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Two rhodamine derivatives: 9-[2-(ethoxycarbonyl)phenyl]-3,6-bis-(ethylamino)-2,7-dimethylxanthylium chloride monohydrate and 3,6-diamino-9-[2-(methoxycarbonyl)-phenyl]xanthylium chloride trihydrate

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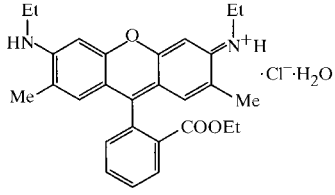
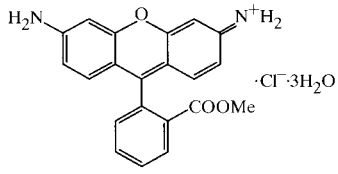
The title compounds, $C_{28}H_{31}N_2O_3^+\cdot Cl^-\cdot H_2O$ (common name rhodamine-6g), (I), and $C_{21}H_{17}N_2O_3^+\cdot Cl^-\cdot 3H_2O$ (common name rhodamine-123), (II), both have planar xanthene skeletons with a formal +1 charge on the amino N atoms delocalized through the π-electron system so that the N—Csp^2 bond distances indicate significant double-bond character. The substituted planar phenyl groups make angles of 63.29 (8) and 87.96 (11)° with the xanthene planes in (I) and (II), respectively. In both molecules, the carbonyl bond vectors point toward the xanthene rings. The ethylamine groups in (I) are oriented similarly with their CH_2–CH_3 bond vectors pointing nearly perpendicular to the xanthene plane. The chloride ions and water molecules are disordered in both structures. In (I), the chloride ion and water molecule are disordered between two sites. One water and chloride alternately occupy the same site with occupancy factors of 0.5. The other 0.5-chloride and 0.5-water occupy two distinct positions separated by 0.747 (8) Å. In (II), the chloride ion is disordered between three sites and one of the waters is disordered about two other sites. Both crystal structures are stabilized by hydrogen bonds involving the chloride ions, amino groups and water molecules, as well as by π–π stacking between xanthene planes.

Comment

Rhodamine derivatives are lipophilic cationic dyes that have found wide use in tunable lasers and other electro-optical devices (Wittman *et al.*, 1992; Johnson & McGrane, 1993). Our interest in these compounds, however, is in their use and development as potential anticancer agents. Rhodamine-123 has been shown to be selectively taken up by mitochondria of tumor cells (Summerhayes *et al.*, 1982) and to suppress the growth of rat prostate tumor cells (Arcadi, 1998). These compounds are also substrates for P-glycoprotein, a membrane-bound protein that expels cytotoxic drugs from cells making them resistant to chemotherapy (Eytan *et al.*, 1997). The interactions of the rhodamine molecules with the different cellular components are dependent on the three-dimensional stereochemistries of both ligands and receptors. The two rhodamine structures presented here were determined to provide accurate three-dimensional data that may contribute to elucidating the stereochemical bases of their biological activity.



(I)



(II)

The conformations of (I) and (II) are shown in the displacement ellipsoid plot in Fig. 1. The 14 atoms of the xanthene rings define planes with r.m.s. deviations of the fitted atoms from the planes equal to 0.048 Å for (I) and 0.015 Å for (II). The dihedral angles between the xanthene planes and substituent phenyl-ring planes are 63.29 (8) and 87.96 (11)° in (I) and (II), respectively. These compare with values that range from 76.2 to 88.1° for reported structures of metal complexes of rhodamine-6g (Wang *et al.*, 1997; Liu *et al.*, 1998) and a value of 78.6° for an iodide hydrate of rhodamine-6g (Fun *et al.*, 1997). The ethylamine groups in (I) have similar orientations, with C2—N15—C23—C24 and C10—N16—C27—C28 torsion angles of 84.6 (4) and −76.5 (4)°, respectively. The C17—C18—C29—O30 torsion angle [35.3 (4)°] in (I) and the C17—C18—C23—O24 torsion angle [−2.8 (6)°] in (II) place the phenylcarbonyl groups pointing toward the xanthene rings. This contrasts with the opposite conformation for the phenylcarbonyl group found in the rhodamine–Cu complex (Liu *et al.*, 1998) and in the iodide hydrate (Fun *et al.*, 1997). Delocalization of the positive charge between the N atoms is indicated by the C2—N15 and C10—N16 distances, which show significant double-bond character. In (I), the C2—N15 and C10—N16 bond distances are 1.324 (3) and 1.339 (4) Å, respectively, and in (II), they are 1.343 (5) and 1.341 (5) Å. The short C2—N15 distance observed in (I) is also significantly shorter than equivalent partial double-bond distances found in the other rhodamine derivatives referenced above.

In (I), both amino N atoms are involved in hydrogen bonds to disordered Cl and water O atoms (Table 1). The disorder is unique in that 0.5-chlorine (Cl1) and 0.5-oxygen (O1*W*) share the same position. This position is hydrogen bonded to N16. The other 0.5-chlorine and 0.5-water oxygen started out

sharing a common second position but converged to two distinct sites (O2*W* and Cl2) during refinement. The site assigned to 0.5-water (O2*W*) makes contacts of 2.13 (1) and 2.798 (8) Å to center of symmetry related atoms $O2W^{i}$ and $Cl2^{i}$ [symmetry code: (i) $1-x, -y, 1-z$], respectively. The site occupied by Cl1 or O1*W* makes contacts of 2.814 (6) Å with $Cl2^{ii}$ and 3.276 (7) Å with $O2W^{ii}$ [symmetry code: (ii) $x, 1+y, 1+z$]. Because of the possible short $Cl1\cdots Cl2^{ii}$ and $O2W\cdots O2W^{i}$ contacts, it is proposed that when N16 is hydrogen bonded to Cl1, N15 is hydrogen bonded to O2*W*, and the center of symmetry related rhodamine-6g would have $N16^{i}$ hydrogen bonded to $O1W^{i}$ and $N15^{i}$ hydrogen bonded to $Cl2^{i}$. An equally probable opposite arrangement would occur in other unit cells, *i.e.* N16 hydrogen bonded to O1*W*, N15 hydrogen bonded to Cl2, $N16^{i}$ hydrogen bonded to $Cl1^{i}$ and $N15^{i}$ hydrogen bonded to $O2W^{i}$. In this way, the charge balance is maintained and all contacts between disordered sites are of the water oxygen–chloride ion hydrogen-bonded type. In addition, the average of the two possible arrangements of the disordered atoms taken over all unit cells preserves the centrosymmetric distribution of atoms.

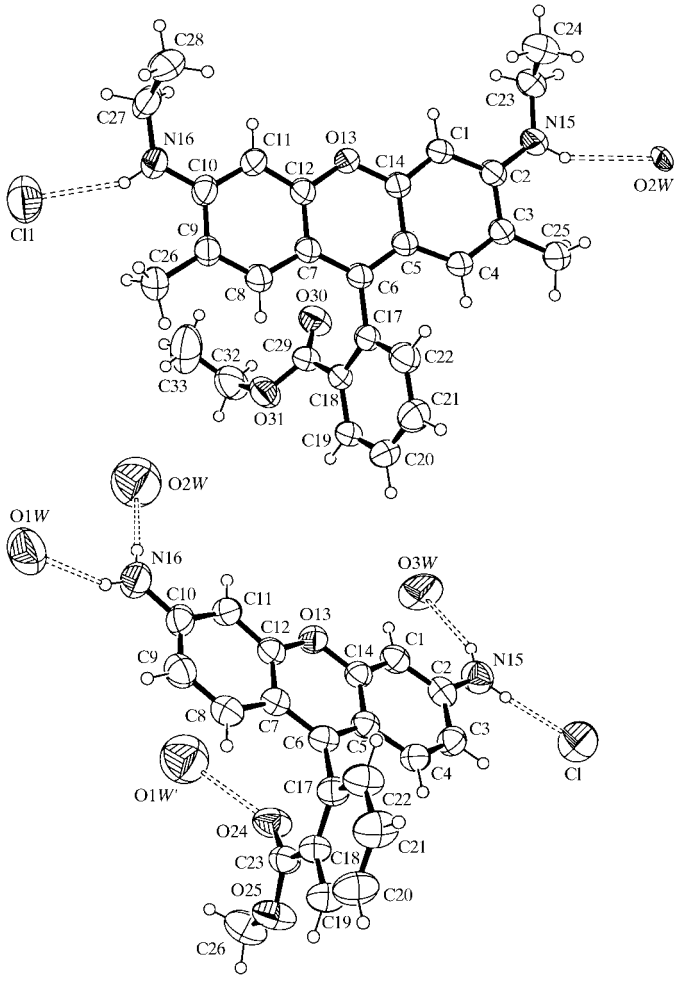


Figure 1
ORTEP-3 (Farrugia, 1997) view of (I) (top) and (II) (bottom) showing 40% probability displacement ellipsoids along with the numbering schemes. Hydrogen bonds to the rhodamine derivatives are represented by dashed bonds.

In (II), the chloride ion is disordered about one major site and two minor sites. The major site (occupancy factor = 0.68) is hydrogen bonded to N15 and one of the minor sites is hydrogen bonded to a water molecule. N15 is also hydrogen bonded to a disordered water O atom (occupancy = 0.5). N16 is hydrogen bonded to two water molecules and a symmetry-related water is hydrogen bonded to the phenylcarbonyl O atom (see Table 2).

The crystal lattices in these structures are also stabilized by π–π-stacking interactions of their xanthene rings. The perpendicular separations between their planes are 3.457 (4) Å in (I) and 3.445 (5) Å in (II).

Experimental

Compounds (I) and (II) were supplied by the Eastman–Kodak Company. Orange crystals of both compounds were obtained by slow evaporation of a methanol–ethanol–water mixture maintained at room temperature. Crystals of (II) were unstable in air and for data collection were sealed in capillary tubes with some mother liquor.

Compound (I)

Crystal data

$C_{28}H_{31}N_2O_3^{+}\cdot Cl^{-}\cdot H_2O$
$M_r = 496.46$
Triclinic, $P\overline{1}$
$a = 9.1947$ (13) Å
$b = 11.240$ (3) Å
$c = 13.1995$ (13) Å
$\alpha = 95.874$ (13)°
$\beta = 91.525$ (10)°
$\gamma = 102.63$ (2)°
$V = 1322.6$ (4) Å^3
$Z = 2$
$D_x = 1.243$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 8$–15°
$\mu = 0.18$ mm^{-1}
$T = 293$ (2) K
Plate, orange
0.6 × 0.4 × 0.4 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
4642 measured reflections
4642 independent reflections
3182 reflections with $I > 2\sigma(I)$
$\theta_{max} = 25.0°$
$h = -10 \rightarrow 10$
$k = -13 \rightarrow 13$
$l = 0 \rightarrow 15$
3 standard reflections
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.067$
$wR(F^2) = 0.217$
$S = 1.03$
4642 reflections
333 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1160P)^2 + 0.4678P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.33$ e Å^{-3}
$\Delta\rho_{min} = -0.26$ e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
N15—H15···Cl2	0.86	2.20	2.992 (5)	152
N15—H15···O2*W*	0.86	2.45	3.247 (7)	154
N16—H16···Cl1	0.86	2.34	3.133 (3)	154

Compound (II)

Crystal data

$C_{21}H_{17}N_2O_3^+\cdot Cl^-\cdot 3H_2O$
M_r = 434.88
Monoclinic, $C2/c$
a = 13.5624 (14) Å
b = 21.468 (3) Å
c = 15.427 (3) Å
β = 95.409 (12)°
V = 4471.5 (11) Å^3
Z = 8
D_x = 1.286 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 21 reflections
θ = 6–14°
μ = 0.21 mm^{-1}
T = 293 (2) K
Plate, orange
0.4 × 0.3 × 0.2 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
3924 measured reflections
3924 independent reflections
2256 reflections with $I > 2\sigma(I)$
θ_{max} = 25.0°
$h = 0 \rightarrow 16$
$k = 0 \rightarrow 25$
$l = -18 \rightarrow 18$
3 standard reflections
frequency: 180 min
intensity decay: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.072
$wR(F^2)$ = 0.268
S = 1.05
3924 reflections
314 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.1558P)^2 + 2.1805P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.005
$\Delta\rho_{max}$ = 0.41 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.0030 (8)

Table 2
Hydrogen-bonding geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
N15—H15A···O3W	0.86	2.34	3.140 (10)	156
N15—H15B···Cl^{i}	0.86	2.24	3.103 (5)	177
N16—H16A···O1W^{ii}	0.86	2.12	2.909 (5)	153
N16—H16B···O2W^{ii}	0.86	2.23	3.086 (7)	172
O1W—H1WA···O24^{iii}	0.95 (2)	1.97 (5)	2.810 (5)	146 (6)
O1W—H1WB···Cl	0.98 (2)	2.06 (2)	3.008 (5)	163 (5)
O2W—H2WA···Cl2A	0.99 (2)	1.88 (3)	2.861 (18)	170 (7)

Symmetry codes: (i) $\frac{1}{2}-x, \frac{1}{2}-y, -z$; (ii) $\frac{1}{2}-x, \frac{1}{2}-y, 1-z$; (iii) $\frac{1}{2}+x, \frac{1}{2}-y, z-\frac{1}{2}$.

Methyl group H-atom positions were located from difference Fourier maps, idealized and refined as riding atoms using *SHELXL*97 (Sheldrick, 1997) instructions, which also allowed for rotation about the C—C bonds. Isotropic displacement parameters for these atoms were assigned to a free variable which was refined. All other rhodamine H atoms were fixed geometrically and treated as riding atoms using *SHELXL*97 defaults. A second free variable was assigned to the displacement parameters for the amino and aromatic H atoms, a third for methylene H atoms and all were refined isotropically. The O1W and O2W H atoms in (II) were positioned based on hydrogen-bond geometry and restrained with *SHELXL*97 instructions *DFIX* and *DANG* [O—H = 0.95 (2) and H···H = 1.52 (4) Å]. H atoms on the disordered water molecules in (I) and (II) were not located. Occupancy factors for disordered atoms were estimated from electron-density maps and consideration of the refined displacement parameters.

For both compounds, data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *DATRDN* in *X-RAY*76 (Stewart *et al.*, 1976); program(s) used to solve structure: *MULTAN*80 (Main *et al.*, 1980); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1307). Services for accessing these data are described at the back of the journal.

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