

## Data Report

### Identification of cannabidiol from *Humulus Kriya* using x-ray crystallography

D. Cushing<sup>1\*</sup> & B. Joseph<sup>1</sup>

<sup>1</sup>: Peak Health Center, Los Gatos, CA

\*For inquiries, email corresponding author at donish@peakhealth.center

Received: June 19, 2018

Accepted: June 20, 2018

Published: June 26, 2018

Copyright: © Cushing & Joseph (2018c).

This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Citation: Cushing, C., Joseph, B. (2018c).

Identification of cannabidiol from *Humulus Kriya* using x-ray crystallography. Retrieved from <https://doi.org/10.31013/2002d>

#### Abstract

The crystal structure of cannabidiol, was determined by the application of Cu K $\alpha$  radiation single-crystal X-ray crystallography. The unsaturated alkyl chain of the cannabidiol molecule was found to be freely rotatable. We found two molecules with different orientations of this side chain within the asymmetric unit. These independent molecules are both found to have the R,R configuration, just like cannabidiol from *Cannabis Sativa*.

The crystal structure of cannabidiol, C<sub>21</sub>H<sub>30</sub>O<sub>2</sub>, {2-[(1R,6R)-3-methyl-6-(prop-1-en-2-yl)cyclohex-2-enyl]-5-pentylbenzene-1,3-diol}, was first determined by Jones et al. (1977) and Ottersen & Rosenqvist (1977). Mechoulam (1967) identified and represented the structure as R,R by chemical means, which was a laborious and remarkable feat.

We used advanced single-crystal X-ray diffractometers to study the structure of a fraction isolated

from the *Humulus kriya* plant. The unique Cu K $\alpha$  wavelength radiation determined that the absolute structure was R,R— the same as the Cannabidiol structure represented by Mechoulam. We found an identical crystal structure to CBD from cannabis sativa (Mayr, Grassl, Korber, Christoffel & Bodensteiner, 2017).

#### Procedure

The crystal structure of cannabidiol, (Figure 1), was determined by the application of Cu K $\alpha$  radiation

single-crystal X-ray crystallography. This is a rather uncommon wavelength radiation to measure crystal structures. The unsaturated alkyl chain of the cannabidiol molecule was found to be freely rotatable. We found two molecules with different orientations of this side chain within the asymmetric unit (Figures 2 & 3). These independent molecules are both found to have the *R,R* configuration, confirming earlier investigations by Jones *et al.* (1977), Ottersen & Rosenqvist (1977) and Mechoulam *et al.* (1967).

Synthesis and crystallization

Cannabidiol was obtained from ImmunAG LLP, 501, Edcon Mindspace, Campal, Panaji, Goa, India-403001. *n*-Heptane was used to recrystallize the Cannabidiol and further purify it. The crystal was selected using standard preparation techniques, and mounted on a MiTiGen-loop using mineral oil.

Refinement

Crystallographic data, data collection and strucutre refinement details are summarized in Table 1.

<u>Crystal data</u>	
Chemical formula	C21H30O2
Mr	314.45
Crystal system, space group	Monoclinic, <i>P</i> 2 <sub>1</sub>
Temperature (K)	123
a, b, c (Å)	10.4395 (1), 10.8739 (1), 16.7853 (2)
β (o)	95.448 (1)
V (Å <sup>3</sup> )	1896.83 (3)
Z	4
Radiation type	Cu Kβ
μ (mm <sup>-1</sup> )	0.39
Crystal size (mm)	0.28 X 0.16 X 0.15
<u>Data collection</u>	
Diffractometer	Agilent GV1000, TitanS2
Absorption correction	Gaussian ( <i>CrysAlis</i> PRO; Rigaku OD, 2015)
T <sub>min</sub> , T <sub>max</sub>	0.996, 0.997
No. of measured, independent and observed [ <i>I</i> > 2σ( <i>I</i> )] reflections	85198, 10203, 9859
R <sub>int</sub>	0.044
(sin θ/λ) <sub>max</sub> (Å <sup>-1</sup> )	0.695
<u>Refinement</u>	
R[F <sup>2</sup> > 2σ( <i>F</i> <sup>2</sup> )], wR( <i>F</i> <sup>2</sup> ), S	0.032, 0.088, 1.03
No. of reflections	10203
No. of parameters	655
No. of restraints	1
H-atom treatment	All H-atom parameters refined
Δρ <sub>max</sub> , Δρ <sub>min</sub> (e Å <sup>-3</sup> )	0.23, 0.13
Absolute structure	Flack <i>x</i> determined using 4335 quotients [( <i>I</i> <sup>+</sup> ) - ( <i>I</i> )]/[( <i>I</i> <sup>+</sup> )+( <i>I</i> )] (Parsons et al., 2013)
Absolute structure parameter	-0.03 (6)
Table 1: Experimental details.	

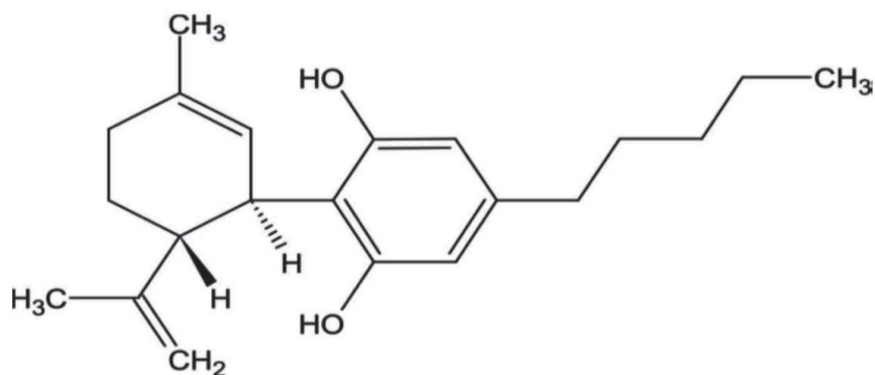


Figure 2: 3-D structure of Cannabidiol isolated from H kriya

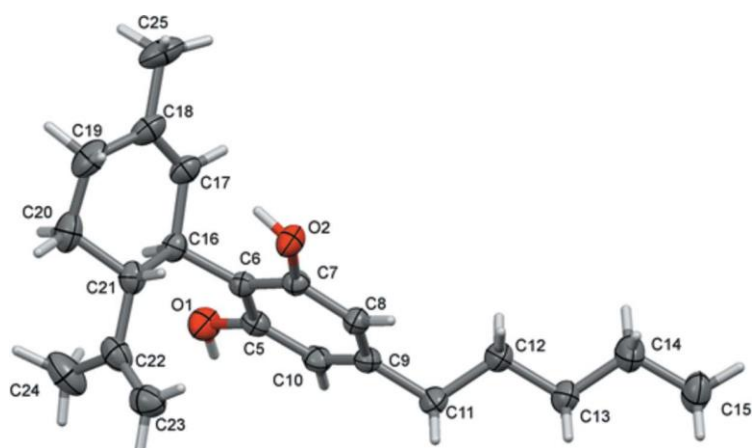


Fig 3: 3-D structure of one independent Cannabidiol molecule isolated from H kriya

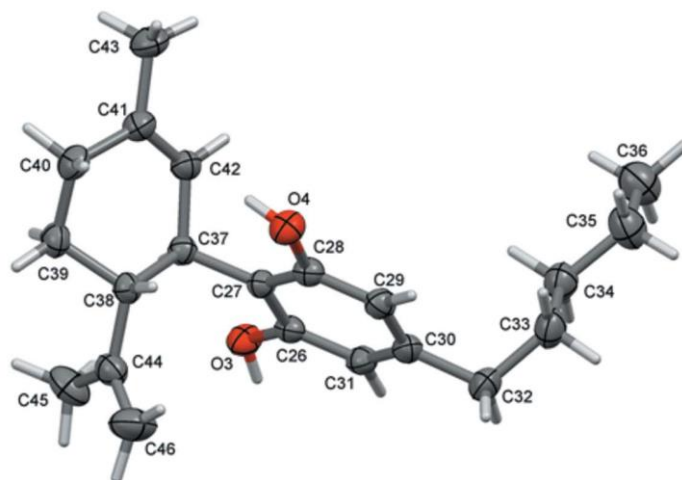


Fig 4: 3-D structure of a second independent Cannabidiol molecule isolated from H kriya

**References:**

- Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A., & Puschmann, H. (2009). OLEX2: a complete structure solution, refinement and analysis program. *Journal of Applied Crystallography*, 42(2), 339-341. <https://doi.org/10.1107/s0021889808042726>
- Jones, P. G., Falvello, L., Kennard, O., Sheldrick, G. M., & Mechoulam, R. (1977). Cannabidiol. *Acta Crystallographica Section B: Structural Crystallography and Crystal Chemistry*, 33(10), 3211-3214. <https://doi.org/10.1107/s0567740877010577>
- Macrae, C.F., Bruno, I.J., Chisholm, J.A., Edgington, P.R., McCabe, P., Pidcock, E., ... & Wood, P.A. (2008) New Features for the Visualization and Investigation of Crystal Structures. *Journal of Applied Crystallography*, 41, 466-470. <http://dx.doi.org/10.1107/S0021889807067908>
- Mayr, T., Grassl, T., Korber, N., Christoffel, V., & Bodensteiner, M. (2017). Cannabidiol revisited. *IUCrData*, 2(2), x170276. <https://doi.org/10.1107/s2414314617002760>
- Mechoulam, R., Braun, P., & Gaoni, Y. (1967). Stereospecific synthesis of (-)- DELTA. 1-and (-)- DELTA. 1 (6)-tetrahydrocannabinols. *Journal of the American Chemical Society*, 89(17), 4552-4554. <https://doi.org/10.1021/ja00993a072>
- Ottersen, T. & Rosenqvist, E. (1977). The crystal and molecular structure of cannabidiol. *Acta Chem. Scand.* 31b, 749– 755. <https://doi.org/10.3891/acta.chem.scand.31b-0807>
- Parsons, S., Flack, H. D., & Wagner, T. (2013). Use of intensity quotients and differences in absolute structure refinement. *Acta Crystallographica Section B: Structural Science, Crystal Engineering and Materials*, 69(3), 249-259. <https://doi.org/10.1107/s2052519213010014>
- Sheldrick, G. M. (2015). Crystal structure refinement with SHELXL. *Acta Crystallographica Section C: Structural Chemistry*, 71(1), 3-8.

## Full crystallographic report

*Crystal data* $C_{21}H_{30}O_2$  $M_r = 314.45$ Monoclinic,  $P2_1$  $a = 10.4395$  (1) Å $b = 10.8739$  (1) Å $c = 16.7853$  (2) Å $\beta = 95.448$  (1)° $V = 1896.83$  (3) Å<sup>3</sup> $Z = 4$  $F(000) = 668$  $D_x = 1.101$  mg m<sup>-3</sup>

Melting point = 339-340 K

Cu  $K\beta$  radiation,  $\lambda = 1.39222$  Å

Cell parameters from 54306 reflections

 $\theta = 3.6$ -74.8° $\mu = 0.39$  mm<sup>-1</sup> $T = 123$  K

Prism, clear colorless

*Data collection*

Agilent GV1000, TitanS2 diffractometer

Radiation source: gradient vacuum rotating-anode X-ray  
tube, GV1000 (Cu) X-ray source

Mirror monochromator

Detector resolution: 4.1818 pixels mm<sup>-1</sup> $\omega$  scans

Absorption correction: gaussian

(CrysAlisPro; Rigaku OD, 2015)

 $T_{\min} = 0.996$ ,  $T_{\max} = 0.997$ 

85198 measured reflections

9859 reflections with  $I > 2\sigma(I)$  $R_{\text{int}} = 0.044$  $\theta_{\max} = 75.3^\circ$ ,  $\theta_{\min} = 2.4^\circ$  $h = -14 \rightarrow 14$  $k = -15 \rightarrow 14$  $l = -23 \rightarrow 23$ *Refinement*Refinement on  $F^2$ 

Least-squares matrix: full

 $R[F^2 > 2\sigma(F^2)] = 0.032$  $wR(F^2) = 0.088$  $S = 1.03$ 

10203 reflections

655 parameters

1 restraint

Primary atom site location: dual

Hydrogen site location: difference Fourier map  
2013)*Special details*

All H-atom parameters refined

 $w = 1/\sigma^2(F^2) + (0.0493P)^2 + 0.1553P]$ where  $P = (F^2 + 2F^2)/3$  $(\Delta/\sigma)_{\max} < 0.001$  $\Delta\rho_{\max} = 0.23$  e Å<sup>-3</sup> $\Delta\rho_{\min} = -0.13$  e Å<sup>-3</sup>Absolute structure: Flack  $x$  determined using 4335quotients  $[(I^+) - (I^-)] / [(I^+) + (I^-)]$  (Parsons *et al.*,

Absolute structure parameter: -0.03 (6)

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ( $\text{\AA}^2$ )*

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O2	0.45873 (9)	0.27113 (11)	0.68801 (7)	0.0350 (2)
O3	0.22910 (10)	0.31909 (11)	0.75679 (7)	0.0361 (2)
O4	−0.01007 (11)	0.64952 (12)	0.85698 (7)	0.0370 (2)
O1	0.89037 (10)	0.39186 (12)	0.65474 (7)	0.0401 (2)
C7	0.56191 (12)	0.35049 (13)	0.70250 (8)	0.0280 (2)
C27	0.11199 (12)	0.47899 (13)	0.81028 (7)	0.0276 (2)
C28	0.06220 (12)	0.59824 (14)	0.80142 (8)	0.0298 (2)
C26	0.18235 (11)	0.43560 (13)	0.74901 (7)	0.0285 (2)
C6	0.68036 (12)	0.32428 (13)	0.67315 (7)	0.0272 (2)
C5	0.77497 (12)	0.41511 (14)	0.68514 (8)	0.0297 (2)
C29	0.08240 (13)	0.67195 (14)	0.73595 (9)	0.0337 (3)
C41	−0.10203 (14)	0.40126 (16)	0.96293 (9)	0.0360 (3)
C37	0.09170 (12)	0.39998 (14)	0.88271 (7)	0.0290 (2)
C9	0.63810 (13)	0.54375 (14)	0.75803 (8)	0.0317 (3)
C16	0.70534 (12)	0.20447 (14)	0.63181 (8)	0.0301 (2)
C8	0.54143 (13)	0.45499 (14)	0.74650 (8)	0.0309 (2)
C10	0.75383 (13)	0.52378 (14)	0.72519 (8)	0.0328 (3)
C38	0.16926 (12)	0.44801 (14)	0.96000 (8)	0.0309 (3)
C31	0.20157 (13)	0.50812 (15)	0.68246 (8)	0.0327 (3)
C42	−0.05071 (13)	0.39038 (15)	0.89332 (8)	0.0329 (3)
C30	0.15332 (13)	0.62697 (15)	0.67583 (8)	0.0334 (3)
C17	0.61190 (15)	0.18610 (16)	0.55797 (8)	0.0359 (3)
C18	0.56273 (18)	0.07793 (18)	0.53315 (9)	0.0432 (4)
C44	0.31309 (14)	0.43548 (17)	0.95708 (9)	0.0381 (3)
C21	0.70272 (14)	0.09214 (15)	0.68849 (9)	0.0352 (3)
C22	0.80132 (16)	0.10349 (17)	0.76024 (11)	0.0426 (3)

C11	0.61657 (16)	0.66019 (16)	0.80361 (10)	0.0390 (3)
C39	0.12060 (15)	0.38200 (17)	1.03236 (8)	0.0374 (3)
C32	0.17722 (17)	0.70713 (19)	0.60483 (10)	0.0434 (4)
C12	0.49874 (18)	0.73187 (17)	0.77039 (10)	0.0429 (3)
C33	0.0558 (2)	0.74656 (19)	0.55280 (11)	0.0475 (4)
C40	−0.01885 (16)	0.41677 (18)	1.04074 (9)	0.0408 (3)
C13	0.47857 (18)	0.85021 (16)	0.81437 (10)	0.0414 (3)
C23	0.7641 (2)	0.12371 (19)	0.83228 (11)	0.0498 (4)
C20	0.7152 (2)	−0.02482 (18)	0.63891 (13)	0.0494 (4)
C43	−0.24537 (17)	0.3974 (2)	0.96703 (12)	0.0503 (4)
C34	−0.01477 (18)	0.64082 (19)	0.50915 (11)	0.0449 (4)
C14	0.3597 (2)	0.9199 (2)	0.78214 (16)	0.0630 (6)
C25	0.4721 (3)	0.0678 (3)	0.45807 (12)	0.0607 (6)
C45	0.36871 (18)	0.3090 (2)	0.95561 (14)	0.0528 (5)
C46	0.38685 (19)	0.5344 (3)	0.95736 (16)	0.0603 (5)
C19	0.5994 (2)	−0.03921 (19)	0.57671 (13)	0.0540 (4)
C15	0.3401 (2)	1.0401 (2)	0.82410 (13)	0.0543 (5)
C35	−0.1338 (2)	0.6820 (2)	0.45576 (15)	0.0578 (5)
C24	0.9415 (2)	0.0943 (3)	0.74624 (18)	0.0663 (6)

C36	−0.1995 (2)	0.5757 (3)	0.40974 (17)	0.0636 (6)
H40A	−0.025 (2)	0.504 (2)	1.0609 (14)	0.043 (5)*
H38	0.1488 (18)	0.538 (2)	0.9650 (11)	0.027 (4)*
H8	0.459 (2)	0.466 (2)	0.7688 (13)	0.042 (5)*
H33A	−0.005 (3)	0.789 (3)	0.5860 (17)	0.062 (7)*
H39A	0.177 (2)	0.401 (2)	1.0813 (13)	0.041 (5)*
H21	0.617 (2)	0.089 (2)	0.7084 (12)	0.033 (5)*
H33B	0.085 (3)	0.807 (3)	0.5148 (17)	0.063 (8)*
H19A	0.527 (3)	−0.071 (3)	0.6008 (16)	0.060 (7)*
H42	−0.107 (2)	0.374 (2)	0.8461 (12)	0.035 (5)*
H32A	0.235 (3)	0.665 (3)	0.5677 (16)	0.055 (7)*
H37	0.1249 (18)	0.315 (2)	0.8712 (11)	0.030 (4)*
H16	0.7917 (18)	0.210 (2)	0.6121 (11)	0.030 (4)*
H39B	0.127 (2)	0.290 (3)	1.0247 (14)	0.046 (6)*
H40B	−0.055 (2)	0.365 (3)	1.0835 (15)	0.050 (6)*
H17	0.591 (2)	0.264 (3)	0.5272 (15)	0.047 (6)*
H31	0.251 (2)	0.476 (2)	0.6408 (13)	0.043 (5)*
H45A	0.356 (4)	0.256 (4)	1.004 (2)	0.092 (11)*
H20A	0.798 (3)	−0.018 (3)	0.6132 (16)	0.060 (7)*
H34A	−0.042 (2)	0.578 (3)	0.5498 (15)	0.050 (6)*
H10	0.823 (2)	0.585 (2)	0.7311 (13)	0.039 (5)*
H11A	0.608 (2)	0.639 (3)	0.8615 (15)	0.050 (6)*
H13A	0.550 (3)	0.902 (3)	0.8117 (18)	0.069 (8)*
H1	0.943 (3)	0.444 (3)	0.6727 (15)	0.054 (7)*
H13B	0.473 (3)	0.835 (3)	0.8723 (17)	0.058 (7)*
H29	0.049 (2)	0.756 (2)	0.7327 (13)	0.043 (6)*
H24A	0.961 (3)	0.150 (3)	0.7046 (19)	0.070 (8)*
H24B	0.993 (3)	0.106 (3)	0.793 (2)	0.077 (9)*
H3	0.290 (2)	0.307 (2)	0.7284 (14)	0.046 (6)*
H35A	−0.111 (3)	0.746 (3)	0.4193 (18)	0.063 (8)*
H35B	−0.190 (3)	0.721 (3)	0.4888 (19)	0.068 (8)*
H46A	0.483 (3)	0.524 (3)	0.9616 (18)	0.071 (9)*

H43A	−0.283 (3)	0.469 (3)	0.9898 (19)	0.074 (9)*
H12A	0.416 (3)	0.679 (3)	0.7686 (19)	0.073 (9)*
H46B	0.344 (4)	0.613 (4)	0.958 (2)	0.090 (11)*
H12B	0.499 (3)	0.750 (3)	0.7153 (19)	0.070 (8)*
H15A	0.342 (3)	1.031 (3)	0.883 (2)	0.080 (10)*
H19B	0.617 (3)	−0.104 (3)	0.537 (2)	0.074 (9)*
H32B	0.223 (3)	0.781 (3)	0.6257 (17)	0.064 (8)*
H14A	0.365 (4)	0.935 (4)	0.720 (3)	0.113 (14)*
H34B	0.048 (2)	0.596 (3)	0.4745 (15)	0.052 (6)*
H20B	0.721 (3)	−0.098 (3)	0.6747 (16)	0.057 (7)*
H43B	−0.293 (3)	0.386 (3)	0.9146 (17)	0.060 (7)*
H23A	0.676 (3)	0.132 (3)	0.8403 (16)	0.059 (7)*
H23B	0.818 (3)	0.130 (3)	0.8784 (17)	0.061 (7)*
H2	0.475 (2)	0.223 (2)	0.6496 (14)	0.044 (5)*
H4	−0.036 (3)	0.593 (3)	0.8864 (16)	0.054 (7)*
H43C	−0.264 (3)	0.331 (3)	1.0030 (19)	0.073 (9)*

H25A	0.443 (3)	0.156 (4)	0.438 (2)	0.075 (9)*
H15B	0.415 (3)	1.097 (4)	0.815 (2)	0.082 (10)*
H36A	−0.142 (3)	0.538 (3)	0.3720 (17)	0.063 (8)*
H25B	0.512 (3)	0.020 (3)	0.4207 (19)	0.069 (8)*
H25C	0.401 (3)	0.024 (3)	0.4684 (19)	0.073 (9)*
H45B	0.463 (3)	0.312 (3)	0.9515 (18)	0.068 (8)*
H11B	0.692 (3)	0.713 (3)	0.8057 (18)	0.072 (8)*
H45C	0.331 (3)	0.264 (3)	0.914 (2)	0.078 (9)*
H36B	−0.222 (3)	0.515 (4)	0.448 (2)	0.076 (9)*
H14B	0.280 (5)	0.877 (5)	0.788 (3)	0.125 (16)*
H36C	−0.284 (4)	0.611 (4)	0.377 (2)	0.088 (11)*
H24C	0.955 (4)	0.003 (4)	0.723 (2)	0.093 (11)*
H15C	0.261 (4)	1.085 (4)	0.808 (2)	0.098 (12)*

*Atomic displacement parameters ( $\text{\AA}^2$ )*

	$U^{11}$	$U^{22}$	$U^{33}$	$U^{12}$	$U^{13}$	$U^{23}$
O2	0.0289 (4)	0.0337 (5)	0.0438 (5)	−0.0053 (4)	0.0102 (4)	−0.0110 (4)
O3	0.0349 (5)	0.0343 (6)	0.0409 (5)	0.0056 (4)	0.0121 (4)	−0.0004 (4)
O4	0.0416 (5)	0.0330 (6)	0.0380 (5)	0.0046 (4)	0.0113 (4)	−0.0038 (4)
O1	0.0277 (4)	0.0454 (7)	0.0481 (6)	−0.0063 (4)	0.0074 (4)	−0.0059 (5)
C7	0.0276 (5)	0.0280 (6)	0.0281 (5)	−0.0018 (4)	0.0016 (4)	−0.0003 (4)

C27	0.0256 (5)	0.0302 (6)	0.0271 (5)	−0.0014 (4)	0.0027 (4)	−0.0013 (4)
C28	0.0273 (5)	0.0313 (7)	0.0309 (5)	−0.0008 (5)	0.0034 (4)	−0.0028 (5)
C26	0.0237 (5)	0.0316 (7)	0.0302 (5)	−0.0003 (4)	0.0027 (4)	−0.0026 (5)
C6	0.0277 (5)	0.0279 (6)	0.0258 (5)	0.0000 (4)	0.0018 (4)	0.0007 (4)
C5	0.0264 (5)	0.0331 (7)	0.0292 (5)	−0.0011 (5)	0.0003 (4)	0.0028 (5)
C29	0.0312 (6)	0.0311 (7)	0.0386 (6)	−0.0008 (5)	0.0028 (5)	0.0025 (5)
C41	0.0335 (6)	0.0392 (8)	0.0361 (6)	−0.0019 (5)	0.0077 (5)	0.0030 (6)
C37	0.0297 (5)	0.0301 (7)	0.0272 (5)	−0.0006 (5)	0.0032 (4)	−0.0002 (4)
C9	0.0332 (6)	0.0290 (7)	0.0314 (6)	0.0017 (5)	−0.0052 (5)	−0.0027 (5)
C16	0.0300 (6)	0.0299 (7)	0.0312 (5)	0.0007 (5)	0.0075 (4)	−0.0016 (5)
C8	0.0294 (5)	0.0315 (7)	0.0315 (5)	0.0020 (5)	0.0014 (4)	−0.0037 (5)
C10	0.0300 (6)	0.0306 (7)	0.0361 (6)	−0.0033 (5)	−0.0049 (5)	−0.0003 (5)
C38	0.0311 (6)	0.0330 (7)	0.0282 (5)	−0.0004 (5)	0.0016 (4)	−0.0004 (5)
C31	0.0277 (5)	0.0415 (8)	0.0294 (5)	−0.0034 (5)	0.0061 (4)	−0.0021 (5)
C42	0.0314 (6)	0.0358 (7)	0.0315 (6)	−0.0042 (5)	0.0026 (5)	0.0016 (5)
C30	0.0295 (6)	0.0394 (8)	0.0311 (6)	−0.0056 (5)	0.0015 (4)	0.0042 (5)
C17	0.0409 (7)	0.0392 (8)	0.0285 (6)	−0.0005 (6)	0.0084 (5)	−0.0053 (5)
C18	0.0503 (8)	0.0465 (10)	0.0342 (6)	−0.0056 (7)	0.0112 (6)	−0.0129 (6)
C44	0.0331 (6)	0.0473 (9)	0.0332 (6)	0.0020 (6)	−0.0008 (5)	−0.0012 (6)
C21	0.0356 (6)	0.0301 (7)	0.0405 (7)	0.0012 (5)	0.0070 (5)	0.0011 (5)
C22	0.0397 (7)	0.0357 (8)	0.0513 (8)	0.0028 (6)	−0.0013 (6)	0.0103 (7)
C11	0.0403 (7)	0.0319 (8)	0.0426 (7)	0.0032 (6)	−0.0069 (6)	−0.0098 (6)
C39	0.0414 (7)	0.0435 (9)	0.0271 (5)	0.0016 (6)	0.0020 (5)	0.0031 (5)
C32	0.0429 (7)	0.0482 (10)	0.0393 (7)	−0.0094 (7)	0.0051 (6)	0.0112 (7)
C12	0.0493 (8)	0.0349 (8)	0.0423 (8)	0.0082 (6)	−0.0073 (6)	−0.0079 (6)

C33	0.0572 (9)	0.0442 (10)	0.0403 (8)	−0.0047 (7)	0.0011 (7)	0.0111 (7)
C40	0.0433 (7)	0.0491 (10)	0.0311 (6)	−0.0003 (6)	0.0093 (5)	0.0014 (6)
C13	0.0501 (8)	0.0306 (8)	0.0427 (7)	0.0049 (6)	0.0006 (6)	−0.0046 (6)
C23	0.0590 (10)	0.0435 (10)	0.0448 (8)	−0.0022 (8)	−0.0065 (7)	0.0068 (7)
C20	0.0574 (10)	0.0300 (8)	0.0621 (10)	0.0052 (7)	0.0128 (8)	−0.0040 (7)
C43	0.0355 (7)	0.0689 (13)	0.0484 (8)	−0.0037 (8)	0.0136 (6)	0.0041 (9)
C34	0.0488 (8)	0.0426 (9)	0.0429 (8)	−0.0007 (7)	0.0022 (6)	0.0068 (7)
C14	0.0641 (12)	0.0452 (12)	0.0756 (14)	0.0181 (9)	−0.0141 (10)	−0.0167 (10)
C25	0.0731 (13)	0.0685 (15)	0.0401 (8)	−0.0155 (11)	0.0037 (9)	−0.0236 (9)
C45	0.0413 (8)	0.0558 (12)	0.0591 (10)	0.0145 (8)	−0.0063 (7)	−0.0074 (9)
C46	0.0366 (8)	0.0613 (14)	0.0833 (15)	−0.0080 (8)	0.0070 (9)	0.0000 (11)
C19	0.0686 (12)	0.0369 (10)	0.0577 (10)	−0.0088 (8)	0.0122 (9)	−0.0156 (8)
C15	0.0680 (12)	0.0384 (10)	0.0581 (10)	0.0133 (9)	0.0143 (9)	−0.0006 (8)
C35	0.0599 (11)	0.0511 (12)	0.0593 (11)	0.0042 (9)	−0.0112 (9)	0.0052 (9)
C24	0.0396 (9)	0.0783 (17)	0.0794 (15)	0.0108 (10)	−0.0016 (9)	0.0226 (14)
C36	0.0584 (12)	0.0607 (14)	0.0692 (13)	0.0005 (10)	−0.0070 (10)	0.0006 (11)

*Geometric parameters (Å, °)*

O2—C7	1.3836 (16)	C11—H11B	0.98 (3)
O2—H2	0.86 (3)	C39—C40	1.523 (2)
O3—C26	1.3595 (18)	C39—H39A	0.98 (2)
O3—H3	0.84 (3)	C39—H39B	1.02 (3)

O4—C28	1.3723 (16)	C32—C33	1.531 (3)
O4—H4	0.85 (3)	C32—H32A	1.02 (3)
O1—C5	1.3756 (17)	C32—H32B	0.98 (3)
O1—H1	0.83 (3)	C12—C13	1.508 (2)
C7—C6	1.4031 (18)	C12—H12A	1.03 (3)
C7—C8	1.3829 (19)	C12—H12B	0.95 (3)
C27—C28	1.400 (2)	C33—C34	1.516 (3)
C27—C26	1.4011 (17)	C33—H33A	1.00 (3)
C27—C37	1.5198 (18)	C33—H33B	0.99 (3)
C28—C29	1.392 (2)	C40—H40A	1.01 (3)
C26—C31	1.3973 (19)	C40—H40B	1.01 (3)
C6—C5	1.3978 (18)	C13—C14	1.510 (3)
C6—C16	1.510 (2)	C13—H13A	0.94 (3)
C5—C10	1.388 (2)	C13—H13B	0.99 (3)
C29—C30	1.395 (2)	C23—H23A	0.95 (3)
C29—H29	0.98 (3)	C23—H23B	0.92 (3)
C41—C42	1.3361 (19)	C20—C19	1.529 (3)
C41—C40	1.508 (2)	C20—H20A	1.00 (3)
C41—C43	1.505 (2)	C20—H20B	1.00 (3)
C37—C38	1.5530 (17)	C43—H43A	0.96 (4)
C37—C42	1.5176 (18)	C43—H43B	0.98 (3)
C37—H37	1.01 (2)	C43—H43C	0.97 (4)
C9—C8	1.397 (2)	C34—C35	1.529 (3)
C9—C10	1.392 (2)	C34—H34A	1.02 (3)
C9—C11	1.507 (2)	C34—H34B	1.04 (3)
C16—C17	1.516 (2)	C14—C15	1.507 (3)
C16—C21	1.550 (2)	C14—H14A	1.06 (4)
C16—H16	0.991 (19)	C14—H14B	0.97 (5)
C8—H8	0.98 (2)	C25—H25A	1.05 (4)
C10—H10	0.98 (2)	C25—H25B	0.94 (3)
C38—C44	1.5131	C25—H25C	0.91 (4)

	(19)		
C38—C39	1.5380 (19)	C45—H45A	1.01 (4)
C38—H38	1.01 (2)	C45—H45B	1.00 (3)
C31—C30	1.388 (2)	C45—H45C	0.91 (4)
C31—H31	0.97 (2)	C46—H46A	1.01 (3)
C42—H42	0.96 (2)	C46—H46B	0.97 (4)
C30—C32	1.516 (2)	C19—H19A	0.95 (3)
C17—C18	1.334 (2)	C19—H19B	0.99 (3)
C17—H17	1.01 (3)	C15—H15A	1.00 (3)
C18—C25	1.506 (3)	C15—H15B	1.03 (4)
C18—C19	1.500 (3)	C15—H15C	0.97 (4)
C44—C45	1.494 (3)	C35—C36	1.517 (4)
C44—C46	1.323 (3)	C35—H35A	0.97 (3)
C21—C22	1.513 (2)	C35—H35B	0.94 (3)
C21—C20	1.532 (2)	C24—H24A	0.96 (3)
C21—H21	0.99 (2)	C24—H24B	0.91 (4)
C22—C23	1.323 (3)	C24—H24C	1.09 (4)
C22—C24	1.507 (3)	C36—H36A	1.00 (3)
C11—C12	1.517 (2)	C36—H36B	0.96 (4)
C11—H11A	1.01 (3)	C36—H36C	1.07 (4)
C7—O2—H2	107.9 (16)	C33—C32—H32B	109.2 (18)
C26—O3—H3	112.3 (18)	H32A—C32—H32B	106 (2)
C28—O4—H4	108.9 (19)	C11—C12—H12A	111.8 (19)
C5—O1—H1	108.4 (18)	C11—C12—H12B	112.7 (19)
O2—C7—C6	120.59 (12)	C13—C12—C11	113.86 (13)
C8—C7—O2	116.69 (12)	C13—C12—H12A	109.4 (18)
C8—C7—C6	122.72 (12)	C13—C12—H12B	108 (2)
C28—C27—C26	116.69 (12)	H12A—C12—H12B	100 (3)

C28—C27—C37	122.01 (11)	C32—C33—H33A	110.4 (16)
C26—C27—C37	121.29 (13)	C32—C33—H33B	105.3 (17)
O4—C28—C27	121.79 (13)	C34—C33—C32	113.65 (17)
O4—C28—C29	115.90 (13)	C34—C33—H33A	108.3 (18)
C29—C28—C27	122.32 (12)	C34—C33—H33B	111.2 (17)
O3—C26—C27	116.85 (12)	H33A—C33—H33B	108 (2)
O3—C26—C31	121.68 (12)	C41—C40—C39	111.66 (12)
C31—C26—C27	121.46 (13)	C41—C40—H40A	110.2 (13)
C7—C6—C16	122.20 (12)	C41—C40—H40B	109.2 (14)
C5—C6—C7	116.12 (12)	C39—C40—H40A	111.0 (13)
C5—C6—C16	121.68 (11)	C39—C40—H40B	110.6 (14)
O1—C5—C6	116.65 (13)	H40A—C40—H40B	103.9 (19)
O1—C5—C10	121.43 (13)	C12—C13—C14	113.65 (15)
C10—C5—C6	121.92 (12)	C12—C13—H13A	109.9 (19)
C28—C29—C30	119.97 (14)	C12—C13—H13B	111.2 (18)
C28—C29—H29	120.1 (13)	C14—C13—H13A	108 (2)
C30—C29—H29	119.9 (13)	C14—C13—H13B	108.2 (17)
C42—C41—C40	121.44 (13)	H13A—C13—H13B	105 (2)
C42—C41—C43	121.36 (14)	C22—C23—H23A	121.3 (17)
C43—C41—C40	117.19 (13)	C22—C23—H23B	124.9 (18)
C27—C37—C38	112.15 (11)	H23A—C23—H23B	114 (2)
C27—C37—H37	106.6 (11)	C21—C20—H20A	106.8

			(18)
C38—C37—H37	107.8 (11)	C21—C20—H20B	109.9 (16)
C42—C37—C27	110.20 (11)	C19—C20—C21	110.68 (15)
C42—C37—C38	111.34 (10)	C19—C20—H20A	111.8 (16)
C42—C37—H37	108.5 (11)	C19—C20—H20B	109.1 (16)
C8—C9—C11	120.68 (13)	H20A—C20—H20B	108 (2)
C10—C9—C8	118.71 (13)	C41—C43—H43A	116 (2)
C10—C9—C11	120.60 (14)	C41—C43—H43B	112.6 (16)
C6—C16—C17	111.32 (12)	C41—C43—H43C	107.7 (19)
C6—C16—C21	112.57 (11)	H43A—C43—H43B	106 (3)
C6—C16—H16	107.6 (12)	H43A—C43—H43C	104 (3)
C17—C16—C21	110.52 (12)	H43B—C43—H43C	111 (3)
C17—C16—H16	105.6 (11)	C33—C34—C35	113.08 (17)
C21—C16—H16	108.9 (12)	C33—C34—H34A	109.5 (14)
C7—C8—C9	119.71 (12)	C33—C34—H34B	108.6 (15)
C7—C8—H8	119.2 (14)	C35—C34—H34A	109.1 (14)
C9—C8—H8	121.1 (14)	C35—C34—H34B	109.3 (14)
C5—C10—C9	120.58 (13)	H34A—C34—H34B	107 (2)
C5—C10—H10	118.7 (13)	C13—C14—H14A	108 (2)
C9—C10—H10	120.7 (13)	C13—C14—H14B	114 (3)
C37—C38—H38	107.4 (11)	C15—C14—C13	114.30 (18)
C44—C38—C37	112.51 (11)	C15—C14—H14A	110 (3)
C44—C38—C39	112.76 (12)	C15—C14—H14B	103 (3)
C44—C38—H38	108.0 (11)	H14A—C14—H14B	107 (4)
C39—C38—C37	108.52 (11)	C18—C25—H25A	110.3 (18)
C39—C38—H38	107.4 (11)	C18—C25—H25B	108.3

			(19)
C26—C31—H31	119.9 (15)	C18—C25—H25C	110 (2)
C30—C31—C26	120.74 (12)	H25A—C25—H25B	115 (3)
C30—C31—H31	119.4 (15)	H25A—C25—H25C	108 (3)
C41—C42—C37	125.11 (12)	H25B—C25—H25C	105 (3)
C41—C42—H42	118.5 (13)	C44—C45—H45A	116 (2)
C37—C42—H42	116.4 (12)	C44—C45—H45B	111 (2)
C29—C30—C32	120.33 (15)	C44—C45—H45C	112 (2)
C31—C30—C29	118.81 (13)	H45A—C45—H45B	106 (3)
C31—C30—C32	120.86 (14)	H45A—C45—H45C	103 (3)
C16—C17—H17	113.6 (14)	H45B—C45—H45C	109 (3)
C18—C17—C16	124.76 (16)	C44—C46—H46A	119 (2)
C18—C17—H17	121.6 (14)	C44—C46—H46B	117 (2)
C17—C18—C25	121.23 (19)	H46A—C46—H46B	124 (3)
C17—C18—C19	121.57 (16)	C18—C19—C20	113.24 (16)
C19—C18—C25	117.16 (18)	C18—C19—H19A	109.6 (18)
C45—C44—C38	118.15 (15)	C18—C19—H19B	109 (2)
C46—C44—C38	120.39 (17)	C20—C19—H19A	110.7 (16)
C46—C44—C45	121.46 (17)	C20—C19—H19B	110.3 (19)
C16—C21—H21	107.7 (13)	H19A—C19—H19B	103 (3)
C22—C21—C16	111.96 (13)	C14—C15—H15A	113 (2)
C22—C21—C20	114.41 (15)	C14—C15—H15B	108 (2)
C22—C21—H21	107.7 (12)	C14—C15—H15C	117 (3)
C20—C21—C16	108.26 (13)	H15A—C15—H15B	105 (3)
C20—C21—H21	106.5 (13)	H15A—C15—H15C	105 (3)
C23—C22—C21	120.27 (16)	H15B—C15—H15C	107 (3)
C23—C22—C24	121.83 (19)	C34—C35—H35A	110.3 (17)
C24—C22—C21	117.87 (18)	C34—C35—H35B	107.5 (19)
C9—C11—C12	113.57 (12)	C36—C35—C34	112.3 (2)
C9—C11—H11A	109.0 (16)	C36—C35—H35A	110.5 (18)
C9—C11—H11B	110.9 (19)	C36—C35—H35B	112 (2)

C12—C11—H11A	109.1 (14)	H35A—C35—H35B	104 (3)
C12—C11—H11B	110 (2)	C22—C24—H24A	110.2 (18)
H11A—C11—H11B	104 (2)	C22—C24—H24B	111 (2)
C38—C39—H39A	110.1 (14)	C22—C24—H24C	106 (2)
C38—C39—H39B	109.3 (14)	H24A—C24—H24B	113 (3)
C40—C39—C38	110.32 (12)	H24A—C24—H24C	106 (3)
C40—C39—H39A	111.6 (13)	H24B—C24—H24C	110 (3)
C40—C39—H39B	109.4 (14)	C35—C36—H36A	111.6 (18)
H39A—C39—H39B	105.9 (19)	C35—C36—H36B	108 (2)
C30—C32—C33	114.85 (14)	C35—C36—H36C	108 (2)
C30—C32—H32A	112.2 (16)	H36A—C36—H36B	110 (3)
C30—C32—H32B	107.4 (17)	H36A—C36—H36C	109 (3)
C33—C32—H32A	106.6 (15)	H36B—C36—H36C	110 (3)
O2—C7—C6—C5	174.74 (12)	C9—C11—C12—C13	−178.47 (15)
O2—C7—C6—C16	−5.95 (19)	C16—C6—C5—O1	2.37 (18)
O2—C7—C8—C9	−175.02 (12)	C16—C6—C5—C10	−178.04 (12)
O3—C26—C31—C30	−179.81 (12)	C16—C17—C18—C25	−178.89 (16)
O4—C28—C29—C30	−179.15 (13)	C16—C17—C18—C19	−1.5 (3)
O1—C5—C10—C9	−177.67 (13)	C16—C21—C22—C23	109.34 (19)
C7—C6—C5—O1	−178.32 (12)	C16—C21—C22—C24	−69.1 (2)
C7—C6—C5—C10	1.27 (18)	C16—C21—C20—C19	−63.94 (19)
C7—C6—C16—C17	59.51 (16)	C8—C7—C6—C5	−5.08 (19)
C7—C6—C16—C21	−65.22 (16)	C8—C7—C6—C16	174.22 (12)
C27—C28—C29—C30	0.7 (2)	C8—C9—C10—C5	−3.1 (2)
C27—C26—C31—C30	1.3 (2)	C8—C9—C11—C12	−55.2 (2)
C27—C37—C38—C44	−67.06 (16)	C10—C9—C8—C7	−0.6 (2)
C27—C37—C38—C39	167.46 (12)	C10—C9—C11—C12	123.46 (16)
C27—C37—C42—C41	−135.63 (17)	C38—C37—C42—C41	−10.5 (2)
C28—C27—C26—O3	−178.98 (11)	C38—C39—C40—C41	50.55 (19)
C28—C27—C26—C31	−0.02 (18)	C31—C30—C32—C33	118.00 (18)
C28—C27—C37—C38	−70.38 (15)	C42—C41—C40—C39	−16.2 (2)
C28—C27—C37—C42	54.26 (16)	C42—C37—C38—C44	168.94 (13)
C28—C29—C30—C31	0.6 (2)	C42—C37—C38—C39	43.46 (16)

C28—C29—C30—C32	-179.24 (13)	C30—C32—C33—C34	-66.3 (2)
C26—C27—C28—O4	178.87 (12)	C17—C16—C21—C22	176.17 (13)
C26—C27—C28—C29	-0.96 (18)	C17—C16—C21—C20	49.14 (16)
C26—C27—C37—C38	109.37 (14)	C17—C18—C19—C20	-11.9 (3)
C26—C27—C37—C42	-125.99 (13)	C44—C38—C39—C40	169.73 (14)
C26—C31—C30—C29	-1.5 (2)	C21—C16—C17—C18	-18.05 (19)
C26—C31—C30—C32	178.27 (13)	C21—C20—C19—C18	44.8 (2)
C6—C7—C8—C9	4.8 (2)	C22—C21—C20—C19	170.46 (16)
C6—C5—C10—C9	2.8 (2)	C11—C9—C8—C7	178.12 (13)
C6—C16—C17—C18	-143.92 (15)	C11—C9—C10—C5	178.21 (13)
C6—C16—C21—C22	-58.66 (16)	C11—C12—C13—C14	-178.8 (2)
C6—C16—C21—C20	174.31 (13)	C39—C38—C44—C45	57.14 (19)
C5—C6—C16—C17	-121.22 (13)	C39—C38—C44—C46	-121.6 (2)
C5—C6—C16—C21	114.05 (13)	C32—C33—C34—C35	-178.50 (17)
C29—C30—C32—C33	-62.2 (2)	C12—C13—C14—C15	-178.5 (2)
C37—C27—C28—O4	-1.37 (19)	C33—C34—C35—C36	177.4 (2)
C37—C27—C28—C29	178.80 (12)	C40—C41—C42—C37	-4.0 (3)
C37—C27—C26—O3	1.26 (18)	C20—C21—C22—C23	-127.02 (19)
C37—C27—C26—C31	-179.78 (11)	C20—C21—C22—C24	54.5 (2)
C37—C38—C44—C45	-66.00 (18)	C43—C41—C42—C37	176.55 (17)
C37—C38—C44—C46	115.25 (19)	C43—C41—C40—C39	163.23 (17)
C37—C38—C39—C40	-64.94 (16)	C25—C18—C19—C20	165.63 (17)