Supporting Information:

Analogs of the ATP-Sensitive Potassium (K_{ATP}) Channel Opener Cromakalim with in Vivo Ocular Hypotensive Activity

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Synthesis of Compounds (±)-1 and (±)-2

(±)-Dibenzyl ((3*S*,4*R*)-6-cyano-2,2-dimethyl-4-(2-oxopyrrolidin-1-yl)chroman-3-yl) phosphate [(±)-1]. To a stirred suspension of racemic cromakalim (50 mg, 0.175 mmol) in CH_2Cl_2 (5 mL) was added 0.45 M tetrazole in acetonitrile (3.9 mL, 1.76 mmol) followed by dibenzyl *N*,*N*-dimethylphosphoramidite (0.200 mL, 0.75 mmol). The reaction mixture was stirred at rt for 2.5 h. After cooling the mixture in an ice bath, THF (5 mL) was added, followed by dropwise addition of 30% H_2O_2 (1 mL). After stirring for 5 min., saturated aqueous $Na_2S_2O_3$ (30 mL) was added slowly. The mixture was diluted with water (50 mL) and extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Purification by flash chromatography (35% ethyl acetate/hexanes) on silica gel followed by a second flash chromatography (60% ethyl acetate/hexanes) on silica gel furnished 89.8 mg product (94% yield) as a clear colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.47 (dd, J = 8.5, 1.5 Hz, 1H), 7.39-7.31 (m, 10H), 7.26 (s, 1H), 6.90 (d, J = 8.6 Hz, 1H), 5.55 (d, J = 9.9 Hz, 1H), 5.10-4.96 (m, 4H), 4.60 (dd, J = 9.9 Hz, J_{31P} = 10 Hz, 1H), 3.55-3.46 (m, 1H), 2.93-2.83 (m, 1H), 2.51-2.39 (m, 1H), 2.35-2.23 (m, 1H), 2.02-1.89 (m, 2H), 1.51 (s, 3H), 1.28 (s, 3H). LC/MS calculated for $C_{30}H_{31}N_2O_6P+ H^+$, 547.2; observed 547.8.

(±)-Sodium (3*S*,4*R*)-6-cyano-2,2-dimethyl-4-(2-oxopyrrolidin-1-yl)chroman-3-yl phosphate [(±)-2]. To a solution of (±)-**1** (65.5 mg, 0.120 mmol) in dry CH_2Cl_2 (3 mL) was added TMSBr (53 µL, 0.40 mmol) by syringe. After stirring for 6 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by chromatography (0% acetonitrile/20 mM triethylammonium acetate buffer to 100% acetonitrile, C_{18} column) to yield 53.5 mg white solid after lyophilization. To prepare the sodium salt of (±)-**2**, a 1 cm wide column was filled with 12 cm of DOWEX 50W2 (50-100 mesh, strongly acidic) ion exchange resin. The column was prepared by sequentially washing with 1:1 acetonitrile/water, 1M aqueous $NaHCO_3$ (lots of gas evolution), water, and then finally 1:1 acetonitrile/water. The reaction product was dissolved in 1:1 acetonitrile/water and loaded onto the column, which was eluted with 1:1 acetonitrile/water. The product containing fractions were lyophilized to furnish (±)-**2** as a white solid (40.9

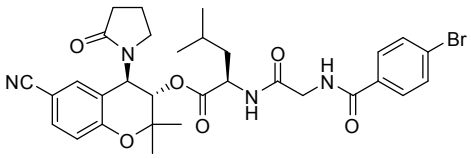
mg, 83% yield). ^{1}H NMR (400 MHz, D_2O): 7.64 (dd, J = 8.6, 1.8 Hz, 1H), 7.47 (bs, 1H), 7.01 (d, J = 8.6 Hz, 1H), 5.27 (d, J = 9.8 Hz, 1H), 4.46 (dd, J = 10.0, J_{31P} = 10 Hz, 1H), 3.68-3.56 (m, 1H), 3.21-3.07 (m, 1H), 2.68-2.52 (m, 2H), 2.22-1.99 (m, 2H), 1.59 (s, 3H), 1.32 (s, 3H).

Sodium (3*R*,4*S*)-6-cyano-2,2-dimethyl-4-(2-oxopyrrolidin-1-yl)chroman-3-yl phosphate [(-)-2]. Compound (-)-**2** was synthesized from dexcromakalim using the same sequence of synthetic steps used to synthesize (±)-**2** from cromakalim. ^{1}H NMR (400 MHz, D_2O): 7.64 (dd, J = 8.6, 1.7 Hz, 1H), 7.45 (bs, 1H), 7.00 (d, J = 8.6 Hz, 1H), 5.23 (d, J = 10.2 Hz, 1H), 4.42 (dd, J = 10, J_{31P} = 10 Hz, 1H), 3.76-3.65 (m, 1H), 3.19-3.06 (m, 1H), 2.73-2.50 (m, 2H), 2.23-1.98 (m, 2H), 1.60 (s, 3H), 1.32 (s, 3H). $[\alpha]_D^{22}$ -24.6 (*c* 0.35, H_2O).

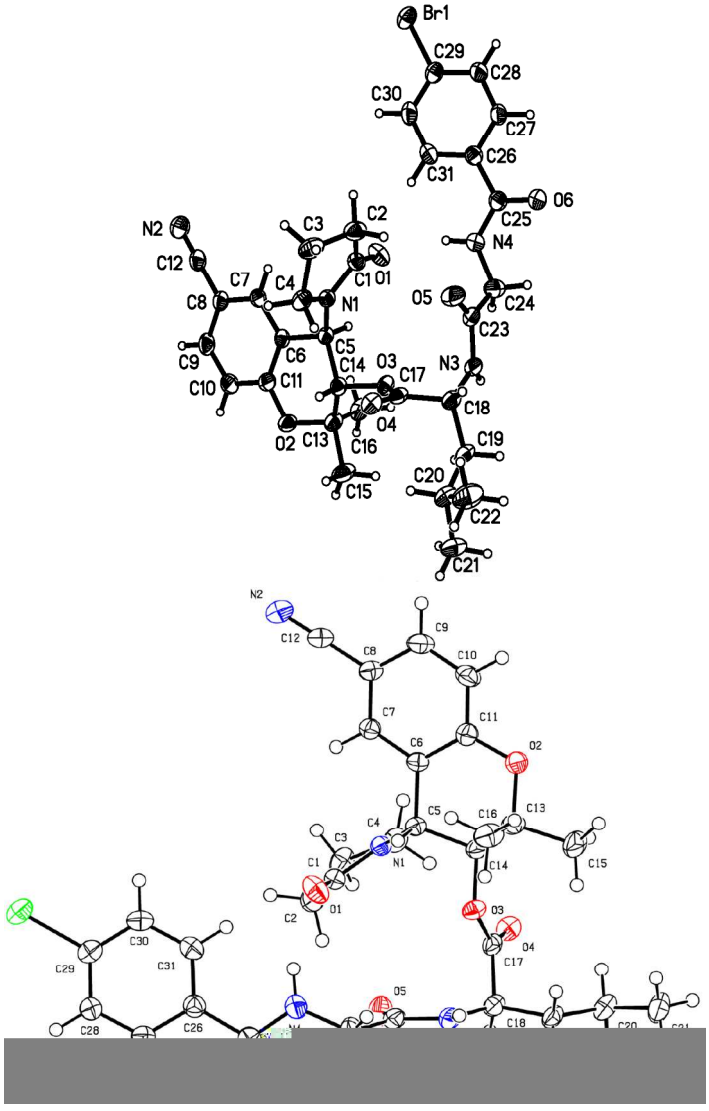
Table S1, Effect of Compounds (3*S*,4*R*)-**2**, (±)-**2**, and (±)-**4** on IOP in Mice.

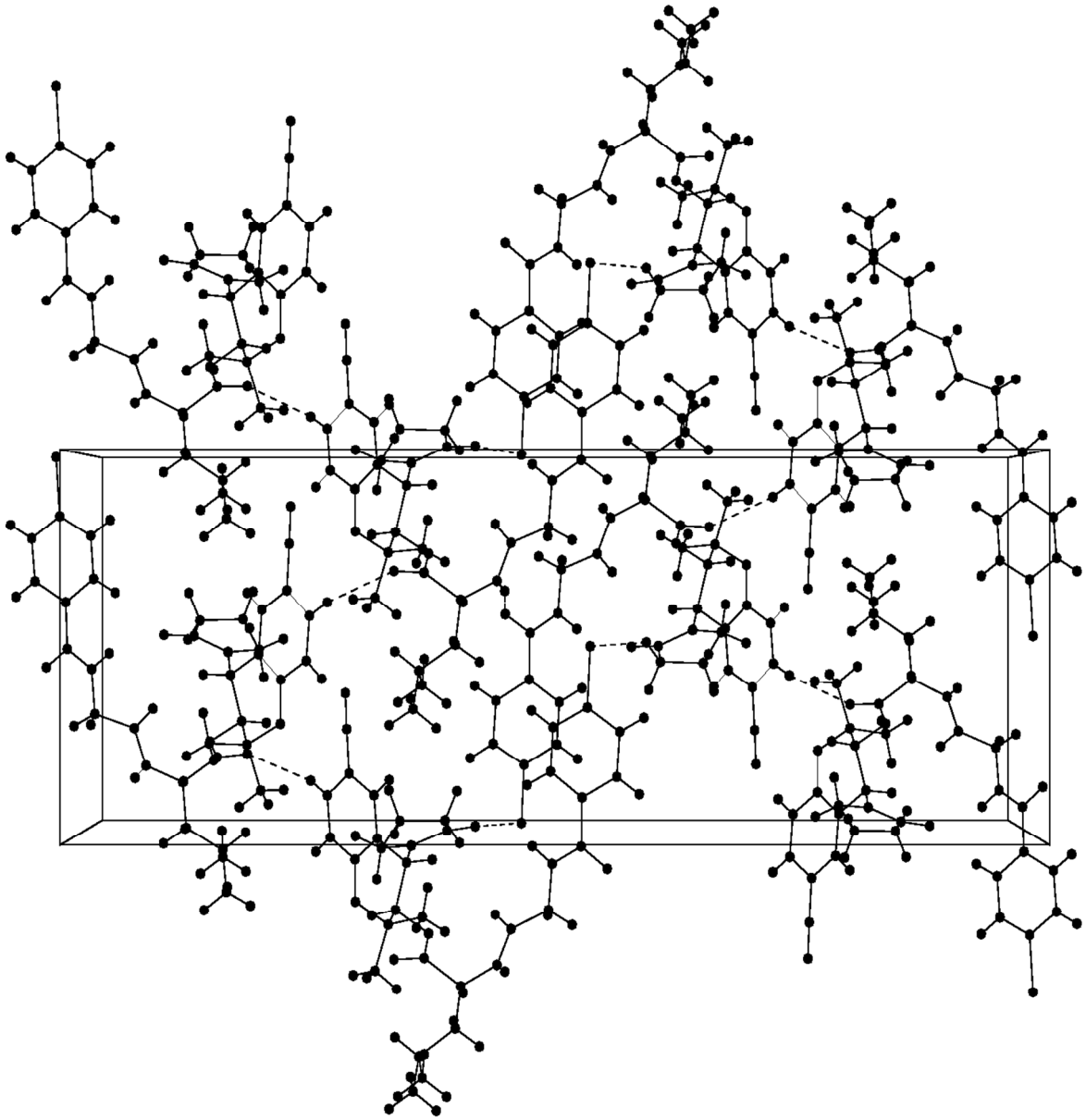
	IOP (mm Hg)			
	Right eye (vehicle control)		Left eye (treated)	
Prodrugs	Baseline	After vehicle treatment	Baseline	After prodrug treatment
(3*S*,4*R*)-**2**	15.77 ± 0.38	16.25 ± 0.19	15.81 ± 0.38	13.11 ± 0.5
(±)-**4**	16.24 ± 0.14	16.41 ± 0.12	16.20 ± 0.43	14.60 ± 0.51
(±)-**2**	16.38 ± 0.30	16.63 ± 0.06	16.53 ± 0.21	14.13 ± 0.22

Crystal Structure Report for Compound **14**



$C_{31}\ H_{35}\ Br\ N_4\ O_6$





Data collection

A crystal (approximate dimensions 0.180 x 0.180 x 0.045 mm^3) was placed onto the tip of a 0.1 mm diameter glass capillary and mounted on a Bruker Photon-100 CMOS diffractometer for a data collection at 123(2) K.[1] A preliminary set of cell constants was calculated from reflections harvested from three sets of frames. These initial sets of frames were oriented such that orthogonal wedges of reciprocal space were surveyed. This produced an initial orientation matrix determined from 231 reflections. The data collection was carried out using CuKα radiation (parabolic mirrors) with a frame time of 10 seconds and a detector distance of 4.0 cm. A strategy program was used to assure complete coverage of all unique data to a resolution of 0.83 Å. All major sections of frames were collected with 0.80º steps in ω or ϕ at different detector positions in 2θ. The intensity data were corrected for absorption and decay (SADABS).[2] Final cell constants were calculated from 2710 strong reflections from the actual data collection after integration (SAINT).[3] Please refer to Table 1 for additional crystal and refinement information.

Structure solution and refinement

The structure was solved using SHELXS-97 (Sheldrick 2008)[4] and refined using SHELXL-2013 (Sheldrick 2013).[4] The space group $P2_12_12_1$ was determined based on systematic absences and intensity statistics. A direct-methods solution was calculated which provided most non-hydrogen atoms from the E-map. Full-matrix least squares / difference Fourier cycles were performed which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters. The final full matrix least squares refinement converged to $R1 = 0.0240$ and $wR2 = 0.0572$ (F^2, obs. data).

Structure description

The structure is the one suggested. Stereochemistry found: C5=R, C14=S, and C18=R. See the CheckCIF report for additional details.

Data collection and structure solution were conducted at the X-Ray Crystallographic Laboratory, 192 Kolthoff Hall, Department of Chemistry, University of Minnesota. All calculations were performed using Pentium computers using the current SHELXTL suite of programs. All publications arising from this report MUST either 1) include Victor G. Young, Jr. as a coauthor or 2) acknowledge Victor G. Young, Jr. and the X-Ray Crystallographic Laboratory. **The Bruker-AXS D8 Venture diffractometer was purchased through a grant from NSF/MRI (#1224900) and the University of Minnesota.**

[1] APEX2, Bruker Analytical X-ray Systems, Madison, WI (2004).

[2] SADABS, Bruker Analytical X-ray Systems, Madison, WI (2004).

[3] SAINT Bruker Analytical X-ray Systems, Madison, WI (2004).

[4] SHELXTL 2013, Bruker Analytical X-Ray Systems, Madison, WI (2013); G. M. Sheldrick, *Acta Cryst.* **A64**, 112-122 (2008).

Some equations of interest:

$$R_{int} = \Sigma\ |F_o^2 - < F_o^2 >| \ / \ \Sigma |F_o^2|$$

$$R_1 = \Sigma ||F_o| - |F_c|| \ / \ \Sigma |F_o|$$

$$wR2 = [\Sigma [w(F_o^2 - F_c^2)^2] \ / \ \Sigma\ [w(F_o^2)^2]]^{1/2}$$

$$\text{where } w = q \ / \ [\sigma^2 (F_o^2) + (a*P)^2 + b*P + d + e*\sin(\theta)]$$

$$\text{GooF} = S = [\Sigma [w(F_o^2 - F_c^2)^2] \ / \ (n-p)]^{1/2}$$

Table 1. Crystal data and structure refinement for **14**.

Identification code	14030a	
Empirical formula	C_{31} H_{35} Br N_4 O_6	
Formula weight	639.54	
Temperature	123(2) K	
Wavelength	1.54178 Å	
Crystal system	orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.9252(7) Å	α = 90°
	b = 11.9152(9) Å	β = 90°
	c = 32.299(3) Å	γ = 90°
Volume	3050.0(4) Å^3	
Z	4	
Density (calculated)	1.393 Mg/m^3	
Absorption coefficient	2.246 mm^{-1}	
F(000)	1328	
Crystal color, morphology	purple, plate	
Crystal size	0.180 x 0.180 x 0.045 mm^3	
Theta range for data collection	2.736 to 68.409°	
Index ranges	$-9 \le h \le 8$, $-14 \le k \le 14$, $-38 \le l \le 38$	
Reflections collected	36670	
Independent reflections	5592 [R(int) = 0.0374]	
Observed reflections	5248	
Completeness to theta = 67.679°	99.9%	
Absorption correction	multi-scan	
Max. and min. transmission	0.7531 and 0.5939	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5592 / 2 / 389	
Goodness-of-fit on F^2	1.066	
Final R indices [I>2sigma(I)]	R1 = 0.0240, wR2 = 0.0572	
R indices (all data)	R1 = 0.0269, wR2 = 0.0585	
Absolute structure parameter	-0.032(5)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.196 and -0.253 e.Å^{-3}	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **14**. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
Br1	3103(1)	45(1)	-365(1)	39(1)
O1	4316(2)	4800(2)	839(1)	42(1)
O2	7415(2)	7040(2)	2158(1)	34(1)
O3	4396(2)	7635(1)	1330(1)	26(1)
O4	1975(2)	8078(1)	1658(1)	31(1)
O5	1412(3)	6873(2)	612(1)	41(1)
O6	1748(3)	5729(2)	-535(1)	38(1)
N1	3674(2)	5270(2)	1502(1)	23(1)
N2	7457(4)	1412(2)	2266(1)	49(1)
N3	3208(1)	8338(1)	604(1)	28(1)
N4	3428(1)	5728(1)	31(1)	36(1)
C1	3301(3)	4847(2)	1126(1)	29(1)
C2	1494(4)	4466(2)	1128(1)	38(1)
C3	1004(3)	4444(2)	1582(1)	38(1)
C4	2250(3)	5239(2)	1793(1)	31(1)
C5	5271(3)	5829(2)	1575(1)	22(1)
C6	6337(3)	5262(2)	1902(1)	23(1)
C7	6369(3)	4105(2)	1938(1)	25(1)
C8	7410(3)	3583(2)	2225(1)	29(1)
C9	8448(4)	4228(2)	2483(1)	36(1)
C10	8428(4)	5376(2)	2449(1)	36(1)
C11	7374(3)	5897(2)	2161(1)	30(1)
C12	7433(4)	2381(2)	2250(1)	35(1)
C13	6749(4)	7607(2)	1792(1)	32(1)
C14	5053(3)	7064(2)	1688(1)	25(1)
C15	6513(4)	8818(2)	1930(1)	44(1)
C16	8019(4)	7517(2)	1441(1)	40(1)
C17	2877(3)	8125(2)	1359(1)	26(1)
C18	2480(3)	8820(2)	975(1)	28(1)
C19	3197(3)	10004(2)	1038(1)	30(1)
C20	2521(4)	10658(2)	1408(1)	36(1)

C21	3607(4)	11695(2)	1482(1)	44(1)
C22	669(4)	10977(3)	1351(1)	52(1)
C23	2611(3)	7355(2)	456(1)	31(1)
C24	3505(5)	6935(2)	69(1)	42(1)
C25	2557(3)	5214(2)	-270(1)	30(1)
C26	2684(3)	3951(2)	-280(1)	29(1)
C27	2180(3)	3393(2)	-637(1)	32(1)
C28	2282(4)	2231(2)	-668(1)	33(1)
C29	2890(3)	1629(2)	-336(1)	31(1)
C30	3409(4)	2162(2)	20(1)	42(1)
C31	3303(4)	3313(2)	47(1)	41(1)

Table 3. Bond lengths [Å] and angles [°] for **14**.

Br1-C29	1.898(3)	C7-H7A	0.9500
O1-C1	1.229(3)	C8-C9	1.400(4)
O2-C11	1.362(3)	C8-C12	1.435(4)
O2-C13	1.459(3)	C9-C10	1.372(4)
O3-C17	1.341(3)	C9-H9A	0.9500
O3-C14	1.440(3)	C10-C11	1.398(4)
O4-C17	1.204(3)	C10-H10A	0.9500
O5-C23	1.219(3)	C13-C16	1.519(4)
O6-C25	1.233(3)	C13-C15	1.521(4)
N1-C1	1.348(3)	C13-C14	1.529(4)
N1-C5	1.450(3)	C14-H14A	1.0000
N1-C4	1.470(3)	C15-H15A	0.9800
N2-C12	1.155(4)	C15-H15B	0.9800
N3-C23	1.350(2)	C15-H15C	0.9800
N3-C18	1.448(2)	C16-H16A	0.9800
N3-H3A	0.91000(7)	C16-H16B	0.9800
N4-C25	1.339(2)	C16-H16C	0.9800
N4-C24	1.445(3)	C17-C18	1.523(3)
N4-H4A	0.91000(5)	C18-C19	1.535(3)
C1-C2	1.502(4)	C18-H18A	1.0000
C2-C3	1.518(4)	C19-C20	1.524(4)
C2-H2A	0.9900	C19-H19A	0.9900
C2-H2B	0.9900	C19-H19B	0.9900
C3-C4	1.528(4)	C20-C21	1.525(4)
C3-H3B	0.9900	C20-C22	1.527(4)
C3-H3C	0.9900	C20-H20A	1.0000
C4-H4B	0.9900	C21-H21A	0.9800
C4-H4C	0.9900	C21-H21B	0.9800
C5-C6	1.511(3)	C21-H21C	0.9800
C5-C14	1.526(3)	C22-H22A	0.9800
C5-H5A	1.0000	C22-H22B	0.9800
C6-C7	1.383(4)	C22-H22C	0.9800
C6-C11	1.395(3)	C23-C24	1.522(4)
C7-C8	1.389(3)	C24-H24A	0.9900

C24-H24B	0.9900	C28-C29	1.378(4)
C25-C26	1.508(3)	C28-H28A	0.9500
C26-C27	1.389(3)	C29-C30	1.376(4)
C26-C31	1.391(4)	C30-C31	1.376(4)
C27-C28	1.390(4)	C30-H30A	0.9500
C27-H27A	0.9500	C31-H31A	0.9500

C11-O2-C13	117.40(18)	N1-C4-H4C	111.2
C17-O3-C14	118.36(19)	C3-C4-H4C	111.2
C1-N1-C5	120.6(2)	H4B-C4-H4C	109.1
C1-N1-C4	113.5(2)	N1-C5-C6	113.36(19)
C5-N1-C4	125.29(19)	N1-C5-C14	112.55(19)
C23-N3-C18	119.82(15)	C6-C5-C14	109.10(19)
C23-N3-H3A	121.71(12)	N1-C5-H5A	107.2
C18-N3-H3A	116.06(10)	C6-C5-H5A	107.2
C25-N4-C24	122.59(16)	C14-C5-H5A	107.2
C25-N4-H4A	118.13(11)	C7-C6-C11	118.6(2)
C24-N4-H4A	118.75(12)	C7-C6-C5	120.9(2)
O1-C1-N1	123.6(2)	C11-C6-C5	120.4(2)
O1-C1-C2	127.9(2)	C6-C7-C8	120.9(2)
N1-C1-C2	108.5(2)	C6-C7-H7A	119.5
C1-C2-C3	104.7(2)	C8-C7-H7A	119.5
C1-C2-H2A	110.8	C7-C8-C9	120.0(3)
C3-C2-H2A	110.8	C7-C8-C12	119.6(2)
C1-C2-H2B	110.8	C9-C8-C12	120.4(2)
C3-C2-H2B	110.8	C10-C9-C8	119.6(3)
H2A-C2-H2B	108.9	C10-C9-H9A	120.2
C2-C3-C4	104.8(2)	C8-C9-H9A	120.2
C2-C3-H3B	110.8	C9-C10-C11	120.1(3)
C4-C3-H3B	110.8	C9-C10-H10A	119.9
C2-C3-H3C	110.8	C11-C10-H10A	119.9
C4-C3-H3C	110.8	O2-C11-C6	123.5(2)
H3B-C3-H3C	108.9	O2-C11-C10	115.8(2)
N1-C4-C3	103.0(2)	C6-C11-C10	120.7(3)
N1-C4-H4B	111.2	N2-C12-C8	179.1(3)
C3-C4-H4B	111.2	O2-C13-C16	109.3(2)

O2-C13-C15	104.3(2)	C18-C19-H19B	108.2
C16-C13-C15	111.5(2)	H19A-C19-H19B	107.3
O2-C13-C14	107.5(2)	C19-C20-C21	109.8(2)
C16-C13-C14	112.9(2)	C19-C20-C22	111.7(3)
C15-C13-C14	110.9(2)	C21-C20-C22	111.1(2)
O3-C14-C5	107.72(18)	C19-C20-H20A	108.0
O3-C14-C13	107.14(19)	C21-C20-H20A	108.0
C5-C14-C13	111.2(2)	C22-C20-H20A	108.0
O3-C14-H14A	110.2	C20-C21-H21A	109.5
C5-C14-H14A	110.2	C20-C21-H21B	109.5
C13-C14-H14A	110.2	H21A-C21-H21B	109.5
C13-C15-H15A	109.5	C20-C21-H21C	109.5
C13-C15-H15B	109.5	H21A-C21-H21C	109.5
H15A-C15-H15B	109.5	H21B-C21-H21C	109.5
C13-C15-H15C	109.5	C20-C22-H22A	109.5
H15A-C15-H15C	109.5	C20-C22-H22B	109.5
H15B-C15-H15C	109.5	H22A-C22-H22B	109.5
C13-C16-H16A	109.5	C20-C22-H22C	109.5
C13-C16-H16B	109.5	H22A-C22-H22C	109.5
H16A-C16-H16B	109.5	H22B-C22-H22C	109.5
C13-C16-H16C	109.5	O5-C23-N3	122.4(2)
H16A-C16-H16C	109.5	O5-C23-C24	123.1(2)
H16B-C16-H16C	109.5	N3-C23-C24	114.4(2)
O4-C17-O3	124.6(2)	N4-C24-C23	112.2(2)
O4-C17-C18	123.8(2)	N4-C24-H24A	109.2
O3-C17-C18	111.4(2)	C23-C24-H24A	109.2
N3-C18-C17	112.05(18)	N4-C24-H24B	109.2
N3-C18-C19	109.10(18)	C23-C24-H24B	109.2
C17-C18-C19	108.34(19)	H24A-C24-H24B	107.9
N3-C18-H18A	109.1	O6-C25-N4	122.9(2)
C17-C18-H18A	109.1	O6-C25-C26	121.1(2)
C19-C18-H18A	109.1	N4-C25-C26	115.9(2)
C20-C19-C18	116.4(2)	C27-C26-C31	117.9(2)
C20-C19-H19A	108.2	C27-C26-C25	118.5(2)
C18-C19-H19A	108.2	C31-C26-C25	123.6(2)
C20-C19-H19B	108.2	C28-C27-C26	121.4(2)

C28-C27-H27A	119.3	C28-C29-Br1	120.7(2)
C26-C27-H27A	119.3	C29-C30-C31	119.6(2)
C29-C28-C27	118.8(2)	C29-C30-H30A	120.2
C29-C28-H28A	120.6	C31-C30-H30A	120.2
C27-C28-H28A	120.6	C30-C31-C26	121.3(2)
C30-C29-C28	121.0(2)	C30-C31-H31A	119.4
C30-C29-Br1	118.27(19)	C26-C31-H31A	119.4

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **14**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U_{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U_{12}\ ]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br1	45(1)	28(1)	44(1)	6(1)	4(1)	5(1)
O1	43(1)	53(1)	29(1)	-9(1)	-2(1)	-2(1)
O2	38(1)	25(1)	41(1)	2(1)	-15(1)	-5(1)
O3	21(1)	24(1)	32(1)	5(1)	-1(1)	2(1)
O4	25(1)	31(1)	38(1)	3(1)	3(1)	0(1)
O5	42(1)	32(1)	50(1)	-3(1)	1(1)	-11(1)
O6	47(1)	29(1)	37(1)	2(1)	-10(1)	2(1)
N1	21(1)	22(1)	26(1)	1(1)	-2(1)	-2(1)
N2	65(2)	34(1)	48(1)	7(1)	-16(1)	6(1)
N3	32(1)	22(1)	32(1)	2(1)	-3(1)	-4(1)
N4	49(2)	29(1)	31(1)	-1(1)	-7(1)	-3(1)
C1	32(1)	26(1)	30(1)	-2(1)	-8(1)	2(1)
C2	34(2)	30(1)	51(2)	-1(1)	-15(1)	-4(1)
C3	27(2)	29(1)	59(2)	-2(1)	2(1)	-3(1)
C4	26(1)	29(1)	36(1)	4(1)	6(1)	-5(1)
C5	19(1)	22(1)	25(1)	2(1)	-1(1)	-1(1)
C6	21(1)	26(1)	23(1)	3(1)	-1(1)	0(1)
C7	24(1)	27(1)	24(1)	0(1)	-1(1)	1(1)
C8	30(1)	29(1)	28(1)	6(1)	-2(1)	2(1)
C9	35(2)	39(2)	32(1)	9(1)	-9(1)	1(1)
C10	34(2)	38(2)	34(1)	2(1)	-13(1)	-4(1)
C11	31(1)	27(1)	31(1)	1(1)	-2(1)	-1(1)
C12	38(2)	35(2)	31(1)	6(1)	-8(1)	6(1)
C13	29(1)	25(1)	41(1)	5(1)	-11(1)	-4(1)
C14	23(1)	24(1)	28(1)	2(1)	-3(1)	0(1)
C15	44(2)	25(1)	64(2)	0(1)	-18(2)	-7(1)
C16	25(1)	39(2)	55(2)	13(1)	-6(1)	-8(1)
C17	24(1)	18(1)	36(1)	0(1)	-4(1)	-4(1)
C18	26(1)	22(1)	36(1)	2(1)	-3(1)	1(1)
C19	32(1)	18(1)	40(1)	3(1)	-2(1)	-1(1)
C20	38(2)	23(1)	46(2)	1(1)	2(1)	4(1)

C21	46(2)	26(1)	59(2)	-9(1)	-2(2)	2(1)
C22	39(2)	38(2)	81(2)	-7(2)	4(2)	5(1)
C23	37(2)	23(1)	33(1)	5(1)	-8(1)	-3(1)
C24	59(2)	32(1)	36(1)	-4(1)	0(1)	-13(1)
C25	31(1)	32(1)	28(1)	1(1)	1(1)	-4(1)
C26	29(1)	30(1)	28(1)	-1(1)	0(1)	1(1)
C27	36(2)	32(1)	27(1)	4(1)	-4(1)	4(1)
C28	42(2)	30(1)	29(1)	-2(1)	-4(1)	3(1)
C29	31(1)	29(1)	34(1)	3(1)	4(1)	3(1)
C30	57(2)	37(2)	32(1)	7(1)	-11(1)	6(1)
C31	57(2)	37(2)	29(1)	-1(1)	-11(1)	1(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **14**.

	x	y	z	U(eq)
H3A	4235(1)	8609(1)	528(1)	34
H4A	3866(1)	5298(1)	237(1)	44
H2A	1385	3711	1003	46
H2B	773	4997	972	46
H3B	1104	3676	1696	46
H3C	-170	4708	1620	46
H4B	1753	5994	1831	37
H4C	2605	4944	2066	37
H5A	5921	5801	1310	27
H7A	5669	3662	1764	30
H9A	9162	3873	2679	43
H10A	9133	5817	2623	43
H14A	4257	7143	1927	30
H15A	7583	9110	2036	67
H15B	5654	8851	2147	67
H15C	6149	9272	1693	67
H16A	9063	7903	1520	60
H16B	7551	7865	1192	60
H16C	8262	6724	1386	60
H18A	1228	8869	941	34
H19A	4437	9942	1067	36
H19B	2970	10446	785	36
H20A	2607	10166	1658	43
H21A	4780	11466	1528	66
H21B	3193	12097	1727	66
H21C	3545	12189	1240	66
H22A	281	11400	1593	79
H22B	-10	10294	1321	79
H22C	548	11441	1102	79
H24A	2978	7281	-178	51

H24B	4701	7173	78	51
H27A	1757	3813	-864	38
H28A	1938	1859	-914	40
H30A	3839	1738	246	50
H31A	3659	3678	293	49

Table 6. Torsion angles [°] for **14**.

C5-N1-C1-O1	7.6(4)	C11-O2-C13-C15	164.6(2)
C4-N1-C1-O1	179.7(2)	C11-O2-C13-C14	46.8(3)
C5-N1-C1-C2	-172.3(2)	C17-O3-C14-C5	118.0(2)
C4-N1-C1-C2	-0.2(3)	C17-O3-C14-C13	-122.3(2)
O1-C1-C2-C3	165.9(3)	N1-C5-C14-O3	-66.8(2)
N1-C1-C2-C3	-14.2(3)	C6-C5-C14-O3	166.44(19)
C1-C2-C3-C4	22.3(3)	N1-C5-C14-C13	176.08(19)
C1-N1-C4-C3	14.3(3)	C6-C5-C14-C13	49.3(3)
C5-N1-C4-C3	-174.0(2)	O2-C13-C14-O3	179.42(19)
C2-C3-C4-N1	-22.0(3)	C16-C13-C14-O3	-60.0(3)
C1-N1-C5-C6	-119.0(2)	C15-C13-C14-O3	66.0(3)
C4-N1-C5-C6	69.9(3)	O2-C13-C14-C5	-63.1(3)
C1-N1-C5-C14	116.6(2)	C16-C13-C14-C5	57.5(3)
C4-N1-C5-C14	-54.5(3)	C15-C13-C14-C5	-176.6(2)
N1-C5-C6-C7	36.6(3)	C14-O3-C17-O4	-3.7(3)
C14-C5-C6-C7	162.9(2)	C14-O3-C17-C18	172.32(19)
N1-C5-C6-C11	-146.5(2)	C23-N3-C18-C17	68.3(2)
C14-C5-C6-C11	-20.2(3)	C23-N3-C18-C19	-171.72(17)
C11-C6-C7-C8	-0.1(4)	O4-C17-C18-N3	-151.0(2)
C5-C6-C7-C8	176.9(2)	O3-C17-C18-N3	32.9(3)
C6-C7-C8-C9	-0.1(4)	O4-C17-C18-C19	88.5(3)
C6-C7-C8-C12	-179.1(2)	O3-C17-C18-C19	-87.6(2)
C7-C8-C9-C10	0.0(4)	N3-C18-C19-C20	177.97(19)
C12-C8-C9-C10	179.0(3)	C17-C18-C19-C20	-59.8(3)
C8-C9-C10-C11	0.2(5)	C18-C19-C20-C21	167.9(2)
C13-O2-C11-C6	-18.8(4)	C18-C19-C20-C22	-68.3(3)
C13-O2-C11-C10	162.3(2)	C18-N3-C23-O5	3.7(3)
C7-C6-C11-O2	-178.5(2)	C18-N3-C23-C24	-179.1(2)
C5-C6-C11-O2	4.5(4)	C25-N4-C24-C23	112.8(2)
C7-C6-C11-C10	0.3(4)	O5-C23-C24-N4	-29.7(4)
C5-C6-C11-C10	-176.7(2)	N3-C23-C24-N4	153.1(2)
C9-C10-C11-O2	178.5(3)	C24-N4-C25-O6	-0.4(3)
C9-C10-C11-C6	-0.4(4)	C24-N4-C25-C26	176.8(2)
C11-O2-C13-C16	-76.1(3)	O6-C25-C26-C27	13.2(4)

N4-C25-C26-C27	-164.0(2)	C27-C28-C29-Br1	-178.6(2)
O6-C25-C26-C31	-167.8(3)	C28-C29-C30-C31	0.8(5)
N4-C25-C26-C31	15.0(4)	Br1-C29-C30-C31	178.6(3)
C31-C26-C27-C28	0.2(4)	C29-C30-C31-C26	-0.2(5)
C25-C26-C27-C28	179.3(3)	C27-C26-C31-C30	-0.3(5)
C26-C27-C28-C29	0.3(4)	C25-C26-C31-C30	-179.3(3)
C27-C28-C29-C30	-0.8(4)		

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for **14** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N3-H3A...O6#1	0.9100(1)	2.143(2)	3.027(2)	163.66(5)
N4-H4A...O1	0.9100(1)	2.0612(18)	2.9195(18)	156.75(6)

Symmetry transformations used to generate equivalent atoms:

#1 x+1/2,-y+3/2,-z