SHORT STRUCTURAL PAPERS

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Rubidium D-1,2-Dihydronaphtho[2,1-*b*]furan-2-carboxylate, a Substrate Analogue of Chymotrypsin

By P. S. Rodgers and L. C. G. Goaman

Department of Physics, Portsmouth Polytechnic, Portsmouth PO1 2DZ, England

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Abstract. $C_{13}H_9O_3Rb.H_2O$, monoclinic, $P2_1$, $a=6{\cdot}531$ (7), $b=4{\cdot}33$ (1), $c=21{\cdot}84$ (1) Å, $\beta=97{\cdot}80$ (1)°, $Z=2$, $D_m=1{\cdot}71$, $D_x=1{\cdot}72$ g cm^{-3}, $\lambda=1{\cdot}5418$ (Cu $K\bar{\alpha}$). The carboxylate group adopts a pseudo 'axial' conformation with respect to the aromatic plane. The furan ring has an angle of buckle of 14°. The rubidium ion is eight-coordinated. A comparison of bond lengths and angles with those found for the methyl ester (a chymotrypsin substrate) is given.

Introduction. The rubidium salt was prepared by Dr T. N. Pattabiraman (Department of Biochemistry, College of Science, Osmania University, Hyderabad-7, India) by neutralization of the free acid with rubidium hydrogen carbonate and precipitating the product with ethanol. Transparent needle-shaped crystals were grown from an aqueous methanol solution at −5 °C. X-ray intensities were obtained from a crystal 0·4 × 0·08 × 0·12 mm mounted about the unique (needle) axis, using the equi-inclination Weissenberg photographic method. Unit-cell dimensions were obtained from zero-level Weissenberg photographs calibrated by superposition of a powder pattern from a gold wire. The space group was $P2_1$ (systematic absences: $0k0$, $k=2n+1$). 1239 non-zero reflexions, out of a total possible 1398, were recorded. Lorentz, polarization and spot-shape corrections were applied with the program *PODAR*. No absorption corrections were applied ($\mu R=0{\cdot}6$). Interlayer scales, overall scale and mean isotropic temperature factors were calculated by a modified Wilson method with the program *POSCALE*. The structure was solved by standard heavy-atom methods with the y coordinate of the rubidium ion initially set to zero to define an origin in this direction. Least-squares refinement, minimizing $\sum w(|F_o|-|F_c|)^2$ with weights $w=1$ if $|F_o|<F^*$ or $w=F^*/|F_o|$ if $|F_o|>F^*$, ($F^*=70{\cdot}0$), was carried out with the program *PABLO*.

The final value of $\sum w(|F_o|-|F_c|)^2$ was 5190 and the final R was 0·09 with anisotropic refinement of all non-hydrogen atoms. The H atoms were given fixed isotropic temperature factors of 3·0 Å^2. Positional and thermal parameters of the former are listed in Table 1

Table 1. *Fractional coordinates and anisotropic thermal parameters* (× 10^4) *for non-hydrogen atoms*

$$B_{\text{aniso}}=\exp\left[-(b_{11}h^2+b_{12}hk+b_{13}hl+b_{22}k^2+b_{23}kl+b_{33}l^2)\right].$$

	x	y	z	b_{11}	b_{12}	b_{13}	b_{22}	b_{23}	b_{33}
C(1)	0·194 (3)	0·429 (5)	0·2733 (9)	262	−69	40	573	−14	22
C(2)	0·340 (3)	0·376 (6)	0·2332 (9)	243	128	−5	849	−46	19
C(3)	0·521 (3)	0·176 (8)	0·2511 (11)	205	−328	24	1375	16	26
C(4)	0·553 (3)	0·078 (6)	0·3085 (10)	252	−1	−8	545	−52	33
C(5)	0·441 (3)	−0·044 (6)	0·4108 (10)	461	29	11	236	19	31
C(6)	0·302 (4)	0·036 (10)	0·4523 (9)	489	−639	11	1033	64	20
C(7)	0·126 (4)	0·210 (7)	0·4345 (11)	503	−289	79	629	−84	26
C(8)	0·081 (4)	0·336 (6)	0·3772 (10)	374	−164	67	656	−43	22
C(9)	0·223 (3)	0·296 (6)	0·3318 (9)	301	−47	51	571	−28	18
C(10)	0·406 (3)	0·109 (7)	0·3519 (10)	280	27	3	911	38	23
C(11)	0·021 (3)	0·627 (6)	0·2401 (9)	257	41	35	666	−6	19
C(12)	0·087 (3)	0·645 (6)	0·1736 (9)	233	250	10	788	56	18
C(13)	−0·061 (2)	0·451 (3)	0·1281 (8)	227	−77	33	1	19	24
O(1)	0·297 (2)	0·537 (5)	0·1782 (5)	212	−110	20	758	55	20
O(2)	0·016 (2)	0·278 (3)	0·0908 (6)	262	−42	41	282	−17	22
O(3)	−0·249 (2)	0·520 (6)	0·1273 (5)	195	38	23	611	50	25
O(4)	0·247 (2)	0·543 (4)	0·0061 (6)	241	68	26	378	−27	27
Rb	−0·5365 (3)	0·0020 (0)	0·0883 (1)	215	−82	30	488	−23	21

Table 2. *Fractional coordinates of hydrogen atoms*

Isotropic temperature factor fixed at 3·0 Å^2

	x	*y*	*z*
H(1)	0·14 (3)	0·51 (8)	0·001 (8)
H(2)	0·23 (3)	0·95 (7)	0·000 (8)
H(3)	0·69 (3)	0·16 (–)	0·216 (9)
H(4)	0·66 (3)	−0·04 (7)	0·332 (8)
H(5)	0·56 (3)	−0·25 (6)	0·431 (9)
H(6)	0·35 (3)	−0·15 (5)	0·497 (9)
H(7)	−0·02 (3)	0·29 (6)	0·465 (8)
H(8)	−0·07 (3)	0·70 (6)	0·359 (9)
H(9)	0·09 (3)	0·83 (6)	0·262 (9)
H(10)	−0·11 (3)	0·60 (6)	0·232 (8)
H(11)	−0·01 (3)	1·00 (7)	0·169 (8)

and for the H atoms in Table 2. The atom labelling scheme is depicted in Fig. 1.*

Discussion. The methyl ester of the title compound (DI) is a locked substrate of chymotrypsin. Its conformation in the enzyme active site has been the subject of much study and controversy [see, for example, Silver, Stoddard, Sone & Matta (1970) and references therein]. Hayashi & Lawson (1969) have interpreted kinetic data on DI as favouring an 'axial' binding conformation of the ester group in relation to the aromatic part of the molecule. The crystallographic work on the enzyme itself (Steitz, Henderson & Blow, 1969), however, suggests a preferred 'equatorial' position for the ester group. The crystal structure of DI has recently been determined by Rodgers, Goaman & Blow (1976) and we wish to compare the results of that study with those reported here for the rubidium salt (hereinafter referred to as Rb–DI).

Despite their entirely different electrostatic environments in the two crystal lattices, the two compounds have very similar conformations. Both crystallize in the 'axial' form although the furan ring of DI is more highly buckled than Rb–DI. The angle between the plane containing C(11), C(12) and O(1) and the least-squares best fit plane through the aromatic part of the molecule is 18° for DI and 14° for Rb–DI. This compares with the value of 19° found by Green (1969) from far infrared measurements on the related compound 2,3-dihydrofuran. The distances of C(12) and C(13) from the aromatic plane are 0·27 and 1·717 Å respectively for DI and 0·17 and 1·58 Å for Rb–DI.

Table 3 lists heavy-atom bond lengths for the two structures. As expected, in each case, the furan ring is highly asymmetric leading to a displacement of C(12) to the O(1) side of the meridian line ML drawn through the midpoints of the C(4)–C(10) and C(1)–C(2) bonds of the adjoining benzene ring (Fig. 1). Numerical values and the full significance of this displacement for the stereospecificity of DI towards chymotrypsin are discussed by Rodgers *et al.* (1976).

Table 4 compares bond angles in the two structures. The strain in the furan ring is evident from the unusually small C(1)–C(11)–C(12) angle of 99·3° for DI or 101° for Rb–DI.

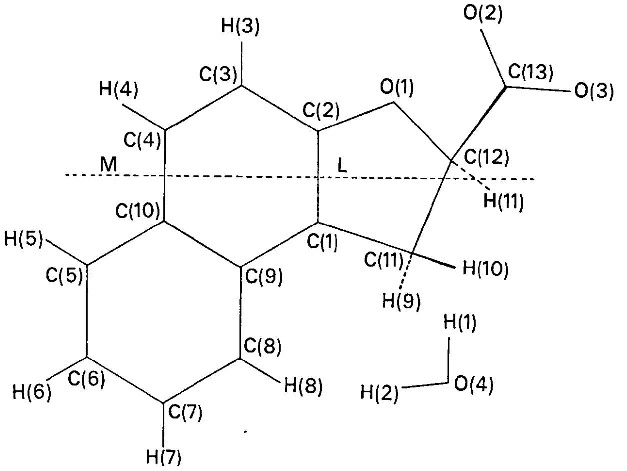

Fig. 1. Atom labelling scheme for Rb–DI. ML is the meridian line through the midpoints of the C(1)–C(2) and C(4)–C(10) bonds.

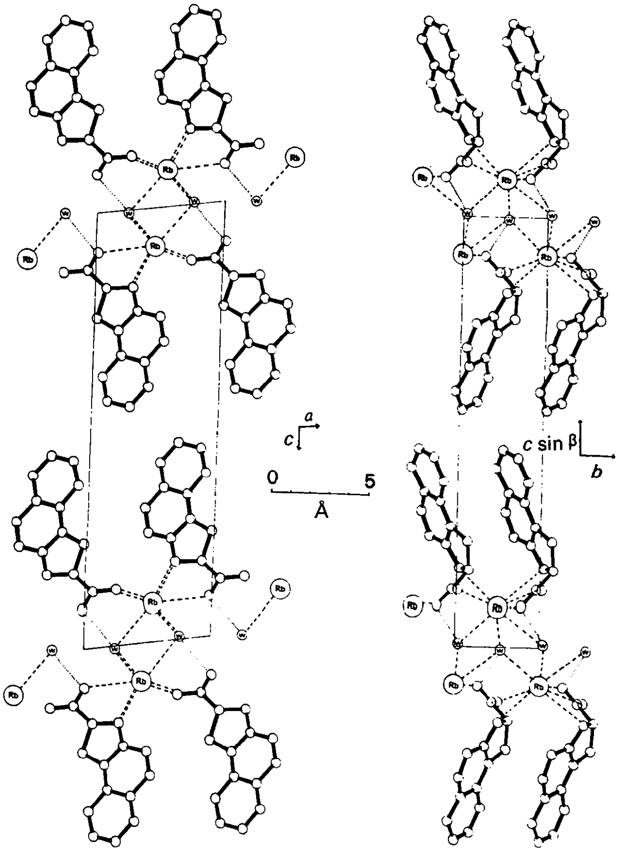

Fig. 2. [010] and [100] projections showing the molecular packing in Rb–DI crystals. Dotted lines denote hydrogen bonds and dashed lines the Rb–O coordinate bonds.

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* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31318 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

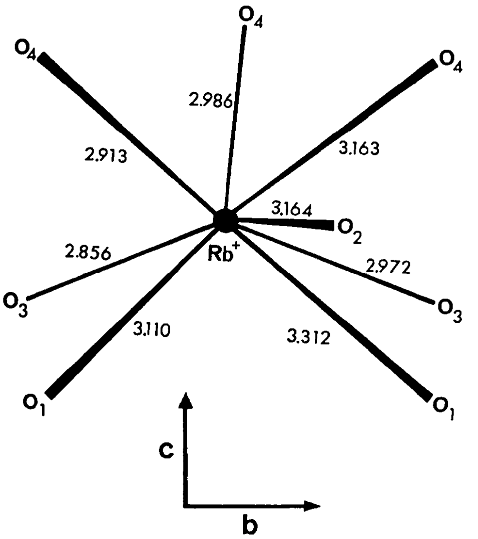

Fig. 3. Coordinate bond lengths (Å) round the rubidium ion.

Table 3. *A comparison of the bond lengths* (Å) *in* Rb–DI *and* DI (*e.s.d.'s in parentheses*)

	Rb–DI	DI
C(1)—C(2)	1·40 (3)	1·356 (9)
C(1)—C(9)	1·39 (3)	1·409 (8)
C(1)—C(11)	1·52 (3)	1·527 (9)
C(2)—C(3)	1·47 (4)	1·402 (11)
C(2)—O(1)	1·38 (3)	1·394 (8)
C(3)—C(4)	1·31 (3)	1·372 (10)
C(4)—C(10)	1·44 (3)	1·430 (10)
C(5)—C(6)	1·41 (3)	1·351 (12)
C(5)—C(10)	1·44 (3)	1·411 (10)
C(6)—C(7)	1·39 (4)	1·427 (12)
C(7)—C(8)	1·36 (3)	1·389 (10)
C(8)—C(9)	1·46 (3)	1·422 (10)
C(9)—C(10)	1·46 (3)	1·420 (10)
C(11)-C(12)	1·57 (3)	1·558 (9)
C(12)-C(13)	1·54 (3)	1·535 (10)
C(12)-O(1)	1·44 (2)	1·442 (8)
C(13)-O(2)	1·26 (2)	1·171 (10)
C(13)-O(3)	1·26 (2)	1·346 (9)

The crystal structure of Rb–DI is maintained by strong hydrogen bonds *via* the water of crystallization [O(2)–O(4) = 2·79 Å] and by the eightfold coordination involving all the O atoms in the molecule to the rubidium ion.

Table 4. *A comparison of the bond angles* (°) *in* Rb–DI *and* DI (*e.s.d.'s in parentheses*)

	Rb–DI	DI
C(1)—C(2)—C(3)	122 (2)	124·0 (6)
C(1)—C(2)—O(1)	113 (2)	113·1 (6)
C(1)—C(9)—C(8)	124 (2)	122·5 (6)
C(1)—C(9)—C(10)	121 (2)	117·5 (6)
C(1)—C(11)-C(12)	101 (2)	99·3 (5)
C(2)—C(1)—C(9)	119 (2)	120·7 (6)
C(2)—C(1)—C(11)	108 (2)	109·9 (5)
C(2)—C(3)—C(4)	118 (2)	116·2 (7)
C(2)—O(1)—C(12)	108 (1)	106·2 (5)
C(3)—C(2)—O(1)	126 (2)	122·9 (6)
C(3)—C(4)—C(10)	124 (2)	122·4 (7)
C(4)—C(10)-C(5)	120 (2)	121·2 (7)
C(4)—C(10)-C(9)	116 (2)	119·2 (6)
C(5)—C(6)—C(7)	122 (2)	121·2 (7)
C(5)—C(10)-C(9)	123 (2)	119·6 (6)
C(6)—C(5)—C(10)	115 (2)	120·2 (7)
C(6)—C(7)—C(8)	123 (2)	120·2 (7)
C(7)—C(8)—C(9)	120 (2)	118·8 (7)
C(8)—C(9)—C(10)	116 (2)	120·0 (6)
C(9)—C(1)—C(11)	132 (2)	129·4 (6)
C(11)-C(12)-C(13)	110 (2)	113·7 (5)
C(11)-C(12)-O(1)	107 (2)	107·9 (5)
C(12)-C(13)-O(2)	118 (2)	126·3 (6)
C(12)-C(13)-O(3)	114 (2)	107·8 (6)
C(13)-C(12)-O(1)	112 (2)	107·6 (6)
O(2)—C(13)-O(3)	127 (2)	125·8 (7)

Fig. 2 shows two projections of the molecular packing arrangement and Fig. 3 gives the coordinate bond lengths to the rubidium ion.

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