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Tetramethyl 1,2-bis(2-aminophenoxy)-ethane-*N*,*N*,*N*′,*N*′-tetraacetate

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In this crystal structure, the methyl derivative of the BAPTA (bisaminophenol tetraacetic acid) ligand, $C_{26}H_{32}N_2O_{10}$, exhibits two molecular geometries. The asymmetric unit consists of one and one-half molecules. One molecule is located on a centre of inversion. The other has an interesting conformation between that of the first, and the geometry observed in a complex of a similar ligand.

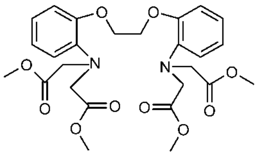
Key indicators

Single-crystal X-ray study
T = 120 K
Mean σ(C–C) = 0.002 Å
R factor = 0.047
wR factor = 0.128
Data-to-parameter ratio = 24.9

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Comment

Since the early 1980's, significant advances in the elucidation of the role that alkali-earth metal cations play in cellular biochemistry have been reported (Campbell, 1983). Calcium in particular has been shown to be intimately involved in many biological processes (Carafoli & Penniston, 1985). This research has been made possible by the development of optical sensor molecules capable of reporting the position of calcium cations within localized cellular domains. Tsien reported the first example of such a system, which was capable of monitoring intracellular calcium levels. The molecule bisaminophenol tetraacetic acid (BAPTA) showed a UV absorption shift on complexation with calcium (Tsien, 1980). After these initial studies, derivatives were synthesized capable of visualizing calcium concentrations using internal charge transfer fluorescence as the signalling response (Pozzan *et al.*, 1982; Tsien, 1989; Pozzan & Tsien, 1989). This led to the commercial promotion of such molecules, which are used widely within the biological community (Desilva *et al.*, 1997). We have previously reported similar sensor molecules which employ a photoinduced electron-transfer mechanism capable of 'switching on' fluorescence upon complexation of the calcium ion (Bissell *et al.*, 1992; Bissell *et al.*, 1993; Desilva *et al.*, 1995). BAPTA is the common feature within all of the calcium sensor molecules reported.



(I)

Despite the importance of the BAPTA ligand, no crystal structure of a derivative of the free ligand, or of the ligand coordinated to a metal has been reported. The single-crystal structure of a derivative of the BAPTA ligand, the FBAPTA ligand (BAPTA ligand with two F atoms in positions *para* to the N atoms) coordinated to a Ca^{2+} metal ion has been determined (Gerig *et al.*, 1987). In this complex, the octa-coordinate calcium ion is bonded to two ether O atoms, to four acetate carboxyl groups, and to two N atoms.

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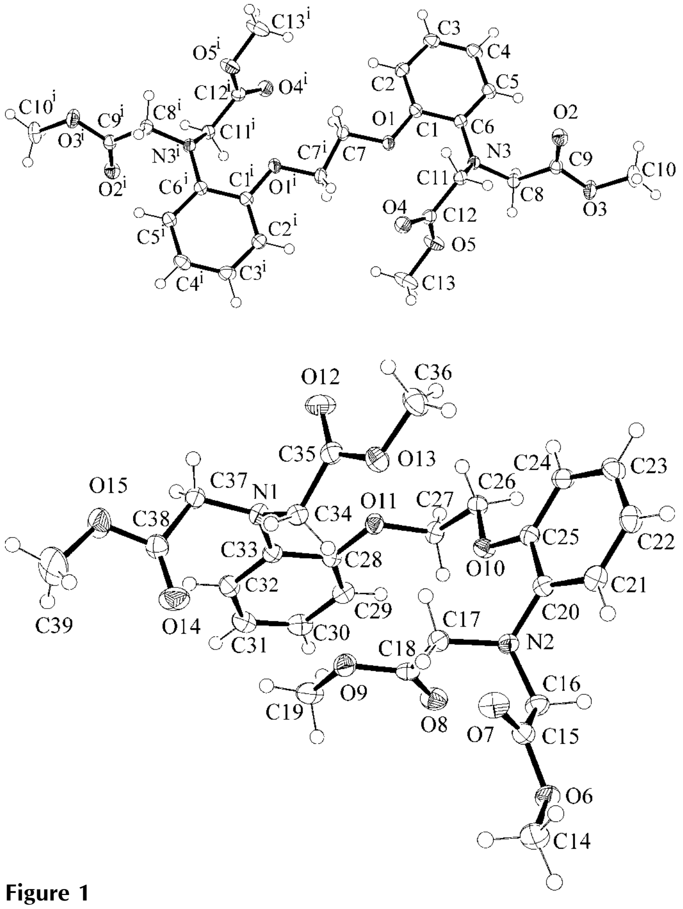

Figure 1

The molecular structure of (I), showing the atomic numbering scheme and ellipsoids at the 50% probability level (*ORTEP*-3; Farrugia, 1997). [Symmetry code (i): $-x$, $-y$, $-z$.]

We report here the structure of tetramethyl 1,2-bis(2-aminophenoxy)ethane-*N*,*N*,*N*′,*N*′-tetraacetate, (I), which crystallizes as two crystallographically different molecules. The two geometries are labelled *A* and *B*, and the numbering schemes and displacement ellipsoids are illustrated in Fig. 1. The asymmetric unit contains half a molecule of type *A* and one molecule of type *B*.

The type A molecule lies on an inversion centre that bisects the C7—C7^{i} bond [symmetry code: (i) $-x$, $-y$, $-z$], and atoms N3, N3^{i}, O1, O1^{i}, C7 and C7^{i} and the aromatic rings are coplanar with a standard uncertainty of 0.031 Å. In the central ethylene glycol moiety, the O1—C7—C7^{i}—O1^{i} torsion angle has a value of 179.98 (12)°. This value indicates an all-*trans* conformation which is expected for the uncomplexed ligand in solution (Desilva *et al.*, 1995). In solution, the complexed form displays a *gauche* bond in the ether part of the molecule, as observed in the structure of FBAPTA coordinated to Ca^{2+}. In this complex, the ethylene glycol segment has a torsion angle of 60.8°.

In the type B molecule, atoms N2 and O10 and the aromatic ring formed by atoms C20–C25 are coplanar with a standard uncertainty of 0.009 Å. In addition, atoms N1 and O11 and the aromatic ring consisting of atoms C28–C33 are coplanar, with a standard uncertainty of 0.011 Å. The angle between the two planes is 88.00 (4)°. For this conformation, the torsion angle O10—C26—C27—O11 has a value of 78.99 (12)°, indicating a conformation between that expected for the coordinated form and the uncoordinated form of the ligand in solution.

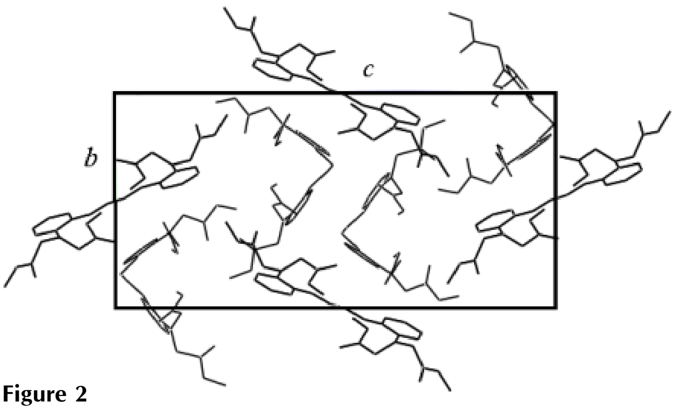

Figure 2

Packing diagram for (I), viewed down the *a* axis. Hydrogen atoms have been omitted (Mercury; Bruno *et al.*, 2002).

The three-dimensional packing of molecules is illustrated in Fig. 2. Viewed along the *a* axis, the two molecular conformations are evident. No π–π stacking interactions are observed and the shortest ring centroid-to-centroid distance is 4.8801 (15) Å.

Experimental

The title compound was synthesized according to the literature procedure of Tsien (1980) (m.p. = 360–362 K). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.78–6.91 (8H, *m*, ArH), 4.23 (4H, *s*, OCH_2), 4.13 (8H, *s*, NCH_2), 3.54 (12H, *s*, OMe) p.p.m.

Crystal data

$C_{26}H_{32}N_2O_{10}$
$M_r = 532.54$
Monoclinic, $P2_1/c$
$a = 11.201$ (3) Å
$b = 13.187$ (3) Å
$c = 27.217$ (5) Å
$\beta = 91.390$ (17)°
$V = 4019.0$ (16) Å^3
$Z = 6$

$D_x = 1.320$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 229 reflections
$\theta = 2$–31°
$\mu = 0.10$ mm^{-1}
$T = 120$ (2) K
Block, colourless
0.40 × 0.40 × 0.30 mm

Data collection

Oxford Excalibur2 diffractometer
ω–2θ scans
Absorption correction: none
36677 measured reflections
12774 independent reflections
9331 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.031$
$\theta_{\rm max} = 31.9°$
$h = -16 \rightarrow 15$
$k = -17 \rightarrow 19$
$l = -40 \rightarrow 39$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.047$
$wR(F^2) = 0.128$
$S = 1.08$
12774 reflections
514 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0581P)^2 + 0.8495P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} = 0.001$
$\Delta\rho_{\rm max} = 0.33$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.27$ e Å^{-3}

All H atoms were placed in calculated positions and refined using a riding model (C—H = 0.96–0.97 Å; $U_{\rm iso} = 1.2$ or $1.5U_{\rm eq}$ of the parent atom.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2003); cell refinement: *CrysAlis CCD*; data reduction: *CrysAlis RED* (Oxford Diffraction, 2003); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997) and *Mercury* (Bruno *et al.*, 2002); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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