

An exceptional 5:4 enantiomeric structure

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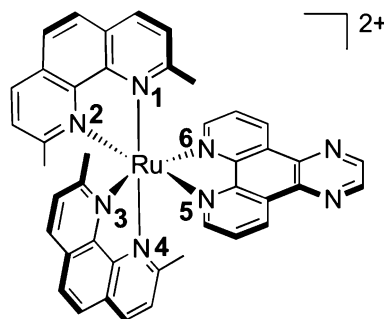
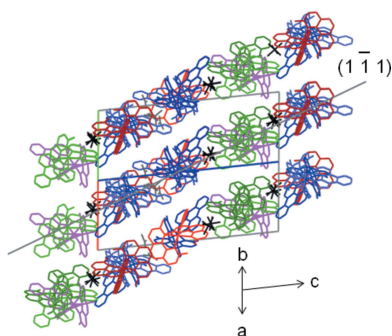
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The only crystals that could be grown from racemic solutions of the PF_6^- salt of the resolvable cation $[\text{Ru}(2,9\text{-dimethyl-1,10-phenanthroline})_2(\text{dipyrido}[3,2-d:2',3'-f]\text{quinoxaline})]^{2+}$ have translational symmetry only (space group $P1$), contain nine independent sets of ions, and include numerous independent solvent molecules (11 acetone, one diethyl ether and possibly several water molecules). Layers of hydrophobic cations alternate with layers containing most of the anions and solvent molecules. All nine cations have the same basic conformation, which is distorted by the presence of the methyl substituents on the two 1,10-phenanthroline ligands. Four pairs of enantiomeric cations within a layer are related by approximate inversion centers; the ninth cation, which shows no sign of disorder, makes the layer chiral. Within the cation layers stripes parallel to $[110]$ of six cations alternate with stripes of three; the local symmetry and the cation orientations are different in the two stripes. These stripes are reflected in the organization of the anion/solvent layer. The *ca* 80:20 inversion twinning found indicates that enantiomeric preference is transmitted less perfectly across the anion/solvent layer than within the cation layer. The structure is exceptional in having nine independent formula units and an unbalanced set (ratio 4:5) of resolvable enantiomers. The difficulty in growing crystals of this material is consistent with its structural complexity.

1. Introduction

The $[\text{Ru}(2,9\text{-dimethyl-1,10-phenanthroline})_2(\text{dipyrido}[3,2-d:2',3'-f]\text{quinoxaline})]^{2+}$ cation was synthesized as one of a series of six-coordinate Ru^{II} complexes with 2,2'-bipyridyl and 1,10-phenanthroline (hereafter, phen) ligands being investigated as photoactivated DNA intercalation agents (Wachter *et al.*, 2014; Hidayatullah *et al.*, 2014). The dipyridoquinoxaline ligand promotes intercalation; the methyl substituents of the 2,9-dimethyl-1,10-phenanthroline ligands (hereafter, dmphen) were added to increase steric strain, which should raise the probability of dissociation upon irradiation. The goal of the structure determination was characterization of the distortions caused by the methyl substituents.



Growing crystals that gave usable diffraction data was an unexpected challenge, even when measurements were made at

Table 1
Crystal data.

Crystal data	
Chemical formula	$9\text{C}_{42}\text{H}_{32}\text{N}_8\text{Ru}\cdot 18\text{F}_6\text{P}\cdot\text{C}_4\text{H}_{10}\text{O}\cdot 11\text{C}_3\text{H}_6\text{O}$
M_r	10 070.85
Crystal system, space group	Triclinic, $P1$
Temperature (K)	90
a, b, c (Å)	18.3127 (3), 21.3286 (4), 29.2640 (6)
α, β, γ (°)	81.874 (1), 89.211 (1), 69.108 (1)
V (Å ³)	10563.1 (3)
Z	1
Radiation type	Cu $K\alpha$
μ (mm ⁻¹)	4.19
Crystal size (mm)	0.11 × 0.10 × 0.05
Data collection	
Diffractometer	Bruker X8 Proteum
Absorption correction	Multi-scan <i>SADABS</i> (Krause <i>et al.</i> , 2015)
T_{\min}, T_{\max}	0.608, 0.753
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	139 158, 41 744, 38 577
R_{int}	0.059
$(\sin \theta/\lambda)_{\text{max}}$ (Å ⁻¹)	0.603
Refinement	
$R[F^2 > 2\sigma(F^2)], wR(F^2), S$	0.057, 0.153, 1.03
No. of reflections	41 744
No. of parameters	5769
No. of restraints	6050
H-atom treatment	H-atom parameters constrained $w = 1/[\sigma^2(F_o^2) + (0.0881P)^2 + 31.8949P]$ where $P = (F_o^2 + 2F_c^2)/3$
$\Delta\rho_{\text{max}}, \Delta\rho_{\text{min}}$ (e Å ⁻³)	2.00, -1.30
Absolute structure	Refined as an inversion twin
Absolute structure parameter	0.188 (9)

Computer programs used: *APEX2* (Bruker, 2006), *SHELXT* (Sheldrick, 2015a), *SHELXL-2014/7* (Sheldrick, 2015b), *XP* in *SHELXTL*, *SHELX* (Sheldrick, 2008) and *CIFFIX* (Parkin, 2013).

90 K with Cu $K\alpha$ radiation from a rotating-anode source equipped with focusing mirrors. Most crystallization attempts used the PF_6^- salt because structures in the Cambridge Structural Database (Allen, 2002; hereafter, the CSD) of similar cations all have PF_6^- or ClO_4^- anions. Twelve solvent combinations were tried; solvent evaporation at room temperature took place over weeks. Only two of the 24 attempts gave any crystals at all, with the first of these giving crystals too small to use. Six attempts to grow crystals of the nitrate salt were also unsuccessful.

A number of similar complexes have been studied in this laboratory and elsewhere. The space groups and numbers of independent formula units (Z') have all been unremarkable. The structure reported here, however, has nine independent cations, 18 anions, and at least 12 solvent molecules and so is exceptionally large. Furthermore, the $P1$ space group and the odd number of resolvable enantiomers means they cannot all be paired; there are five of one chirality and four of the other in the unit cell. Four pairs of enantiomers are related by good pseudo-inversion centers but those centers are broken by the ninth cation and, to a lesser extent, by the anions and included solvent molecules. The chances of an ordered, unmodulated structure having $Z' > 8$ and an unbalanced set of enantiomers are so small as to be impossible to estimate.

2. Structure determination

2.1. Crystal growth

Information about the solvent combinations used during the many attempts to grow crystals is given with the supporting information. In all cases solvent evaporation was at room temperature and took place over several weeks. The solid was dark red. The macroscopic crystals found were in clusters of semi-regular blocks that were thinner in one direction than in the other two. Data were collected for a crystal with dimensions $0.11 \times 0.10 \times 0.05$ mm that was cut to remove several smaller satellite crystals.

2.2. Data collection, structure solution and refinement

X-ray data were collected at 90 K using a Bruker–Nonius X8 Proteum diffractometer equipped with a rotating anode Cu $K\alpha$ X-ray generator, graded multilayer focusing optics (Bruker AXS, Madison, WI), and a CRYOCOOL-LN2 low-temperature device (CryoIndustries of America, Manchester, NH). Although the unit cell was large by small-molecule crystal standards [$V = 10563.1$ (3) Å³], the longest cell edge [$c = 29.2640$ (6) Å] was not excessively long. Data collection was, by and large, routine. Data processing using the standard Bruker *APEX2* package (Bruker, 2006) was also routine, although after structure solution and refinement, many attempts were made to improve the data quality by optimizing the parameters used by the data integration (*SAINT-Plus*; Bruker, 2006), absorption correction and merging programs (*SADABS*; Krause *et al.*, 2015).

The structure solved easily using *SHELXT* (Sheldrick, 2015a), which found the 634 non-H atoms present in the final model. All of these atoms appear to be ordered. The program also located three ‘atoms’ that were placed in small, but diffuse, blobs of electron density that were tentatively assigned as water O atoms. As the model neared completion, those three poorly defined ‘atoms’ failed to improve but neither did they generate too-short contacts with other species. These regions were therefore treated using the latest version of the *SQUEEZE* routine (Spek, 2015), which leaves the original dataset intact. Because of the uncertainty about these three ‘atoms’ and because there are other regions where it seems there might be space for a water molecule the exact number of solvent molecules in this compound is uncertain.

Structure refinement using various iterations of *SHELXL-2014* (Sheldrick, 2015b) was surprisingly straightforward. The solvent molecules, but not the ions, had to be restrained geometrically (*SHELXL-2014* commands *SADI*, *DFIX*, *FLAT*; see the CIF for details). The *RIGU* restraint was applied to all bonds to improve the appearance of the displacement parameters and reduce correlations. If the *RIGU* instruction is applied only to the anions and solvent molecules some of the displacement ellipsoids for the cation atoms become more eccentric but they all remain positive definite.

All H atoms were placed in calculated positions and included using riding models. Since the structure contains both cation enantiomers in space group $P1$, twinning by inversion

Table 2

Some angles and distances averaged over the nine independent cations.

Bond angles, average s.u. and population standard uncertainty (°)				
N1—Ru—N2, N3—Ru—N4	79.7 (3) (6)	N5—Ru—N6	79.4 (3) (4)	
N1—Ru—N4	178.1 (3) (7)	N2—Ru—N5, N3—Ru—N6	172.7 (3) (12)	
N1—Ru—N6, N4—Ru—N5	81.5 (3) (12)	N1—Ru—N5, N4—Ru—N6	97.6 (3) (16)	
N2—Ru—N6, N3—Ru—N5	93.8 (3) (10)	N2—Ru—N3	93.2 (3) (6)	
N1—Ru—N3, N2—Ru—N4	101.2 (3) (11)			

Cation	Angle (°) between planes of the C ₆ N rings containing:		Distance (Å) of the attached Me group from the planes of the C ₆ N ring containing:	
	N1 and N2	N3 and N4	N1, N2	N3, N4
<i>A</i>	6.9	8.5	0.17, 0.14	0.21, 0.05
<i>B</i>	6.9	9.2	0.17, 0.05	0.24, 0.08
<i>C</i>	9.2	10.7	0.06, 0.21	0.01, 0.19
<i>D</i>	5.1	6.0	0.16, 0.20	0.20, 0.09
<i>E</i>	10.7	3.8	0.12, 0.06	0.08, 0.17
<i>F</i>	9.8	6.0	0.18, 0.06	0.04, 0.27
<i>G</i>	12.4	11.6	0.07, 0.09	0.07, 0.10
<i>H</i>	14.6	13.0	0.10, 0.08	0.04, 0.12
<i>I</i>	14.0	17.2	0.13, 0.06	0.02, 0.20
QOZDEQ_A	9.0	9.1	0.10, 0.12	0.13, 0.13
QOZDEQ_B	10.4	11.4	0.09, 0.09	0.08, 0.19

seemed likely. It was modeled with the standard *SHELXL* commands *TWIN* and *BASF*; the minor component fraction converged to 0.188 (9).

The final refinement (Table 1) was surprisingly satisfactory given the size of the structure and the loose packing (as indicated by larger displacement ellipsoids) in some regions. The data were not especially weak; the fraction of reflections

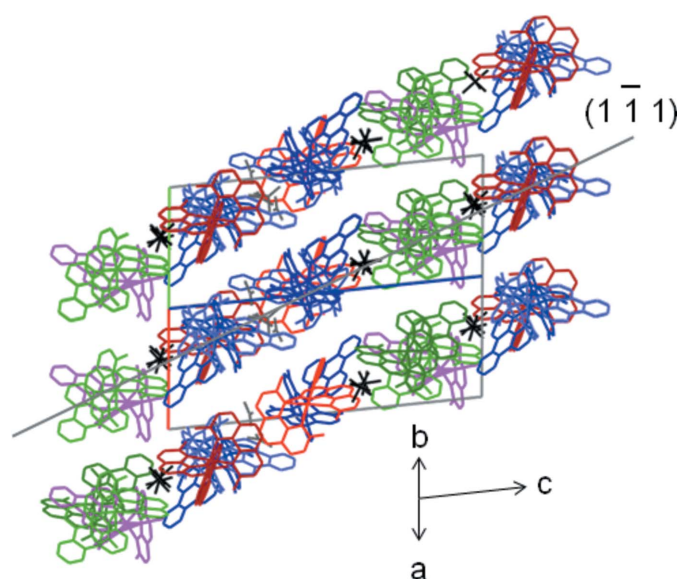


Figure 1
View along $[110]$ of the cation layers $(1\bar{1}1)$. H atoms have been omitted, as have the anions and solvent molecules that are not deeply embedded in the layer. The only cation that clearly protrudes from the layer is (I) (colored magenta).

to 0.603 \AA^{-1} with $I > 2\sigma(I)$ was 0.92. The second parameter in the weighting scheme is large but the many attempts to find a ‘better’ weighting scheme were unsuccessful. The peaks and troughs in the final difference map are generally located near the Ru atoms or near anions (e.g. anion *R*) or solvent molecules (e.g. acetone *SC*) that have displacement ellipsoids that are larger than average.

2.3. Distances and angles

The agreement of the chemically equivalent but symmetry independent distances is a measure of the precision of the structure. The average of the 36 Ru—N distances to the *dmphen* ligands is 2.108 Å; the 36 estimated standard uncertainties average 0.008 Å while the population standard uncertainty is only twice as large (0.015 Å). The corresponding values for the 18 Ru—N distances to the dipyridoquinoxaline ligand are 2.080, 0.008 and 0.015 Å. Tables of corresponding Ru—N and P—F distances and N—Ru—N angles are given in the supporting information.

Since the standard uncertainties for the means of the two types of Ru—N bonds are 0.003 and 0.002 Å the Ru—N bonds to the dipyridoquinoxaline ligand are shorter by 0.028 (4) Å than the Ru—N distances to the *dmphen* ligands. Both types of Ru—N bonds are long, presumably as a result of the steric strain; the median Ru—N bond length in the Ru-phenanthroline complexes in the CSD having $R \leq 0.075$ is 2.073 Å. The Ru—N distances in this compound are essentially the same as in the very similar salt QOZDEQ (Hidayatullah *et al.*, 2014), where the corresponding means [2.112 (4) and 2.092 (8) Å] are just 0.004 and 0.012 Å longer.

The 108 P—F distances average 1.579 Å but vary from that value by -0.107 to $+0.060$ Å. The distribution is skewed towards shorter distances, probably because of the larger apparent thermal motion in some of the anions (see the supporting information). The standard uncertainty that measures the width of the distribution of P—F distances is 0.029 Å.

The steric strain in the cations can also be seen in the N—Ru—N angles and especially in the dihedral angles between the two C₅N rings of a *dmphen* ligand (Table 2). All the *dmphen* ligands are buckled in the same way, with the methyl groups bent even farther away from the dipyridoquinoxaline ligand. The *dmphen* ligands are buckled in the same way in QOZDEQ.

3. Results

3.1. The structure is layered

The cations in this structure are segregated into layers ($1\bar{1}1$) (Fig. 1). Four of the 18 PF₆[−] anions (*A–D*) are deeply embedded in the layer, as are four of the 11 acetone molecules (*SA–SD*) (Fig. 2). The layers are separated by regions

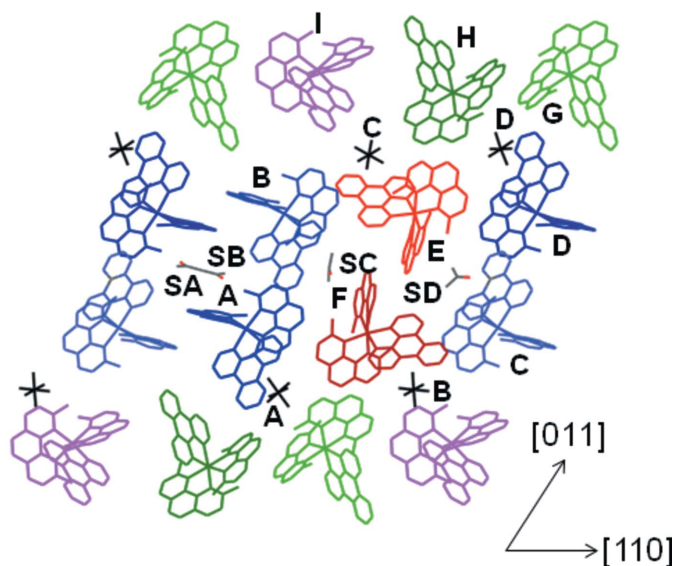


Figure 2
Part of the cation layer $[1\bar{1}1]$ showing the labels for the nine independent cations, the four embedded anions, and the four embedded solvent molecules. In this and the other drawings the colors have been chosen to emphasize the cation groups in which there is local symmetry. The anions are shown in black, and the included solvent molecules in gray with red O atoms. The full atom-numbering scheme for the cations is given in the supporting information.

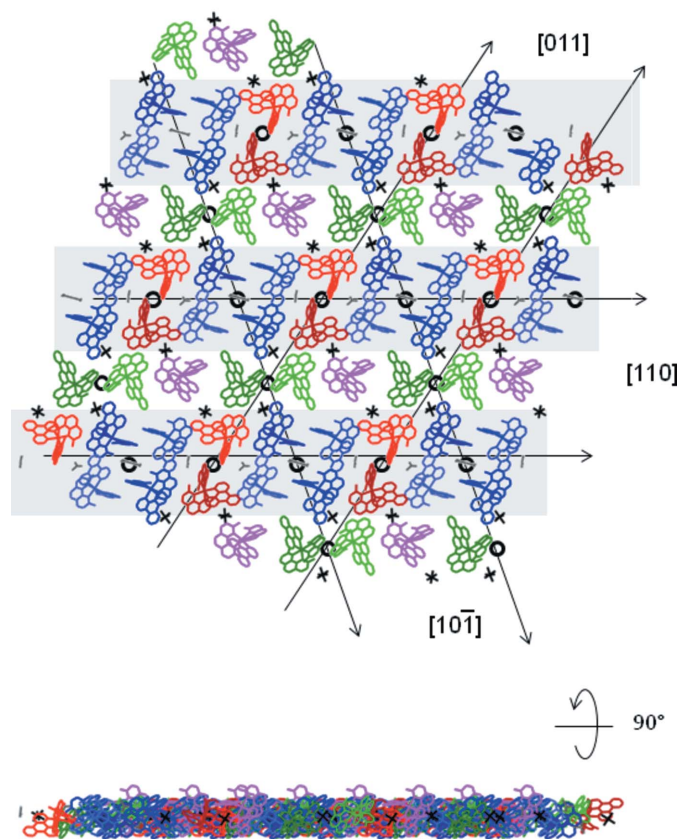


Figure 3
A larger drawing of the cation layer $(1\bar{1}1)$ showing the locations of the approximate layer inversion centers and the two different kinds of cation stripe.

containing the remaining anions and solvent molecules. Layers are common in compounds of this type, especially when the anions are small, because the formation of alternating hydrophobic and hydrophilic regions is favorable (Russell *et al.*, 2001; Horn *et al.*, 2002). There are, however, four cation···cation interlayer contacts shorter than $\Sigma_{VDW} - 0.20 \text{ \AA}$ (where Σ_{VDW} is the sum of the van der Waals radii) and nine shorter than $\Sigma_{VDW} - 0.10 \text{ \AA}$.

3.2. Stripes in the layers include very good local pseudo-inversion centers between cations

In the cation layer there is a stripe parallel to $[110]$ (Figs. 2 and 3) that contains six cations (*A–F*) arranged in a parallelogram with a very good pseudo-inversion center in the middle. The centroids of the three pairs of cations related by local inversion centers vary by no more than 0.002, 0.001 and 0.008 in *x*, *y* and *z* (or by 0.04, 0.02 and 0.23 \AA). There are also excellent pseudo-inversion centers between adjacent parallelograms.

There is a second stripe along $[110]$ containing a pair of cations (*G, H*) related by a pseudo-inversion center; this cation pair alternates with the one unbalanced enantiomer (*I*), which protrudes from the layer. The two types of stripe alternate.

These pseudo-inversion centers are so good that *PLATON* (Spek, 2009) run for the four cation pairs alone recommends space-group symmetry $P\bar{1}$ with 98% certainty. If all the anions and solvent molecules are included the certainty decreases to

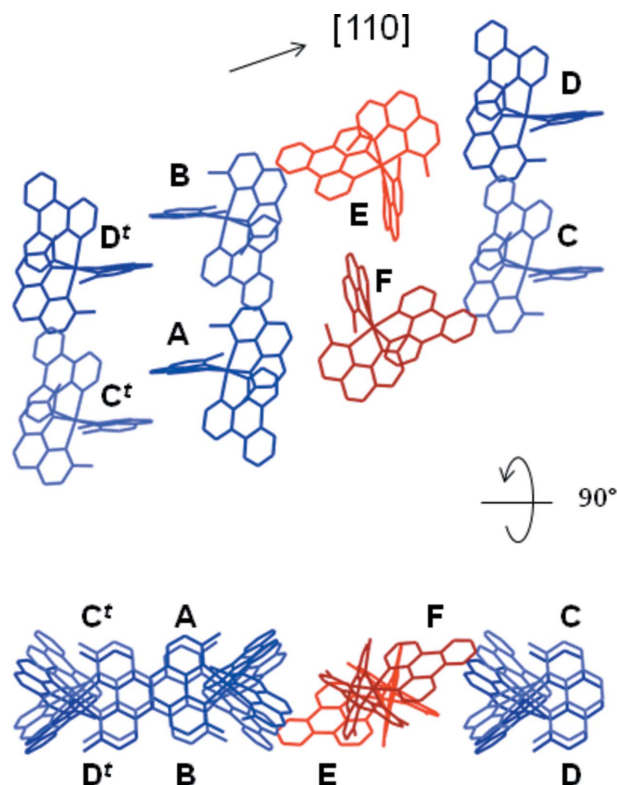


Figure 4
Drawings of cations *A–F* illustrating the approximate local symmetry.

89%, and if the unpaired cation is included *PLATON* issues no alert. If the pseudo-inversion centers were crystallographic the unpaired cation would have to be disordered over a $\bar{1}$ site, but there is no evidence of any such disorder.

In the wider stripe four cations ($\#1,2,3',4'$, where t is $[\bar{1}10]$) form a nearly centrosymmetric unit that has approximate local glide planes (which relate A and B as well as C and D) and twofold axes (which relate A and C as well as B and D); these relationships are illustrated in Fig. 4. The nine independent cations can then be sorted into four groups having different orientations: one set of four (A – D), two sets of two (E,F and G,H), and the one unpaired cation (I).

The Ru atom of cation (I) is 2.12 Å removed along the $(1\bar{1}1)$ normal from the average position of the other eight Ru atoms (standard uncertainty for the eight around their average is 0.54 Å).

3.3. The anion layers are also striped

The layers containing most of the anions and solvent molecules (Figs. 5 and 6) are striped in a way that matches the stripes in the cation layer. Eleven of the anions (E – P but not I) are in or at the edge of the thicker stripe; they form an approximate grid. All the included solvent molecules are either in the thinner stripe or at the border between the two kinds of stripe.

A projection of part of a cation layer with the adjacent anions and solvent molecules (see the supporting information) shows that anions on the two sides of the cation layer line up well (although not by translation), especially in the thicker stripe.

3.4. The cation conformations are all very similar

The eight paired cations all have essentially the same conformation. For the 28 pairwise overlays calculated using

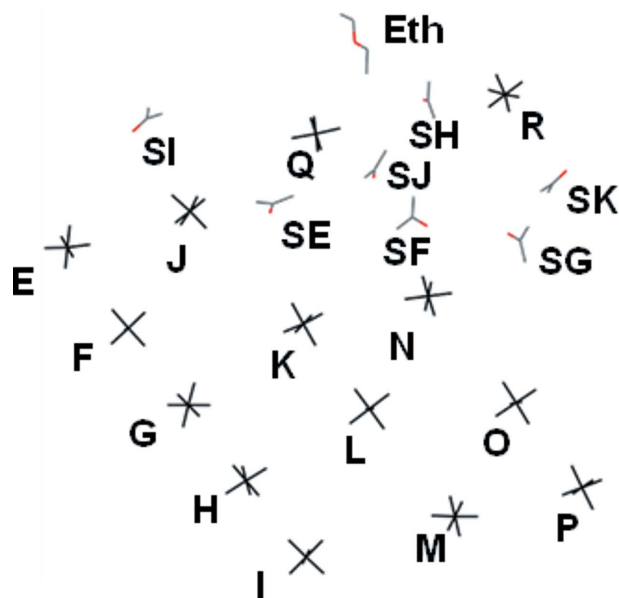


Figure 5
The unique part of the anion layer.

Mercury (Macrae *et al.*, 2008) and allowing inversion the average r.m.s. deviation for the 51 corresponding non-H atoms is 0.17 Å (range 0.07–0.23 Å). The conformation of the ninth unpaired cation is only a little different; its r.m.s. deviations with the other eight average 0.33 Å (range 0.22–0.41 Å). The differences are concentrated in one of the dmphen ligands of (I) (*i.e.* in the ligand that does not protrude from the layer). There are also small differences at the far end of the dipyridoquinoxaline ligand.

3.5. The cation conformation is similar to those seen for closely related compounds

A search of the November 2014 version of the CSD with updates through May 2015 found nine structures containing two dmphen ligands and a third, different 1,10-phen ligand with H atoms at the 2 and 9 positions. All are Ru^{II} cations and all have PF₆[−] or ClO₄[−] counterions. Four have the basic four-ring ligand found in this structure; in QUQLET and XIGNAC there is a fifth, fused benzene ring [dipyrido(3,2-*a*:2,3-*c*)phenazine (dppzs)], in NAQZUC the ligand is 11,12-dichloro-dppz, and in DUMGEY the additional fused ring is saturated. In the fifth structure (QOZDEQ) the dipyrido ring is replaced by a (1,4)dioxino ring. The other four cations (RUVWAH, SALVOR, UJANUO and KOWQAQ) all have a

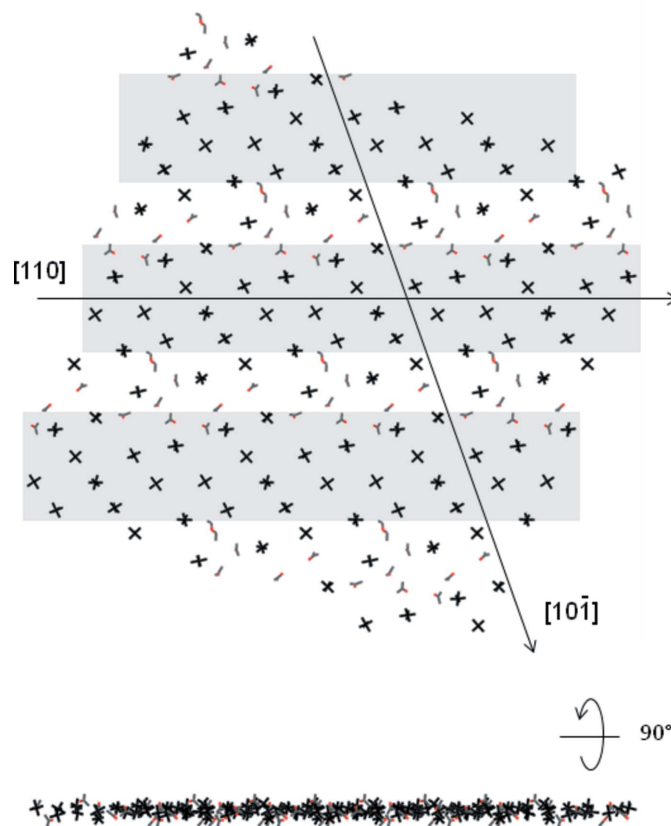


Figure 6
A larger drawing of the anion layer showing the correspondence to the cation stripes shown in Fig. 3. The included solvent molecules are located within and near the edges of the thinner stripes.

fused imidazo ring instead of the dipyrido ring and have phenyl-based substituents off the far side of the imidazo ring.

Pairwise overlays calculated with *Mercury* (Macrae *et al.*, 2008) of the common parts of these nine cations with a typical cation (*A*) of the structure reported here show that the conformations are all very similar. The range of the r.m.s. deviations is 0.12–0.42 Å.

3.6. The methyl substituents have a strong influence on the conformation

A comparison (Fig. 7) of this cation with that of VAMFAQ (Collins *et al.*, 1998) shows the very considerable changes in conformation that result from the introduction of methyl substituents at the 2 and 9 positions of the phen ligands. Except for those Me groups the cations and anions in VAMFAQ and this structure are chemically the same; VAMFAQ, however, has $Z' = 1$ and no included solvent.

3.7. $Z' > 8$ structures are rare

Structures with $Z' > 4$ are unusual (0.08% of the CSD), structures with $Z' > 6$ are scarce (0.03%), and structures with $Z' > 8$ are rare (0.006% of the CSD) (all percentages calculated for structures having $R \leq 0.100$). Large values of Z' that

are odd are less common than those that are even by a factor of about three. There are only four structures (0.0006%) with $Z' = 9$ and $R \leq 0.100$ [IHESIX ($P2_1$, achiral molecules; Sopková-de Oliveira Santos *et al.*, 2002), OQAZUC ($P2_1/n$; Kane *et al.*, 2011), SOYKOH ($P\bar{1}$; Fun *et al.*, 2009), and VARPAG ($C2/c$; Elschenbroich *et al.*, 2003); all have $R \leq 0.060$]. Many of the high- Z' structures are modulated in a simple way (as are OQAZUC and SOYKOH) and many contain hydrogen-bonded aggregates (as do IHESIX and SOYKOH; Brock, 2012); more than 90% of 275 $Z' > 4$ structures have modulations and/or intermolecular interactions similar in strength to a conventional hydrogen bond (Brock, 2016). The structure reported here is therefore exceptional in having neither a hydrogen-bonded aggregate nor a simple modulation.

3.8. Structures with unequal numbers of enantiomers are rare

The phenomenon of an ordered structure containing different numbers of enantiomers has been termed *unbalanced crystallization* (Albano *et al.*, 1971); the first examples (Albano *et al.*, 1969, 1971) were of conformational isomers. A different term, *anomalous racemates*, was used by Jacques *et al.* (1981). The former term is more obviously descriptive, but the latter term seems to have been used more often. Flack (2003) recommended calling the examples *M:N enantiomeric structures*, where *M:N* is the enantiomeric ratio. The phenomenon has been discussed more recently by Tabora *et al.* (2007) and Bredikhin *et al.* (2015).

The number of well documented examples of ordered crystals having an integer ratio of enantiomers other than 1:1 is small. Almost all have a 2:1 ratio. Albano *et al.* (1969, 1971) listed four isostructural examples but coordinates for only one of them were available in the paper or in the CSD [(Ir(NO)(PPh₃)₃, TPNOIR]; coordinates for a second [CuCl(PPh₃)₃, TTPCUC] were published later by Gill *et al.* (1976). Cai *et al.* (2001) described the example QIJWEL ([Co(tren)(AA)](ClO₄)₂, where AA = L-isoleucine and D-alloisoleucine), but in that compound the different enantiomers are actually diastereomers because the configurations of the *sec*-Bu groups in all three cations are the same. Fábíán & Brock (2010) found 11 anomalous racemates composed of separable 'organic' enantiomers during a systematic search for kryptoracemates (*i.e.* racemic compounds that crystallize in a Sohncke space group). That study found 181 kryptoracemates having $R \leq 0.10$ and 11 anomalous racemates. In only two of those 11 is the enantiomeric ratio other than 2:1 (one 3:1, one 5:1; see supporting information). It is clear that solids containing enantiomers in a ratio other than 1:1 are rare (*ca* 1 in 10⁵).

Bernal & Watkins (2015; see their supporting information) identified an organometallic anomalous racemate (TIQHOR; Wang & Sevov, 2007) in which the ratio of resolvable Co^{III} cations is 3:1. They also found three Sohncke-group structures in addition to TPNOIR and TTPCUC in which organometallic conformational enantiomers exist in a ratio other than 1:1.

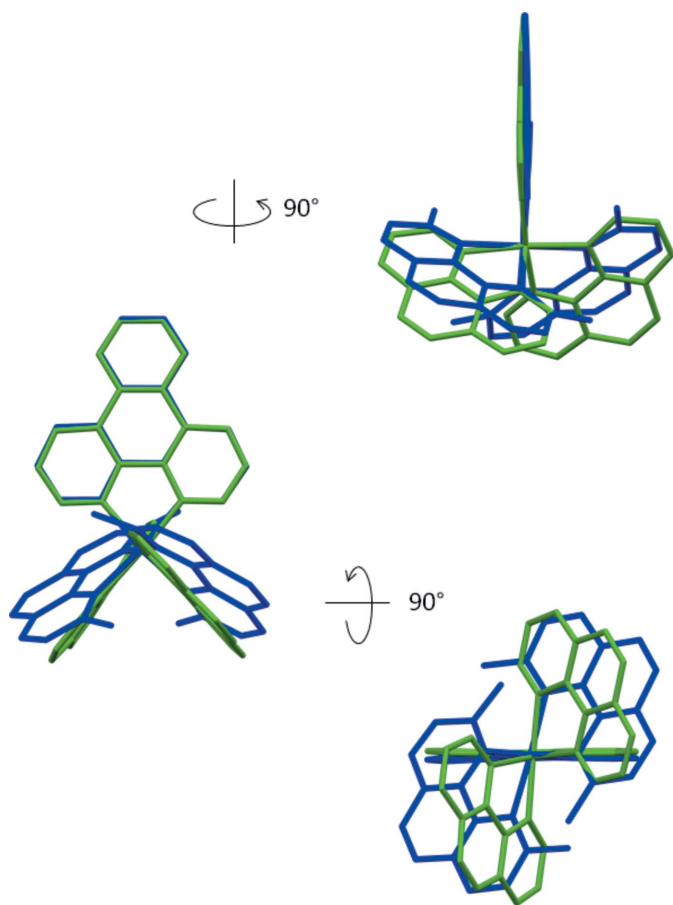


Figure 7
Best superposition of cation *A* with the cation of VAMFAQ, which differs only by the replacement of the four Me groups with H atoms. The distortions caused by the Me groups are large.

3.9. Structures closely related to this one all have low Z' values

The CSD was searched for all transition metal complexes having three phen ligands and $R \leq 0.10$. Of the 561 structures found, 32 (6%) have $Z' > 1$ and none has $Z' > 2$. Two of the nine structures containing two dmphen ligands have $Z' = 2$.

4. Discussion

Why is this 5:4 enantiomeric structure so unusual and so complicated? Why is the crystal structure not simpler? Why is it not like closely related compounds that have $Z' = 1$ or, at most, 2?

4.1. Might the crystal be a metastable form grown under kinetic control?

It has become fashionable to describe high- Z' structures as 'fossil relics' (Steed, 2003) or 'on the way' (Desiraju, 2007). Both of these descriptions imply that high- Z' crystals are sometimes, or even always, formed under kinetic, rather than thermodynamic, control, *i.e.* that the high- Z' form is a metastable form, at least at the temperature at which the crystals were studied. If the conjecture in its stronger form is true there should always be a more stable polymorph having $Z' = 1$ [or $Z' = \frac{1}{2}$ for molecules that can conform to inversion symmetry (Pidcock *et al.*, 2003)]. Since any more stable polymorph may be very difficult to find [consider the late-appearing stable polymorphs of the drugs Ritonavir (Bauer *et al.*, 2001) and Rotigotine (Lee *et al.*, 2011)] it is difficult to counter the conjecture that all $Z' > 1$ crystals grow under kinetic control because it can always be asserted that a lower energy structure with $Z' \leq 1$ exists but has not yet been found. Crystal-structure-prediction (CSP) calculations are not yet reliable enough to identify with certainty the crystal form with the lowest free energy (Price, 2013).

There are, however, studies of two systems in which a $Z' = 1$ polymorph transforms spontaneously near or above room temperature to a quite different $Z' = 6$ polymorph (NAZDIZOn, Franco *et al.*, 2003; ROZRAB, Krishnan & Sureshan, 2015). Furthermore, DFT-d (dispersion-corrected density functional theory) energy calculations for a set of 74 polymorphs that all include a $Z' > 1$ crystal form found that a lower- Z' polymorph is more stable than the higher- Z' polymorph in only 62% of the families (Cruz-Cabeza *et al.*, 2015).¹ Even if there are uncertainties associated with these polymorph comparisons they provide, collectively, strong evidence that a higher- Z' polymorph can have a lower energy.

¹ It has sometimes been asserted that entropy increases with Z' . The Third Law of Thermodynamics, however, says that all well ordered crystals have $S = 0$ at $T = 0$ K. The value of Z' has no effect on the number (three times the number of atoms in the macroscopic crystal) or frequencies of the zero-point vibrations. At higher temperatures S is determined by the amount of thermal motion and by the presence of any disorder. Small, or even moderate, differences in the atomic displacements do not lead to any really significant entropy difference so that entropy differences between polymorphs must be attributed to differences in disorder or to large differences in thermal motion.

In any event, there are several reasons for doubting that the crystals described here represent a metastable phase that grew under kinetic control. First, there is no multi-molecule structural fragment that is likely to have been dominant in the solution (*i.e.* there is no obvious 'fossil relic') because there are no specific interionic interactions like conventional hydrogen bonds. Second, the crystals were grown over a period of weeks, were quite well formed with obvious faces, and were not especially thin or wide in any dimension. Finally, visual examination suggested the crystals grown were all of the same form.

What is certain is that the crystal structure found represents the best solid that could be deposited from the solutions under all sets of conditions attempted, and that that solid was difficult to nucleate and/or grow.

4.2. Why does the compound not have a low- Z' structure like that seen for a related compound?

The 2,9-dimethyl substitution of the dmphen ligands has such a major effect on the conformation that a change in the crystal packing is to be expected. Of the nine structures found in the CSD that contain two dmphen ligands, in only one (QOZDEQ; Hidayatullah *et al.*, 2014) is the third ligand similar in size to the third ligand in this structure; in QOZDEQ a dioxino ring replaces the dipyrido ring so that the fragment $-NCHCHN-$ becomes the slightly larger and somewhat less planar fragment $-OCH_2CH_2O-$. In QOZDEQ Z' is 2 rather than 9 but it would be difficult to view QOZDEQ as a 'better' structure. QOZDEQ is unstable in air because it has very large channels filled with highly disordered solvent. Furthermore, two of the four PF_6^- anions have very large displacement ellipsoids. The $Z' = 9$ compound reported here, however, is stable in air even though it contains quite a lot of solvent, and the structure, although complicated, is very orderly. The displacement ellipsoids are mostly small.

4.3. Is there a basic packing unit?

Russell *et al.* (2001) described packing motifs in metal phenanthroline complexes. The packing of the cation described here must differ somewhat from those because of the distortions caused by the Me substituents (Fig. 7), but the OFF (offset face-to-face) stack Russell *et al.* (2001) describe as very common also occurs in this structure: cations A , B , C' and D' make a tetrameric unit that is an OFF stack (albeit with rather limited overlap) with the two central rings pulled apart to accommodate solvent molecules SA and SB . Local or pseudo-symmetry relates those four cations (Fig. 4). No anion and no other solvent molecule lies within this unit (Fig. 2). The displacement ellipsoids for the atoms of cations $A-D$ are small (see supporting information).

Apparently it is not energetically favorable to extend the $A-D$ unit along $[011]$ or $[110]$. [If it were the layer could have symmetry $p112/a$ (Kopský & Litvin, 2010)]. The OFF motif also occurs in two other cation pairs (E,F and G,H), but the orientations of these pairs are very different from that of the tetramer. The atomic displacement ellipsoids in cation E are

larger than for any of the cations except (I) so the crystal packing in that part of the layer must be relatively loose.

4.4. What is the role of the ninth, 'unbalanced' enantiomer?

If the ninth, unbalanced enantiomer (and its two PF_6^- counterions) were not present the structure would probably be a $P\bar{1}$, $Z' = 4$ structure with the pseudo-inversion centers shown in Fig. 3 converted to crystallographic $\bar{1}$ sites. Solvent molecules would have to fill the void left by the ninth cation (I), and there would have to be an inversion center at the center of that solvent-filled region. Structures with $Z' = 4$ are not common in the CSD but neither are they rare (0.4%).

The fact that the ninth enantiomer protrudes from the layer (Fig. 2) suggests that it might be added relatively late in the development of a new layer. The displacement ellipsoids for cation (I) are also somewhat larger than are those for the other cations; the average U_{iso} is 0.047 \AA^2 versus 0.028 \AA^2 for cations A–D (see supporting information) suggesting a region of looser packing.

The ninth cation in a layer always seems to be the same enantiomer because no cation disorder was found. Since cation (I) sits at a site that would have inversion symmetry if the space group were $P\bar{1}$, and since the eight other cations conform well to that space group (see above) distortions from inversion symmetry involving the intra-layer anions and solvent molecules must be large enough to maintain a strong enantiomeric preference at the site of the ninth cation. Transmission of enantiomeric preference between layers seems less certain (even though there are a number of inter-layer cation...cation contacts shorter than $\Sigma_{\text{VDW}} - 0.10 \text{ \AA}$), and the crystal is indeed an 80:20 inversion twin.

4.5. Other structures with striped layers

An investigation (Brock, 2016) of CSD-archived organic structures with $Z' > 4$ turned up at least five other examples of layered structures in which the layers are composed of alternating ribbons of molecules. The most similar example is KEXLUV [$P\bar{1}$; $Z' = 8$; Mishra *et al.*, 2007; ionic layers (011)]; in that structure stripes parallel to [001] alternate along [011] and are separated by solvent molecules. Other examples are DACGIY [$P\bar{1}$, $Z' = 6$; Filarowski *et al.*, 2004; layers ($\bar{1}20$)], KITQIN [$P1$; $Z' = 6$; Fallon *et al.*, 1999; layers (011)], LAXJUQ [$P2_1/n$, $Z' = 6$; Baruah *et al.*, 2005; layers (100)], and TARNEG [$P\bar{1}$, $Z' = 6$; Gómez *et al.*, 2005; layers (001)]. Drawings of these structures are given with the supporting information.

4.6. Other structures with units in very different orientations

Multiple molecular orientations not related by any pseudo-symmetry are not so unusual when there is strong one-, two- or three-dimensional hydrogen bonding. The structures TARNEG and IHESIX mentioned above are good examples. Structures with multiple molecular orientations but no strong intermolecular interactions (such as conventional hydrogen bonds) are, however, much less common. Two examples are ETCABZ10 ($Pbca$, $Z' = 5$; Kimura *et al.*, 1985) and

NIMRIK08 ($C2/c$, $Z' = 6$; Thakur *et al.*, 2010) (see the supporting information).

5. Summary

The structure described here is exceptional in having both a high (and odd) value of Z' (especially without being modulated or containing hydrogen-bonded aggregates) and different numbers of resolvable enantiomers. The probability of a structure like this one occurring is too small to estimate accurately. The structure is, however, orderly and is just an extreme example of packing features found in lower- Z' structures. The difficulty in growing crystals is consistent with the complexity of the structure. There is no reason to suggest the structure is a kinetic product of crystallization.

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