 1/\Sigma_1^n A_r T_r(x)$ with three coefficients A_r for the Chebyshev polynomial $A_r T_r(x)$ where x was F_c/F_c(max).[43] Models reached convergence with $R = \Sigma(||F_o| - |F_c||)/\Sigma(|F_o|)$ and $R_w = [\Sigma\, w(|F_o| - |F_c|)^2/\Sigma\, w(F_o)^2]^{1/2}$, having values listed in Table 1. Criteria for a satisfactory complete analysis were ratios of rms shift to standard deviation less than 0.1 and no significant features in final difference maps. Details of data collection and refinement are given in Table 1. Calculations were performed with the CRYSTALS package program. The drawings of the molecules were generated using CAMERON.[44] The atomic scattering factors were taken from International Tables for X-ray Crystallography.[45]

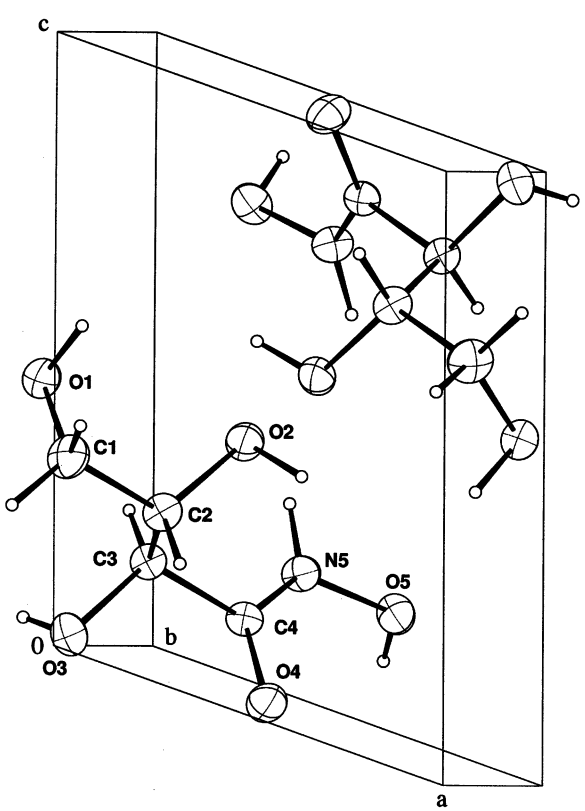

Fig. 2. Molecular packing in L-erythronohydroxamic acid **5**.

D-*Gluconohydroxamic acid* **1**.—The title compound was recrystallized from water, abs EtOH and acetone. Following trituration with

cold abs EtOH, then with Et_2O, it was finally dried under diminished pressure to give a white powder, mp 140–143 °C (lit.[1] 138–140 °C), yield: 110 mg (75%), $[\alpha]_D^{21}$ +20.8° (*c* 1.0, water). IR (KBr) *v* 1654 (CO); 3221, 3445 (NH, OH) cm^{-1}. ^1H NMR (D_2O, 400 MHz): δ 4.38 (d, $J_{2,3}$ 5 Hz, 1 H, H-2); 4.12 (dd, $J_{3,4}$ 3 Hz, 1 H, H-3); 3.86 (dd, $J_{5,6}$ 3, $J_{6,6'}$ −12 Hz, 1 H, H-6); 3.79 (ddd, $J_{4,5}$ 8 Hz, 1 H, H-5); 3.73 (dd, 1 H, H-4); 3.69 (dd, $J_{5,6'}$ 6 Hz, 1 H, H-6′). ^{13}C NMR (D_2O, 50.3 MHz): δ 171.1 (C-1); 73.3, 72.4, 71.9, 71.1 (C-2, C-3, C-4, C-5); 63.5 (C-6). MS (negative mode): 210.1 $[M-H]^-$. Anal. Calcd for $C_6H_{13}NO_7$: C, 34.13; H, 6.21; N, 6.63; Found: C, 33.91; H, 6.14; N, 6.48.

D-*Arabinonohydroxamic acid 5-phosphate, disodium salt* (**2**).—The title compound was obtained from its hydroxylammonium precursor by elution on a Dowex® 50X4-400 column (Na^+ form, water). Following evaporation, then lyophilization, the title compound was obtained as a white fluffy powder, yield: 106 mg (90%). IR, ^1H and ^{13}C NMR data are in agreement with the literature.[5,14] Anal. Calcd for $C_5H_{10}NNa_2O_9P{\cdot}2.5\ H_2O$: C, 17.15; H, 4.32; N, 4.00; Na, 13.13; P, 8.85; Found: C, 16.90; H, 3.98; N, 3.69; Na, 13.30; P, 8.82.

D-*Lyxonohydroxamic acid* **3**.—The title compound was recrystallized from abs EtOH and water, then lyophilized to give a white fluffy powder, mp 147.5–149 °C, yield: 168 mg (33%), $[\alpha]_D^{21}$ +2.5° (*c* 1.0, water). IR (KBr) *v* 1661 (CO); 3261, 3371, 3468 (NH, OH) cm^{-1}. ^1H NMR (D_2O, 250 MHz): δ 4.13 (d, $J_{2,3}$ 7 Hz, 1 H, H-2); 3.87 (ddd, $J_{3,4}$ 2, $J_{4,5}$ 5, $J_{4,5'}$ 8 Hz, 1 H, H-4); 3.77 (dd, 1 H, H-3); 3.65 (dd, $J_{5,5'}$ −12 Hz, 1 H, H-5); 3.60 (dd, 1 H, H-5′). ^{13}C NMR (D_2O, 50.3 MHz): δ 171.6 (C-1); 71.6, 71.3, 71.0 (C-2, C-3, C-4); 63.5 (C-4). MS (TMS deriv.): 420.2 $[C_{14}H_{35}NO_6Si_3+Na]^+$, 398.2 $[C_{14}H_{35}NO_6Si_3+H]^+$, 348.1. Anal. Calcd for $C_5H_{11}NO_6$: C, 33.15; H, 6.12; N, 7.73; Found: C, 33.07; H, 6.04; N, 7.58.

D-*Arabinonohydroxamic acid* **4**.—Lyophilization of the title compound gave a white fluffy powder, mp 146–148 °C (L-arabinonohydroxamic acid: lit.[1] 150 °C), yield: 500 mg (99%), $[\alpha]_D^{20}$ −41.1° (*c* 1.0, water). IR (KBr) *v* 1629, 1665 (CO); 3281 (br NH, OH) cm^{-1}. ^1H NMR (D_2O, 250 MHz): δ 4.47 (d, $J_{2,3}$ 2 Hz, 1 H, H-2); 3.85 (dd, $J_{3,4}$ 9 Hz, 1 H, H-3); 3.71 (m, 1 H, H-4); 3.82 (dd, $J_{4,5}$ 2 Hz, 1 H, H-5); 3.63 (dd, $J_{4,5'}$ 6, $J_{5,5'}$ −11 Hz, 1 H, H-5′). ^{13}C NMR (D_2O, 62.5 MHz): δ 172.9 (C-1); 72.5, 71.7, 71.6 (C-2, C-3, C-4); 64.2 (C-5). MS (negative mode): 180.3 $[M-H]^-$. Anal. Calcd for $C_5H_{11}NO_6$: C, 33.15; H, 6.12; N, 7.73; Found: C, 32.81; H, 5.93; N, 7.77.

L-*Erythronohydroxamic acid* **5**.—The title compound was recrystallized from hot abs EtOH and water to give colorless crystals, mp 131–132.5 °C, yield: 76 mg (40%), $[\alpha]_D^{22}$ −12.9° (*c* 1.0, water). IR (KBr) *v* 1661 (CO); 3318 (br, NH, OH) cm^{-1}. ^1H NMR (D_2O, 250 MHz): δ 4.15 (d, $J_{2,3}$ 5 Hz, 1 H, H-2); 3.89 (m, 1 H, H-3); 3.67 (dd, $J_{3,4}$ 4, $J_{4,4'}$ −12 Hz, 1 H, H-4); 3.60 (dd, $J_{3,4'}$ 7 Hz, 1 H, H-4′). ^{13}C NMR (D_2O, 50.3 MHz): δ 171.2 (C-1); 73.3, 72.0 (C-2, C-3); 62.5 (C-4). MS (negative mode): 150.0 $[M-H]^-$. Anal. Calcd for $C_4H_9NO_5$: C, 31.79; H, 6.00; N, 9.27; Found: C, 31.95; H, 5.79; N, 9.06.

L-*Threonohydroxamic acid* **6**.—Lyophilization of the title compound gave a white fluffy powder, mp 137–138.5 °C, yield: 471 mg (100%), $[\alpha]_D^{24}$ +46.9° (*c* 1.0, water). IR (KBr) *v* 1636, 1670 (CO); 3184, 3266 (br, NH, OH) cm^{-1}. ^1H NMR (D_2O, 200 MHz): δ 4.24 (d, $J_{2,3}$ 3 Hz, 1 H, H-2); 3.98 (ddd, $J_{3,4}$ 6, $J_{3,4'}$ 7 Hz, 1 H, H-3); 3.66 (dd, $J_{4,4'}$ −12 Hz, 1 H, H-4); 3.59 (dd, 1 H, H-4′). ^{13}C NMR (D_2O, 50.3 MHz): δ 171.8 (C-1); 72.6, 71.6 (C-2, C-3); 62.9 (C-4). MS (TMS deriv.): 534.2 $[C_{19}H_{49}NO_5Si_5+Na]^+$, 462.1 $[C_{16}H_{41}NO_5Si_4+Na]^+$, 440.2, 390.1, 285.1. Anal. Calcd for $C_4H_9NO_5$: C, 31.79; H, 6.00; N, 9.27; Found: C, 31.56; H, 5.93; N, 9.06.

L-*Lyxonohydroxamic acid* **7**.—The title compound was recrystallized from abs EtOH and water, then lyophilized to give a white fluffy powder, mp 147.5–148 °C, yield: 137 mg (56%), $[\alpha]_D^{21}$ −2.6° (*c* 1.0, water). IR (KBr) *v* 1661 (CO); 3265, 3371, 3469 (NH, OH) cm^{-1}. ^1H NMR (D_2O, 250 MHz): δ 4.14 (d, $J_{2,3}$ 7 Hz, 1 H, H-2); 3.88 (ddd, $J_{3,4}$ 2, $J_{4,5}$ 5, $J_{4,5'}$ 8 Hz, 1 H, H-4); 3.78 (dd, 1 H, H-3); 3.66 (dd, $J_{5,5'}$ −12 Hz, 1 H, H-5); 3.60 (dd, 1 H, H-5′). ^{13}C NMR (D_2O, 50.3 MHz): δ 171.6 (C-1); 71.6, 71.3, 71.0 (C-2, C-3, C-4); 63.5 (C-4). MS (negative mode): 180.0 $[M-H]^-$. Anal. Calcd for $C_5H_{11}NO_6$: C, 33.15; H, 6.12; N, 7.73; Found: C, 33.07; H, 5.89; N, 7.74.

D-*Erythronohydroxamic acid* **8**.—The title compound was triturated with abs EtOH, and then with Et_2O. It was finally dried under diminished pressure to give a pale yellow powder, mp 129–130.5 °C, yield: 188 mg (99%), $[\alpha]_D^{24}$ +14.1° (*c* 1.0, water). IR (KBr) *v* 1629, 1661 (CO); 3226, 3386, 3432 (NH, OH) cm^{-1}. ^1H NMR (D_2O, 200 MHz): δ 4.16 (d, $J_{2,3}$ 5 Hz, 1 H, H-2); 3.90 (ddd, $J_{3,4}$ 4, $J_{3,4'}$ 7 Hz, 1 H, H-3); 3.69 (dd, $J_{4,4'}$ −12 Hz, 1 H, H-4); 3.61 (dd, 1 H, H-4′). ^{13}C NMR (D_2O, 50.3 MHz): δ 171.0 (C-1); 73.2, 72.0 (C-2, C-3); 62.5 (C-4). MS (TMS deriv.): 462.2 $[C_{16}H_{41}NO_5Si_4 + Na]^+$, 440.2 $[C_{16}H_{41}NO_5Si_4 + H]^+$, 390.1 $[C_{13}H_{33}NO_5Si_3 + Na]^+$, 285.1. Anal. Calcd for $C_4H_9NO_5$: C, 31.79; H, 6.00; N, 9.27; Found: C, 31.84; H, 5.92; N, 9.31.

D-*Ribonohydroxamic acid* **9**.—The title compound was dried under diminished pressure to give a white fluffy powder, mp 133–135 °C (L-ribonohydroxamic acid: lit.[1] 133–136 °C), yield: 181 mg (100%), $[\alpha]_D^{21}$ +16.2° (*c* 1.0, water). IR (KBr) *v* 1642 (CO); 3170, 3290, 3413 (NH, OH) cm^{-1}. ^1H NMR (D_2O, 250 MHz): δ 4.34 (d, $J_{2,3}$ 4 Hz, 1 H, H-2); 3.90 (dd, $J_{3,4}$ 8 Hz, 1 H, H-3); 3.82 (m, 1 H, H-4); 3.79 (m, $J_{4,5}$ 2 Hz, 1 H, H-5); 3.62 (dd, $J_{4,5'}$ 7, $J_{5,5'}$ −12 Hz, 1 H, H-5′). ^{13}C NMR (D_2O, 50.3 MHz): δ 171.0 (C-1); 73.3, 72.5, 71.9 (C-2, C-3, C-4); 63.6 (C-5). MS (TMS deriv.): 614.3 $[C_{23}H_{59}NO_6Si_6 + H]^+$, 571.7, 204.3, 148.2, 132.2. MS (negative mode): 180.2 $[M-H]^-$. HRMS: Calcd for $C_{23}H_{60}NO_6Si_6$ (TMS deriv.): 614.3040; Found: 614.3036. Anal. Calcd for $C_5H_{11}NO_6$: C, 33.15; H, 6.12; N, 7.73; Found: C, 33.08; H, 6.06; N, 7.69.

5-Deoxy-L-*lyxonohydroxamic acid* (**10**).—The title compound was obtained as a colorless syrup, yield: 42 mg (100%). IR (KBr) *v* 1669 (CO); 3379 (br NH, OH) cm^{-1}. ^1H NMR (D_2O, 200 MHz): δ 4.15 (d, $J_{2,3}$ 6 Hz, 1 H, H-2); 3.98 (qd, $J_{3,4}$ 3 Hz, 1 H, H-4); 3.59 (dd, 1 H, H-3); 1.19 (d, $J_{4,5}$ 7 Hz, 1 H, H-5). ^{13}C NMR (D_2O, 62.5 MHz): δ 171.4 (C-1); 75.6, 72.1, 67.2 (C-2, C-3, C-4); 19.5 (C-5). MS (negative mode): 164.0 $[M-H]^-$. Anal. Calcd for $C_5H_{11}NO_5$: C, 36.36; H, 6.71; Found: C, 35.61; H, 6.87.

4. Supplementary material

Full crystallographic details, excluding structure features, have been deposited with the Cambridge Crystallographic Data Center (deposition no. CCDC 166786). These data may be obtained, on request, from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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