Supplementary Material (ESI) for Chemical Communications

Supporting Information

An efficient asymmetric synthesis of the potent β-blocker ICI-118,551 allows the determination of enantiomer dependency on biological activity

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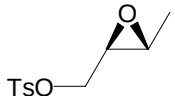
^{1}H and ^{13}C NMR spectra were recorded at room temperature on a Bruker Avance 500 instrument operating at a frequency of 500 MHz for ^{1}H and 125 MHz for ^{13}C. Coupling constants are quoted in Hz to one decimal place. Infra-red spectra were run on a PerkinElmer Spectrum 100 FT-IR spectrometer operating in ATR mode with frequencies given in reciprocal centimeters (cm^{-1}). Mass spectra and high resolution mass data were recorded on a VG70-SE mass spectrometer (EI mode and CI mode). Melting points were taken on a Gallenkamp heating block and are uncorrected. Optical rotation measurements were carried out using a PerkinElmer 343 polarimeter with a cell length of 10 cm. Chromatography (HPLC) was measured using U.V detector type prostar/dynamic system24 (2 Volts) absorbance 218 nm. The analytes were separated and determined by using a Chirapak OD columns. (Daicel; Chiral Technologies Europe, France) 25 cm × 0.46 cm. The polar stationary phase (isopropanol) and the nonpolar mobile phase (hexane) was used as indicated.

(2R,3R)-toluen-4-sulphonic acid-3-methyloxyranylmethyl ester **2**[1]

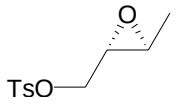


To a flask containing crushed and flame-dried molecular sieves, DCM (30 mL) was added and the solution cooled to -20 °C. Crotyl alcohol (1.00 g, 13.9 mmol), D-(-)-DIPT (0.194 g, 0.83 mmol) and $Ti(O^{i}Pr)_4$ (0.197 g, 0.69 mmol) were added sequentially and stirred for 15 min, followed by the dropwise addition of tert-butylperoxide (5.5 M in decane, 5.04 mL, 27.7 mmol) and the reaction mixture was left to stir for 18 h at -20 °C. The reaction was quenched by the dropwise addition of trimethylphosphite (2.44 mL, 20.8 mmol), followed by the addition of triethylamine (2.8 mL, 20.8 mmol) and dimethylaminopyridine (0.150 g, 1.23 mmol). Tosyl chloride (2.64 g, 13.9 mmol) was dissolved in DCM (30 mL) and then added drop-wise to the reaction mixture. The temperature was raised to -10 °C and stirred for 18 h. The solution was filtered through celite, washed with 10% aqueous tartaric acid (50 mL), saturated aqueous $NaHCO_3$ solution (50 mL) and saturated brine solution (50 mL). The organic layer was removed *in vacuo* and the crude mixture purified by column chromatography (30% ethyl acetate in petroleum ether) to give the desired product **2** as a white solid (1.70 g, 50%).

Mp = 56-58 °C (lit[1] 61-62 °C). 1H NMR (500 MHz, $CDCl_3$) δ 1.29 (d, J = 5.2, 3H, $CHCH_3$), 2.45 (s, 3H, $ArCH_3$), 2.74 - 2.98 (m, 2H, $CHCH_2$ and $CHCH_3$), 3.98 (dd, J = 5.7, 11.3, 1H,

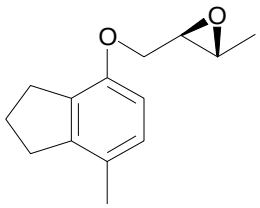
OCH*H*CH), 4.17 (dd, *J* = 3.9, 11.3, 1H, OC*H*HCH), 7.35 (d, *J* = 8.5, 2H, Ar*H*), 7.80 (d, *J* = 8.3, 2H, Ar*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.1 (CH_3), 21.7 (CH_3), 52.9 (CH), 55.6 (CH), 70.1 (CH_2), 128.0 (CH), 130.0 (CH), 132.8 (C), 145.1 (C). CI MS (relative intensity): 243, (M+1, 82%), 225 (26%), 155 (100%), 91 (38%). IR: 2928.5, 1598, 1360, 1176, 1097. $[\alpha]^{20}_D$= +26.7 (*c* 3.29, $CHCl_3$ (lit $[\alpha]^{25}_D$ +34.2)[1]).

(2S,3S)-toluen-4-sulphonic acid-3-methyloxyranylmethyl ester **4**[1]



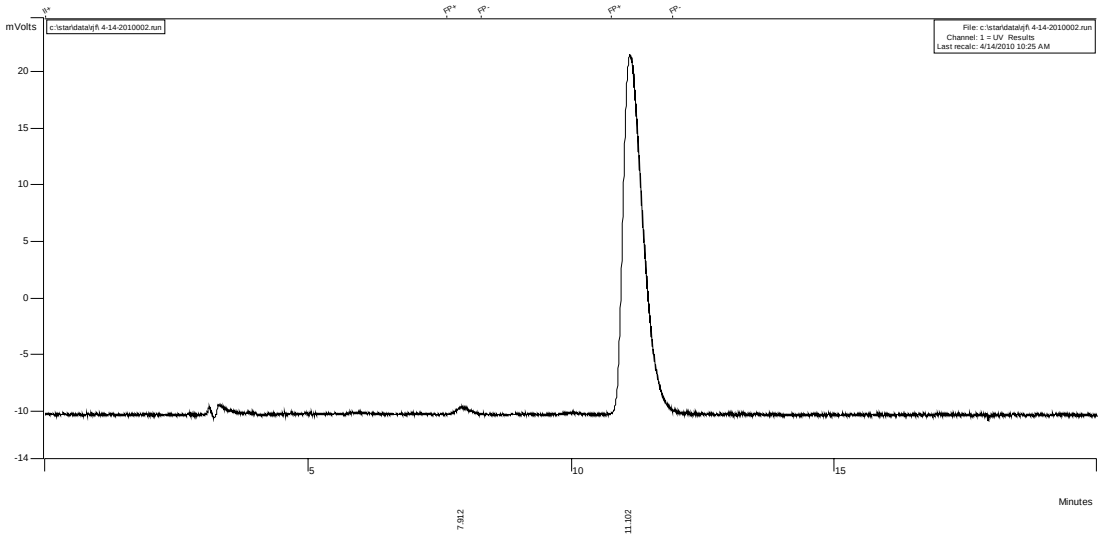
Identical procedure to that described above for the synthesis of the (R,R)-enantiomer **2** was followed, using L-(+)-DIPT, to give the desired product **4** as a white solid (1.40 g, 41%). Data matched that for enantiomer **2**, except; $[\alpha]^{20}_D$ = -25.0 (*c* 3.29, $CHCl_3$).

*(2R,3R)-2-methyl-3-(7-methylindan-4-yloxymethyl)-oxirane **3***

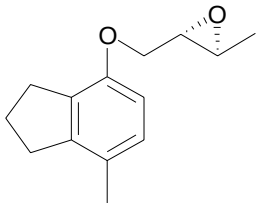


7-methyl-4-indanol **1** (0.89 g, 6.0 mmol) was dissolved in DMF (15 mL) and Cs_2CO_3 (2.93 g, 0.9 mmol) added, followed by the addition of tosylated epoxide **2** (1.6 g, 6.6 mmol). The reaction mixture was stirred under argon at 50 °C for 2.5 hrs, and then partitioned between water (100 mL) and diethyl ether (100 mL). The ether layer was retained, and the water layer washed again with diethyl ether (100 mL). The ether layers were combined, washed with lithium chloride solution (10% w/v, 3 X 100 mL), dried ($MgSO_4$) then filtered and the solvent removed *in vacuo*. The crude product was purified by column chromatography (10% ethyl acetate in petroleum ether, column prewashed with this solution including 1% NEt_3) followed by recrystallisation from ethyl acetate to give **3** as white needles (1.2 g, 92%).

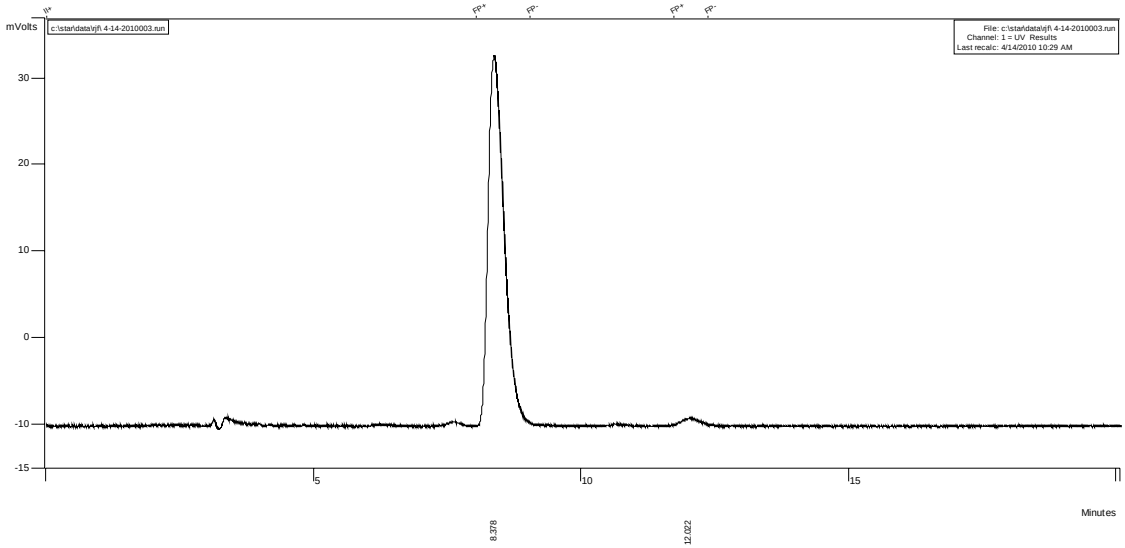
Mp = 62-63 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (d, *J* = 5.1, 3H, CHC*H*$_3$), 2.07 (appt. quintet, *J* = 7.5, 2H, $CH_2CH_2CH_2$), 2.19 (s, 3H ArC*H*$_3$), 2.83 (t, *J* = 7.4, 2H, ArC*H*$_2$CH$_2$), 2.90 (t, *J* = 7.5, 2H, ArC*H*$_2$CH$_2$), 3.05 (m, 2H, C*H*CH$_2$ and C*H*CH$_3$), 3.99 (dd, *J* = 5.1, 11.5, 1H, OC*H*HCH), 4.14 (dd, *J* = 8.8, 11.5, 1H, OCH*H*CH), 6.57 (d, *J* = 8.1, 1H Ar*H*), 6.9 (d, *J* = 8.1, 1H, Ar*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.4 (CH_3), 18.5 (CH_3), 24.6 (CH_2), 29.8 (CH_2), 32.0 (CH_2), 52.7 (CH), 57.4 (CH), 68.5 (CH_2), 109.6 (CH), 126.6 (C), 127.9 (CH), 131.9 (C), 145.1 (C), 153.2 (C). EI MS (relative intensity): 218 (M^+, 100%), 201 (63%), 175 (83%), 148 (91%) 91 (20%). IR: 2997, 2932, 1609, 1501, 1458. $[\alpha]^{20}_D$ = +17.3 (*c* 3.15, $CHCl_3$). Chiral Phase HPLC (99:1 hexane:isopropanol eluent, OD column): 7.9 min and 11.1 min (peak ratio (%): 1 : 99).



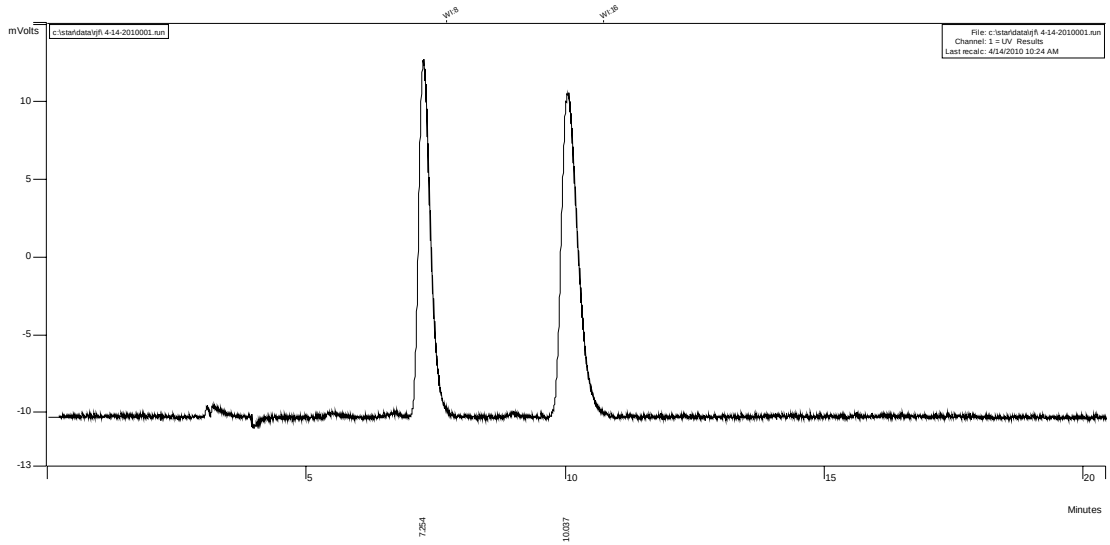
(2S,3S)-2-methyl-3-(7-methylindan-4-yloxymethyl)-oxirane **5**



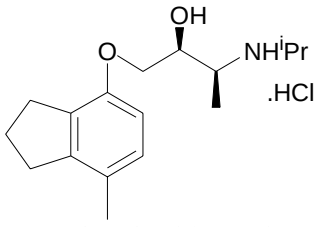
Identical procedure to that described above for the synthesis of the (R,R)-enantiomer **3** was followed using epoxide enantiomer **4** to give the desired product **5** as white needles (1.15 g, 89 %). Data matched that for enantiomer **3**, except; $[\alpha]^{20}_{D}$ = -16.2 (*c* 3.15, $CHCl_3$). Chiral Phase HPLC (99:1 hexane:isopropanol eluent, OD column): 8.4 min and 12.0 min (peak ratio (%): 98 : 2).



HPLC of racemate 2-methyl-3-(7-methylindan-4-yloxymethyl)-oxirane;



(2S,3S)-3-isopropylamino-1-(7-methylindan-4-yloxy)-butan-2-ol ((2S,3S)-ICI 118,551)



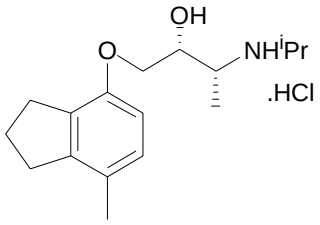
Epoxide **3** (0.040 mg, 0.183 mmol) was dissolved in methanol (1 mL), followed by the addition of isopropylamine (0.054 g, 0.915 mmol), and brought to reflux for 18 h. The methanol was removed on a rotary evaporator, then 6 M HCl (0.5 mL) added. The solid that precipitated was

collected by filtration and washed with water (5 mL), to afford the product as a white crystalline solid (0.020 g, 35%).

Mp = 188-190 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (d, *J* = 6.7, 3H, CHC*H*$_3$), 1.37 (d, 6H, *J* = 6.3, CH(C*H*$_3$)$_2$), 2.05 (appt quintet, *J* = 7.5, 2H, CH$_2$C*H*$_2$CH$_2$), 2.16 (s, 3H, Ar-C*H*$_3$), 2.81 (t, *J* = 7.3, 2H, Ar-C*H*$_2$CH$_2$), 2.85 (t, *J* = 7.3, 2H, Ar-C*H*$_2$CH$_2$), 3.54 (m, 1H, C*H*(CH$_3$)$_2$), 3.63 (m, 1H, CHC*H*CH$_3$), 3.94 (dd, *J* = 6.8 and 9.7, 1H, OCH*H*CH), 4.05 (dd, *J* = 6.0 and 9.7, 1H, OC*H*HCH), 4.28 (m, 1H, CH$_2$C*H*CH), 6.64 (d, *J* = 8.1, 1H, Ar-*H*), 6.87 (d, *J* = 8.1, 1H, Ar-*H*). ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.7 (CH_3), 18.4 (CH_3), 19.2 (CH_3), 19.3 (CH_3), 25.6 (CH_2), 30.6 (CH_2), 32.7 (CH_2), 48.7 (CH), 53.9 (CH), 68.1 (CH_2), 69.4 (CH), 110.4 (CH), 127.7 (C), 129.1 (CH), 132.2 (C), 145.8 (C), 154.1 (C). CI MS (relative intensity): 278 (M+1, 70%), 233 (40%), 189 (23%), 149 (24%), 130 (29%), 86 (100%). Accurate Mass = 278.21200 (Theoretical = 278.21199). IR: 3421, 2928, 1674, 1479, 1262.

The $[\alpha]_D$ of the HCl salt in methanol was too low to measure, and thus the free base was obtained *via* a NaOH wash. Free base $[\alpha]^{20}_D$ = +36.0 (*c* 1.0, $CHCl_3$).

(2R,3R)-3-isopropylamino-1-(7-methylindan-4-yloxy)-butan-2-ol ((2R,3R)-ICI 118,551)



Identical procedure to that described above for the synthesis of the (S,S)-enantiomer was followed using indane-epoxide **5** to give the desired product as a white crystalline solid (0.015 g, 26 %). Data matched that for the opposite enantiomer, except;

The $[\alpha]_D$ of the HCl salt in methanol was too low to measure, and thus the free base was obtained *via* a NaOH wash. $[\alpha]^{20}_D$ = -34.5 (*c* 1.0, $CHCl_3$).

Pharmacology

Materials

(±)-CGP-12177 hydrochloride, and Whatman® grade GF/B glass microfiber filters were from Sigma-Aldrich (UK). (-)-[^{3}H]CGP-12177 was from GE Healthcare (UK). Ultima Gold™ liquid scintillation cocktail was from Perkin Elmer (UK). cDNA clones encoding the genes for the human β_1AR or β_2AR were from the Missouri S&T cDNA Resource Centre (USA). Cell culture materials were from Invitrogen (UK).

Membrane preparation

HEK293 cell lines stably expressing the human β_1AR or β_2AR at 1.64 and 6.64 fmol/μg receptor protein, respectively, were developed. Cells were grown to confluencey in 175 cm^2 flasks. Culture medium was aspirated and the cells washed twice with ice-cold binding buffer (50mM TRIS-base, pH 7.4). Cells were harvested into the same buffer, then an equal volume

of a hypotonic buffer (10 mM TRIS-base, 10 mM EDTA, pH 7.4) was added and the mixture left on ice for 10 min to hypotonically shock the cells. Tonicity was restored by further addition of an equal volume of a sucrose buffer (10 mM TRIS-base, 500 mM sucrose, pH 7.4). Cells were homogenized with > 60 strokes of a glass-on-glass Dounce homogenizer. The resulting homogenate was centrifuged (600 x g, 15 min, 4 °C) to pellet large cell debris and nuclei. The supernatant was centrifuged (100,000 x g, 60 min, 4 °C) and the pellet suspended in binding buffer to give a membrane stock. Membrane was then stored at –20 °C until required for radioligand binding assays.

[^{3}H]CGP-12177 competition binding assay

Membranes were incubated with 0.3 nM [^{3}H]CGP-12177 (a roughly K_d concentration for this radioligand) in the presence of a range of concentrations of racemic or enantiopure preparations of ICI-118,551 for 2 h at room temperature. Additionally, nonspecific binding was determined with incubation of a saturating concentration of cold CGP-12177. The total volume of each binding reaction was 250 µl. Experiments for β_1AR and β_2AR were done in parallel and each treatment was performed in triplicate. Receptor-bound and unbound radioligand were separated by vacuum filtration through Whatman® grade GF/B filter papers, followed by 4 x 2 mL washes with binding buffer. Filter papers were then immersed in 5 mL scintillation cocktail and at least 15 h later a dpm binding signal was measured for 2 min per sample with a Packard Tri-Carb 2100TR liquid scintillation counter.

Data analysis

The nonspecific binding signal for each experiment was subtracted from each binding signal to determine specific binding. These were then expressed as a percentage of maximal binding. This was plotted against the corresponding concentration of ICI-118,551 and the curve was fitted to one-site competition nonlinear regression analysis with GraphPad Prism 4. The Cheng-Prusoff correction was used to calculate the K_i from these curves and the affinity for each βAR subtype was expressed as an averaged pK_i value ± standard deviation from at least three experiments. The statistical significance of differences between the pKi values of these preparations of ICI-118,551 were investigated using ANOVA (Bonferroni's test). This was performed seperately for each receptor In addition, the β_2AR vs. β_1AR selectivity ratio for each preparation was calculated by dividing the K_i at β_1AR by that at β_2AR.

Although a one-site binding model was used for all the data, it was found that (2R,3R)-ICI-118,551 binding to β1AR was actually best fit to a two-site model (F test, $P < 0.005$, $n = 3$). Although this may influence the derivation of pKi values, one-site binding was applied for ease of comparison with the other curves and to represent roughly an average of the two binding sites.

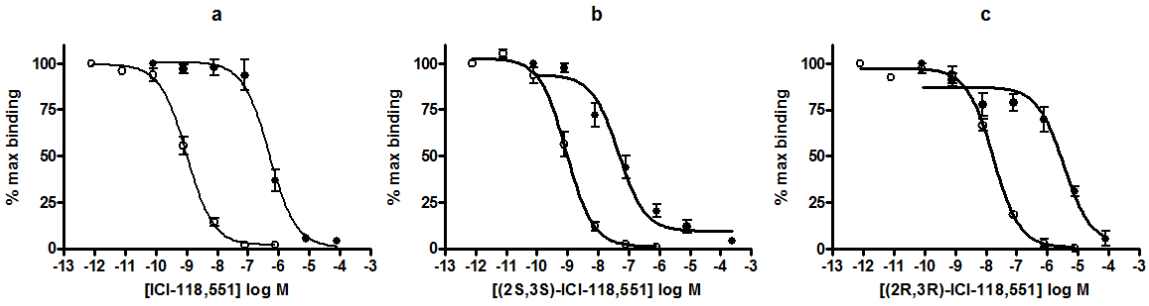
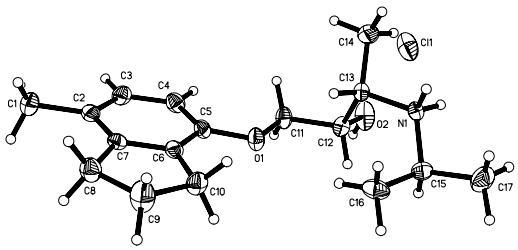


Figure. [^{3}H]CGP-12177 competition binding curves at HEK293 membranes expressing either

β_1AR (closed circels) or β_2AR (open circles) for racemic ICI-118,551 (a), (2S,3S)-ICI-118,551 (b), and (2R,3R)-ICI-118,551 (c).

Table 1. Crystal data and structure refinement for (2S,3S)-ICI 118,551.



Identification code	str0595	
Chemical formula	$C_{17}H_{28}ClNO_2$	
Formula weight	313.85	
Temperature	150(2) K	
Radiation, wavelength	MoK□, 0.71073 Å	
Crystal system, space group	monoclinic, C2	
Unit cell parameters	a = 15.516(2) Å	□ = 90°
	b = 6.0364(7) Å	□ = 109.728(4)°
	c = 19.562(2) Å	□ = 90°
Cell volume	1724.6(4) Å^3	
Z	4	
Calculated density	1.209 g/cm^3	
Absorption coefficient □	0.226 mm^{-1}	
F(000)	680	
Crystal colour and size	colourless, 0.35 × 0.10 × 0.06 mm^3	
Data collection method	Bruker SMART APEX CCD diffractometer □ rotation with narrow frames	
□ range for data collection	2.92 to 28.28°	
Index ranges	h −20 to 20, k −8 to 7, l −25 to 25	
Completeness to □ = 26.00°	99.5 %	
Reflections collected	7495	
Independent reflections	3972 (R_{int} = 0.0263)	
Reflections with F^2>2□	3716	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.9250 and 0.9866	
Structure solution	direct methods	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.0699, 0.4087	
Data / restraints / parameters	3972 / 1 / 190	
Final R indices [F^2>2□]	R1 = 0.0408, wR2 = 0.1070	
R indices (all data)	R1 = 0.0439, wR2 = 0.1099	
Goodness-of-fit on F^2	1.012	
Absolute structure parameter	0.05(6)	

Largest and mean shift/su	0.000 and 0.000
Largest diff. peak and hole	0.417 and −0.366 e Å^{-3}

Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for str0595. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
Cl(1)	0.28516(3)	0.38345(8)	0.06499(2)	0.02943(13)
N(1)	0.32320(9)	0.8837(3)	0.11086(7)	0.0184(3)
O(1)	0.56319(9)	0.7991(2)	0.28014(7)	0.0266(3)
O(2)	0.48059(10)	1.2476(3)	0.15707(9)	0.0361(4)
C(1)	0.87051(14)	0.2764(4)	0.44099(11)	0.0315(5)
C(2)	0.79114(12)	0.4203(3)	0.39814(9)	0.0230(4)
C(3)	0.80222(13)	0.6013(4)	0.35848(10)	0.0256(4)
C(4)	0.72891(13)	0.7337(4)	0.31802(10)	0.0259(4)
C(5)	0.64112(12)	0.6828(3)	0.31740(9)	0.0220(4)
C(6)	0.62848(12)	0.5045(3)	0.35760(9)	0.0207(4)
C(7)	0.70252(12)	0.3758(4)	0.39739(8)	0.0215(3)
C(8)	0.67273(14)	0.1958(4)	0.43764(11)	0.0295(4)
C(9)	0.56886(16)	0.2197(5)	0.41510(14)	0.0453(6)
C(10)	0.54006(13)	0.4236(4)	0.36521(11)	0.0273(5)
C(11)	0.57120(13)	0.9766(3)	0.23471(11)	0.0245(4)
C(12)	0.47320(12)	1.0451(3)	0.19089(10)	0.0221(4)
C(13)	0.42598(11)	0.8608(3)	0.13774(9)	0.0191(3)
C(14)	0.45540(14)	0.8491(4)	0.07120(11)	0.0323(5)
C(15)	0.27483(12)	0.9047(4)	0.16582(9)	0.0234(4)
C(16)	0.30393(16)	0.7219(4)	0.22241(11)	0.0313(5)
C(17)	0.17250(13)	0.9021(5)	0.12387(12)	0.0374(5)

Table 3. Bond lengths [Å] and angles [°] for str0595.

N(1)–C(13)	1.507(2)	N(1)–C(15)	1.510(2)
O(1)–C(5)	1.375(2)	O(1)–C(11)	1.424(2)
O(2)–C(12)	1.413(2)	C(1)–C(2)	1.509(3)
C(2)–C(3)	1.384(3)	C(2)–C(7)	1.396(2)
C(3)–C(4)	1.397(3)	C(4)–C(5)	1.392(3)
C(5)–C(6)	1.385(3)	C(6)–C(7)	1.388(3)
C(6)–C(10)	1.510(2)	C(7)–C(8)	1.504(3)
C(8)–C(9)	1.527(3)	C(9)–C(10)	1.540(3)
C(11)–C(12)	1.529(3)	C(12)–C(13)	1.530(3)
C(13)–C(14)	1.519(2)	C(15)–C(16)	1.519(3)
C(15)–C(17)	1.521(3)		

C(13)–N(1)–C(15)	118.75(13)	C(5)–O(1)–C(11)	117.94(15)
C(3)–C(2)–C(7)	117.01(17)	C(3)–C(2)–C(1)	122.23(17)
C(7)–C(2)–C(1)	120.76(18)	C(2)–C(3)–C(4)	122.54(17)
C(5)–C(4)–C(3)	119.06(18)	O(1)–C(5)–C(6)	115.46(16)
O(1)–C(5)–C(4)	125.05(18)	C(6)–C(5)–C(4)	119.48(17)
C(5)–C(6)–C(7)	120.29(17)	C(5)–C(6)–C(10)	127.92(17)
C(7)–C(6)–C(10)	111.79(17)	C(6)–C(7)–C(2)	121.61(19)

C(6)–C(7)–C(8)	110.84(16)	C(2)–C(7)–C(8)	127.54(18)
C(7)–C(8)–C(9)	105.15(17)	C(8)–C(9)–C(10)	108.11(18)
C(6)–C(10)–C(9)	104.00(16)	O(1)–C(11)–C(12)	105.87(15)
O(2)–C(12)–C(11)	105.90(15)	O(2)–C(12)–C(13)	114.01(15)
C(11)–C(12)–C(13)	109.97(16)	N(1)–C(13)–C(14)	107.09(13)
N(1)–C(13)–C(12)	112.18(15)	C(14)–C(13)–C(12)	113.72(17)
N(1)–C(15)–C(16)	111.16(16)	N(1)–C(15)–C(17)	107.11(14)
C(16)–C(15)–C(17)	112.64(18)		

Table 4. Anisotropic displacement parameters ($Å^2$) for str0595. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2hka^*b^*U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cl(1)	0.0362(2)	0.0150(2)	0.0268(2)	0.00042(19)	–0.00288(17)	0.0013(2)
N(1)	0.0182(6)	0.0182(6)	0.0171(6)	0.0021(7)	0.0036(5)	–0.0008(7)
O(1)	0.0185(6)	0.0305(7)	0.0281(7)	0.0086(6)	0.0041(5)	0.0001(5)
O(2)	0.0304(8)	0.0202(8)	0.0489(9)	0.0090(7)	0.0019(7)	–0.0074(6)
C(1)	0.0236(10)	0.0351(12)	0.0335(11)	0.0021(9)	0.0064(8)	0.0065(9)
C(2)	0.0213(8)	0.0283(12)	0.0181(8)	–0.0042(7)	0.0050(6)	0.0010(7)
C(3)	0.0178(8)	0.0319(11)	0.0275(9)	–0.0019(8)	0.0082(7)	–0.0018(8)
C(4)	0.0251(9)	0.0289(10)	0.0230(9)	0.0031(8)	0.0074(7)	–0.0035(8)
C(5)	0.0204(9)	0.0249(10)	0.0171(8)	–0.0013(7)	0.0017(7)	0.0003(7)
C(6)	0.0179(8)	0.0253(10)	0.0172(8)	–0.0035(7)	0.0037(7)	–0.0018(7)
C(7)	0.0252(8)	0.0234(8)	0.0154(7)	–0.0035(9)	0.0064(6)	0.0003(9)
C(8)	0.0299(10)	0.0280(11)	0.0302(10)	0.0060(9)	0.0096(8)	–0.0001(9)
C(9)	0.0312(11)	0.0533(16)	0.0542(14)	0.0269(13)	0.0184(11)	0.0004(11)
C(10)	0.0206(8)	0.0302(13)	0.0326(10)	0.0040(8)	0.0108(7)	–0.0022(8)
C(11)	0.0178(8)	0.0242(9)	0.0276(10)	0.0035(8)	0.0026(7)	–0.0021(7)
C(12)	0.0190(9)	0.0179(9)	0.0274(9)	0.0005(7)	0.0054(7)	–0.0009(7)
C(13)	0.0167(7)	0.0187(9)	0.0201(7)	0.0009(7)	0.0038(6)	0.0008(7)
C(14)	0.0258(9)	0.0464(15)	0.0275(9)	–0.0022(9)	0.0127(8)	0.0021(9)
C(15)	0.0252(8)	0.0230(10)	0.0251(8)	–0.0010(8)	0.0123(7)	–0.0019(8)
C(16)	0.0450(12)	0.0283(11)	0.0265(9)	0.0035(8)	0.0201(9)	–0.0044(9)
C(17)	0.0238(9)	0.0462(14)	0.0455(11)	0.0031(12)	0.0158(8)	–0.0016(10)

Table 5. Hydrogen coordinates and isotropic displacement parameters ($Å^2$) for str0595.

	x	y	z	U
H(1D)	0.2992	0.7625	0.0823	0.022
H(1E)	0.3084	1.0063	0.0812	0.022
H(2A)	0.5068	1.3418	0.1889	0.054
H(1A)	0.9270	0.3323	0.4354	0.047
H(1B)	0.8597	0.1238	0.4230	0.047
H(1C)	0.8763	0.2798	0.4924	0.047
H(3A)	0.8620	0.6369	0.3588	0.031
H(4A)	0.7388	0.8567	0.2913	0.031
H(8A)	0.7017	0.2149	0.4908	0.035

H(8B)	0.6894	0.0481	0.4239	0.035
H(9A)	0.5506	0.2392	0.4586	0.054
H(9B)	0.5385	0.0851	0.3890	0.054
H(10A)	0.4954	0.3822	0.3174	0.033
H(10B)	0.5125	0.5387	0.3875	0.033
H(11A)	0.6041	0.9275	0.2020	0.029
H(11B)	0.6050	1.1021	0.2643	0.029
H(12A)	0.4386	1.0709	0.2250	0.026
H(13A)	0.4418	0.7163	0.1640	0.023
H(14A)	0.4228	0.7279	0.0397	0.048
H(14B)	0.5215	0.8225	0.0864	0.048
H(14C)	0.4408	0.9894	0.0446	0.048
H(15A)	0.2912	1.0509	0.1909	0.028
H(16A)	0.3701	0.7313	0.2481	0.047
H(16B)	0.2890	0.5775	0.1984	0.047
H(16C)	0.2715	0.7392	0.2572	0.047
H(17A)	0.1572	1.0230	0.0883	0.056
H(17B)	0.1387	0.9216	0.1577	0.056
H(17C)	0.1556	0.7602	0.0986	0.056

Table 6. Torsion angles [°] for str0595.

C(7)–C(2)–C(3)–C(4)	−1.2(3)	C(1)–C(2)–C(3)–C(4)	179.25(18)
C(2)–C(3)–C(4)–C(5)	0.1(3)	C(11)–O(1)–C(5)–C(6)	−176.63(16)
C(11)–O(1)–C(5)–C(4)	4.4(3)	C(3)–C(4)–C(5)–O(1)	179.86(17)
C(3)–C(4)–C(5)–C(6)	0.9(3)	O(1)–C(5)–C(6)–C(7)	−179.92(16)
C(4)–C(5)–C(6)–C(7)	−0.9(3)	O(1)–C(5)–C(6)–C(10)	0.0(3)
C(4)–C(5)–C(6)–C(10)	179.07(19)	C(5)–C(6)–C(7)–C(2)	−0.2(3)
C(10)–C(6)–C(7)–C(2)	179.83(17)	C(5)–C(6)–C(7)–C(8)	178.84(17)
C(10)–C(6)–C(7)–C(8)	−1.1(2)	C(3)–C(2)–C(7)–C(6)	1.2(3)
C(1)–C(2)–C(7)–C(6)	−179.19(17)	C(3)–C(2)–C(7)–C(8)	−177.68(18)
C(1)–C(2)–C(7)–C(8)	1.9(3)	C(6)–C(7)–C(8)–C(9)	2.8(2)
C(2)–C(7)–C(8)–C(9)	−178.2(2)	C(7)–C(8)–C(9)–C(10)	−3.3(3)
C(5)–C(6)–C(10)–C(9)	179.0(2)	C(7)–C(6)–C(10)–C(9)	−1.0(2)
C(8)–C(9)–C(10)–C(6)	2.7(3)	C(5)–O(1)–C(11)–C(12)	170.11(15)
O(1)–C(11)–C(12)–O(2)	168.43(15)	O(1)–C(11)–C(12)–C(13)	−67.96(19)
C(15)–N(1)–C(13)–C(14)	−178.55(19)	C(15)–N(1)–C(13)–C(12)	−53.1(2)
O(2)–C(12)–C(13)–N(1)	−79.59(19)	C(11)–C(12)–C(13)–N(1)	161.66(15)
O(2)–C(12)–C(13)–C(14)	42.1(2)	C(11)–C(12)–C(13)–C(14)	−76.6(2)
C(13)–N(1)–C(15)–C(16)	−51.1(2)	C(13)–N(1)–C(15)–C(17)	−174.52(19)

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