

Promiscuous recognition of the hexapyranose epimers α,β -D-glucuronic and α,β -D-galacturonic acids between corrugated brucine sheets

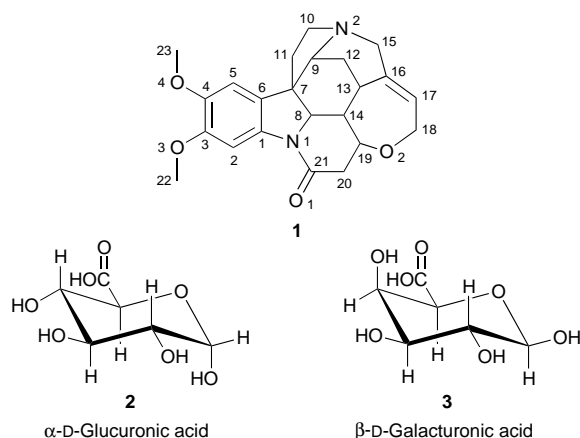
Fokke J. J. Dijkstra,^a Robert O. Gould,^{*a†} Simon Parsons,^a Paul Taylor^b and Malcolm D. Walkinshaw^b

^a Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh, Scotland, UK EH9 3JJ

^b Department of Biochemistry, University of Edinburgh, Michael Swann Building, Edinburgh, Scotland, UK EH9 3JR

The crystal structures of brucinium glucuronate and galacturonate are reported, both of which show layers of uronate between identical corrugated brucine sheets; the change of configuration at C(4) of the acid engineers a reversal in the packing mode of these sheets, while differences at C(1) appear to be relatively unimportant.

For many years the alkaloid brucine **1** has been used to separate racemic mixtures by co-crystallisation, generally with mole-



cules containing acidic functional groups. We have previously reported a motif common to many brucine co-crystals;^{1,2} this feature makes it attractive to examine the possibilities of using brucine as a co-crystallising agent for determining the structures of molecules which crystallise on their own with difficulty or not at all. Carbohydrates provide many examples of this type, and in a preliminary study, we have crystallised glucuronic **2** and galacturonic **3** acids with brucine to examine the specific interactions made. The acids **2** and **3** differ only in the configuration of the OH group at C(4). In addition, both exist in aqueous solution as an equilibrium of anomers [opposite configuration at C(1)] with the approximate anomeric ratio³ $\alpha:\beta = 3:2$. Advances in methods of crystal structure determination, particularly as applied to those structures containing substantial fragments of fixed and known stereochemistry,⁴ make the use of brucine as a co-crystallising agent particularly attractive.

Crystals of brucinium D-glucuronate **4** and brucinium D-galacturonate **5** were obtained from an aqueous solution of an equimolar mixture of **1** and **2** or **1** and **3**. Crystals of **5** were readily obtained within two days as well-formed colourless blocks. Crystals of **4** were only obtained with much greater difficulty as colourless laths after acetonitrile was added to the solution. Both give monoclinic crystals, space group $P2_1$, with unit cell dimensions for **4**: $a = 7.946(1)$, $b = 12.660(1)$, $c = 14.814(2)$ Å, $\beta = 93.676(9)^\circ$; and for **5**: $a = 7.958(4)$, $b = 12.366(5)$, $c = 27.639(10)$ Å, $\gamma = 93.57(3)^\circ$ (in order to

emphasise the relationship of the two structures, **5** has been referred to a cell with c as the unique axis).[‡]

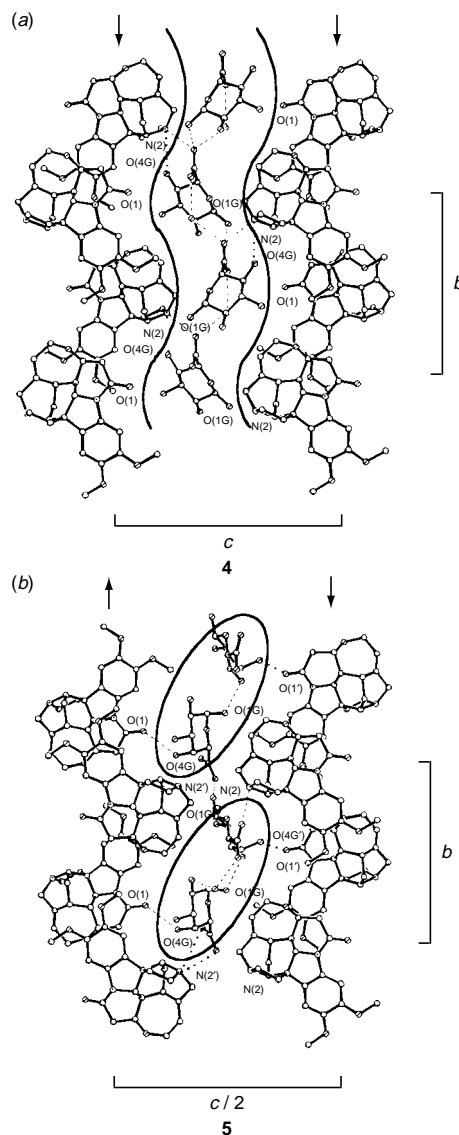


Fig. 1 A view parallel to a brucinium layer (along the a -axis) of the major components of **4** and **5** showing the relative polarities of the brucine sheets, the interstices between them and significant hydrogen bonds. (a) **4**: N(2)⋯O(6G): 2.851(4), N(2)⋯O(4G): 3.065(4), O(3W)⋯O(1) [$1 - x, \frac{1}{2} + y, -z$]: 2.812(4),^a O(1G)⋯O(6G) [$1 - x, \frac{1}{2} + y, 1 - z$]: 2.794(4) O(4G)⋯O(3W) [$x - 1, y, z$]: 2.796(4)^a. (b) **5**: N(2)⋯O(6G'): 2.719(5), N(2)⋯O(5G'): 2.976(5), N(2')⋯O(6G) [$2 - x, 1 - y, \frac{1}{2} + z$]: 2.781(5), N(2')⋯O(7G) [$2 - x, 1 - y, \frac{1}{2} + z$]: 3.184(5), O(1G')⋯O(7G): 2.656(5), O(4G')⋯O(1') [$x, y - 1, z$]: 3.035(5), O(1G)⋯O(3G') [$x, 1 + y, z$]: 2.731(5), O(4G)⋯O(1) [$1 - x, 1 - y, z - \frac{1}{2}$]: 2.832(5), O(1W)⋯O(1) [$-x, 1 - y, z - \frac{1}{2}$]: 3.169(5)^a.

^a Not shown in figure.

Both structures show layers of brucinium ions reported previously,^{1,2} with anions and solvent between the layers as shown in Fig. 1. While the uronates give many opportunities for donation and acceptance of hydrogen bonds, the brucinium ions are limited to two: donation by N(2) and acceptance by O(1) (see Fig. 1). In both structures, O(1) in brucine accepts from water, and in **5** additionally from the hydroxy group (axial) at C(4) of both independent galacturonates, which do not accept hydrogen bonds. In **4** these hydroxy groups (equatorial) donate to water and accept bifurcated bonds from N(2) of a brucinium. This proton is shared in both structures by the O(6) of a uronate; it is shared in **5** with O(5) or O(7) of a uronate. The only disorder in the crystal structures is in the region of the anomeric carbon atoms. In **4** the glucuronate ion is 82.7(8)% in the α -anomeric form. In **5** one of the galacturonate ions is essentially all in the α -anomer, while the other exists as 89.3(8)% β -anomer. These hydroxy groups show hydrogen bonding only with neighbouring uronate ions or water molecules. The water molecules are present mainly as a connecting medium for the uronates. In **5** there are three molecules of water for every one in **4**, and they partially compensate for the poorer fit of glucuronate to brucinium layers. Their requirement may explain the much slower formation of **5**.

In **4**, with one brucinium ion per asymmetric unit, the layers simply repeat along the *c*-axis, giving parallel sheets of brucinium ions and an interstice of roughly uniform thickness [Fig. 1(a)]. In **5**, with the unit cell nearly twice as large, there are two bruciniums in the asymmetric unit, the layers being related by the 2_1 axis parallel to the *c*-axis, while the two crystallographically independent ions in each layer are related by an approximate screw axis parallel to the *b*-axis. This antiparallel packing of layers results in the division of the interstices into channels [Fig. 1(b)].

The crystal structures are remarkable in showing a conserved packing of brucine moieties, although the packing and the hydrogen bonding of the sheets of water and uronate ions is very different. The configuration at C(4), which distinguishes the

two ions, is crucial while the configuration at C(1) is practically irrelevant.

Notes and References

† E-mail: gould@ed.ac.uk

‡ *Crystal data* for $C_{23}H_{26}N_2O_4 + C_6H_{10}O_7 + H_2O$ **5**: $V = 2714.6(9) \text{ \AA}^3$ [cell dimensions from 31 reflections with $40 \leq 2\theta^\circ \leq 44$ and $\lambda = 1.54184 \text{ \AA}$], $Z = 4$, $D_c = 1.484 \text{ Mg m}^{-3}$, $T = 220(2) \text{ K}$, colourless block, $\mu = 0.976 \text{ mm}^{-1}$.

Crystal data for $C_{23}H_{26}N_2O_4 + C_6H_{10}O_7 + 3 H_2O$ **4**: $V = 1487.8(5) \text{ \AA}^3$ [cell dimensions from 56 reflections with $40 \leq 2\theta^\circ \leq 44$ and $\lambda = 1.54184 \text{ \AA}$], $Z = 2$, $D_c = 1.435 \text{ Mg m}^{-3}$, $T = 220(2) \text{ K}$, colourless lath, $\mu = 0.973 \text{ mm}^{-1}$.

Data collection and processing: Stöe STADI-4 four circle diffractometer, graphite-monochromated Cu-K α X-radiation, ω - θ scans, $6.0 < 2\theta < 120.0^\circ$. **4** gave 4246 independent data, including 1929 Friedel pairs ($-8 \leq h \leq 8$, $-14 \leq k \leq 13$, $0 \leq l \leq 16$) and **5** 4171 (155 Friedel pairs), ($-8 \leq h \leq 8$, $-1 \leq k \leq 13$, $0 \leq l \leq 31$). Both structures were solved by DIRDIF-96⁴ and refined anisotropically to give: **4**: $R_1 = 0.0465$ for 3977 data (1785 Friedel pairs), $F > 4\sigma(F)$, $wR_2 = 0.1261$ for all data; **5**: $R_1 = 0.0306$ for 4037 data (133 Friedel pairs), $F > 4\sigma(F)$, $wR_2 = 0.0801$ for all data. All calculations used SHELXL-97.⁵ All hydrogen atoms were placed in calculated positions except those in water molecules, which were placed, and then constrained to give normal geometry. CCDC 182/771.

- 1 S. B. B. Glover, R. O. Gould and M. D. Walkinshaw, *Acta Crystallogr., Sect. C*, 1985, **41**, 990.
- 2 R. O. Gould and M. D. Walkinshaw, *J. Am. Chem. Soc.*, 1984, **106**, 7840.
- 3 L. W. Jaques, J. Burns Macaskill and W. Weltner, Jr., *J. Phys. Chem.*, 1979, **83**, 1412.
- 4 P. T. Beurskens, G. Beurskens, R. de Gelder, S. Garcia-Granda, R. O. Gould, R. Israel and J. M. M. Smits, the DIRDIF-96 program system, Crystallography Laboratory, University of Nijmegen, The Netherlands.
- 5 G. M. Sheldrick, SHELXL-97, University of Göttingen, Germany, 1997.

Received in Cambridge, UK, 7th January 1998; 8/00219C