Crystal structure and molecular docking study of diethyl 2,2′-[[[(1E,1′E)-(hydrazine-1,2-diyldiene)-bis(methanylylidene)]bis(4,1-phenylene)]bis(oxy)]-diacetate

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The title Schiff base, C22H24N2O6, adopts an E configuration. The molecule is planar, the mean planes of the phenyl ring system (r.m.s deviation = 0.0059 Å) forms a dihedral angle of 0.96 (4)° with the mean plane of the phenyl ring moiety (r.m.s deviation = 0.0076 Å). In the crystal, molecules are linked by weak intermolecular C—H···O and C—H···N hydrogen bonds into chains extending along the c-axis and b-axis directions, respectively. A molecular docking study between the title molecule and 5-HT2C, which is a G protein receptor and ligand-gated ion channels found in nervous systems (PDB ID: 6BQH) was executed. The experiment shows that it is a good potential agent because of its affinity and ability to stick to the active sites of the receptor.

1. Chemical context

Compounds with an azomethine group (–C=N–) are known as Schiff bases, which are usually synthesized from the condensation of active carbonyl groups and primary amines (Yang et al., 2001). Furthermore, these derivatives represent an important class of organic compounds, especially in the medicinal and pharmaceutical fields (Murtaza et al., 2014). It is well known from the literature that Schiff bases display excellent biological properties, such as antioxidant and analgesic (Karrouchi et al., 2016), antibacterial and cytotoxic (Maaref et al., 2020), antidiabetic (Karrouchi et al., 2022) and anti-inflammatory activities (Rana et al., 2012). These derivatives are also used as corrosion inhibitors, which relies on their ability to spontaneously form a monolayer on the surface being protected (El Arrouji et al., 2020). In this study, the title compound, diethyl 2,2′-[[[(1E,1′E)-(hydrazine-1,2-diyldiene)-bis(methanylylidene)]bis(4,1-phenylene)]bis(oxy)]-diacetate, was characterized by single crystal X-ray and studied by Hirshfeld surface analysis.
2. Structural commentary

The molecular structure of the title compound is illustrated in Fig. 1. The asymmetric unit contains one independent molecule, which is planar, the mean plane of the C5–C10 phenyl ring (r.m.s deviation = 0.006 Å) forms a dihedral angle of 0.96° with the mean plane of the C16–C20 phenyl ring (r.m.s deviation = 0.008 Å). The C3—O1 and C14—O4 bond lengths in the molecule are 1.213 (8) and 1.212 (8) Å, respectively, while the C11—N1 and C22—N2 bond lengths are 1.274 (7) and 1.275 (7) Å, respectively (Table 1). These results suggest a double-bond character for the C=C bond, is slightly longer than observed for the title compound C10—C11 bond distance of 1.516 (2) Å in WIHDEY, corresponding to a single bond, is slightly longer than observed for the title compound [C3—C4 = 1.493 (10) Å]. This bond length is also longer than in XEWZIJ [C18–C19 = 1.498 (3) Å; Baolin et al., 2013] and 6BQH with a value of 4.38 (8)°. The C10—C11 bond distance of 1.516 (2) Å in WIHDEY, corresponding to a single bond, is slightly longer than observed for the title compound [C3—C4 = 1.498 (10) Å]. This bond length is also longer than in XEWZIJ [C18–C19 = 1.493 (3) Å; Baolin et al., 2007]).

3. Supramolecular features

In the crystal, there are two intermolecular hydrogen bonds. The C6—H6⋅⋅⋅O4′ hydrogen bond links the molecules to each other along the c-axis direction while the C4—H4B⋅⋅⋅N1ii hydrogen bond links the molecules to each other along the b-axis direction (symmetry codes as in Table 1). A view of the crystal packing is shown in Fig. 2.

4. Database survey

A search of the Cambridge Structural Database (CSD, version 5.42, update of May 2021; Groom et al., 2016) for the ethyl 2-(p-tolyloxy)acetate skeleton revealed seven similar compounds, viz: ethyl [4-[(4-bromophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-4-ylaminomethyl]phenoxyacetate (EKEYEY; Thamotharan et al., 2003), di[3-fluoro-6-methoxy-4-(ethoxycarbonylmethoxy)benzyl] ether (HIGLEP; Wallner et al., 2007), ethyl (2-fluoro-4-hydroxymethyl-5-methoxy-phenoxy)acetate (HIGLIT; Wallner et al., 2007), diethyl 3,3-bis[3-[4-(2-ethoxy-2-oxoethoxy)-3-methoxyphenyl]acryloyl]-pentanediol (JUMJEI; Xu et al., 2015), ethyl (4-[3-[2,4-bis[2-ethoxy-2-oxoethoxy]phenyl]-3-oxoprop-1-en-1-yl]phenoxy)acetate (PIXWAW; Liu, 2014), ethyl [2-oxo-2H-chromen-7-yl]oxacylate (WIHDEY; Fun et al., 2013) and ethyl [4-{[(E)-2-(3,4,5-trimethoxyphenyl)vinyl]phenoxy}acetate (XEWZIJ; Baolin et al., 2007). In EKEYEY, the ethoxycarbonyl group is oriented at an angle of 29.42 (15)° with respect to the mean plane of the benzene ring. The mean plane of the 2H-chromene ring system (O1/C1–C9, r.m.s deviation = 0.026 Å) forms a dihedral angle of 81.71 (6)° with the mean plane of ethyl 2-hydroxyacetate moiety (O1/N3/C9/C10, r.m.s deviation = 0.026 Å) in WIHDEY. This dihedral angle for the title compound is smaller than in both EKEYEY and WIHDEY with a value of 4.38 (8)°. The C10—C11 bond distance of 1.516 (2) Å in WIHDEY, corresponding to a single bond, is slightly longer than observed for the title compound [C3—C4 = 1.498 (10) Å]. This bond length is also longer than in XEWZIJ [C18–C19 = 1.493 (3) Å; Baolin et al., 2007]).

5. Molecular docking study

Molecular docking is a substantial process for finding the interactions between small molecules and macromolecules. Intermolecular bonds that occur between ligand and receptor are indicated by molecular docking. In this study, AutoDockVina (Trott & Olson, 2010) was used for predictive binding sites between the title molecule and the 5-HT2C receptor (Peng et al., 2018). 6BQH is a serotonin receptor, which can be efficient for designing drugs to treat ailments.
such as anxiety, aggression, sleep disorders, and other psychological diseases. The three-dimensional structure of 6BQH was taken from the Protein Data Bank (PDB). Before the docking calculations, the receptor must be prepared for efficient insertion. For this reason, all water and ligand molecules were cleared on receptor active sites. According to these active sites, grid box dimensions were defined as $100 \times 80 \times 110 \, \AA$. In addition, $x, y, z$ centres were adjusted to be $-40.569, 33.142, 45.392$, respectively, and then the 5-HT2C receptor was saved in PDBQT format for the calculations. In the next step, rotatable angles for the coupling structure were determined and recorded in PDBQT format. Discovery Studio Visualizer (Biovia, 2017) was used for observations and preparations. All docking calculations were calculated with AutoDockVina. Twenty variable links were decided by AutoDockVina for the ligands connected to the receptor of the protein. The best affinity energy was observed in the first calculation, which is $-6.2 \text{ kcal mol}^{-1}$. The bonding type of interaction is represented in Fig. 3. The 2D and 3D visuals of the intermolecular interactions for the best binding pose of the title compound docked into macromolecule 6BQH can be seen in Fig. 4. In addition, docking conformation can be seen in Fig. 5. Consequently, the title compound could be a possible molecule for drug design to treat psychological disorders, because its ability is suitable to stick to active sites of the receptor.

6. Synthesis and crystallization

Hydrazine hydrate (0.013 g, 0.24 mmol) was added dropwise to a solution of ethyl 2-(4-formylphenoxy)acetate (0.5 g, 0.48 mmol) in ethanol (20 ml), and the mixture was refluxed for 4 h. After cooling, the solvent was removed under reduced pressure, and the residue was purified by recrystallization from ethanol to afford single crystals (yield 80%).

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2. C-bound H atoms were positioned geometrically and refined using a riding model with C−H = 0.93–0.97 Å and $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl H atoms, and $U_{iso}(H) = 1.2U_{eq}(C)$ for all other H atoms. The crystal studied was refined as a two-component inversion twin, but the absolute structure was indeterminate.

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Author contributions are as follows. Conceptualization, SD, SK, and KK; synthesis, SD and KK; writing (review and editing of the manuscript) SD, SK, FAA and KK; formal analysis, SD, KK and NB; crystal-structure determination, KK, SK and ND; validation, KK, ES and NB; project administration, KK, SD, ES and SK; molecular docking, FAA.
Table 2
Experimental details.

| Crystal data | Chemical formula | C_{22}H_{24}N_{2}O_{6} |
|---------------|------------------|------------------------|
| M, (g/mol)    | 412.43           |                        |
| Crystal system, space group | Orthorhombic, P2\_2\_2; |
| Temperature (K) | 296              |                        |
| a, b, c (Å)    | 8.1864 (4), 9.2061 (5), 27.7903 (18) | |
| V (Å³)         | 2094.4 (2)       |                        |
| No. of measured, independent and observed [I > 2σ(I)] reflections | 0.945, 0.979 |
| No. of parameters | 254              |                        |
| No. of reflections | 4091             | 2453                   |
| R_{int} | 0.037            |                        |
| (sin θ/λ)_{max} (Å\(^{-1}\)) | 0.617            |                        |
| R[F^2 > 2σ(F^2)], wR(F^2), S | 0.073, 0.246, 1.01                |
| No. of reflections | 4091             |                        |
| No. of parameters | 254              |                        |
| H-atom treatment | H-atom parameters constrained |                        |
| Δρ_{max}, Δρ_{min} (e Å\(^{-3}\)) | 0.50, −0.67        |
| Absolute structure | Refined as an inversion twin, but the absolute structure was indeterminate | |

Absolute structure parameter −1 (4)

Computer programs: X-AREA and X-RED (Stoe & Cie, 2002), SHELXT2016/1 (Sheldrick, 2016a), SHELXL2017/1 (Sheldrick, 2016b), PLATON (Spek, 2020) and WinGX (Farrugia, 2012).

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Crystal structure and molecular docking study of diethyl 2,2'-([(1E,1' E)-(hydrazine-1,2-diylidene)bis(methanylylidene)]bis(4,1-phenylene))bis(oxy))diacetate

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Computing details

Data collection: X-AREA (Stoe & Cie, 2002); cell refinement: X-AREA (Stoe & Cie, 2002); data reduction: X-RED (Stoe & Cie, 2002); program(s) used to solve structure: SHELXT2017/1 (Sheldrick, 2015a); program(s) used to refine structure: SHELXL2017/1 (Sheldrick, 2015b); molecular graphics: PLATON (Spek, 2020); software used to prepare material for publication: WinGX (Farrugia, 2012).

Diethyl 2,2'-([(1E,1' E)-(hydrazine-1,2-diylidene)bis(methanylylidene)]bis(4,1-phenylene))bis(oxy))diacetate

Crystal data

C22H24N2O6  
Mr = 412.43  
Orthorhombic, P212121  
a = 8.1864 (4) Å  
b = 9.2061 (5) Å  
c = 27.7903 (18) Å  
V = 2094.4 (2) Å³  
Z = 4  
F(000) = 872  

Dₐ = 1.308 Mg m⁻³  
Mo Ka radiation, λ = 0.71073 Å  
Cell parameters from 9754 reflections  
θ = 2.2°-27.8°  
µ = 0.10 mm⁻¹  
T = 296 K  
Prism, colorless  
0.68 x 0.44 x 0.22 mm

Data collection

Stoe IPDS 2  
diffractometer  
Radiation source: sealed X-ray tube, 12 x 0.4 mm long-focus  
Detector resolution: 6.67 pixels mm⁻¹  
rotation method scans  
Absorption correction: integration  
(X-RED32; Stoe & Cie, 2002)  
Tmin = 0.945, Tmax = 0.979  
11156 measured reflections  
4091 independent reflections  
2453 reflections with I > 2σ(I)  
Rint = 0.037  
θmax = 26.0°, θmin = 2.3°  
h = −8→10  
k = −11→11  
l = −27→34

Refinement

Refinement on F²  
Least-squares matrix: full  
R[F² > 2σ(F²)] = 0.073  
wR(F²) = 0.246  
S = 1.00  
4091 reflections  
254 parameters  
2 restraints  
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained

\[ w = \frac{1}{\sigma^2(F_o^2) + (0.1576P)^2} \]

where \( P = (F_o^2 + 2F_c^2)/3 \)

\( (\Delta\sigma)_{\text{max}} < 0.001 \)

\[ \Delta \rho_{\text{max}} = 0.50 \text{ e Å}^{-3} \]

\[ \Delta \rho_{\text{min}} = -0.67 \text{ e Å}^{-3} \]

Absolute structure: Refined as an inversion twin

Absolute structure parameter: \(-1 (4)\)

**Special details**

**Geometry.** All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

**Refinement.** Refined as a 2-component inversion twin.

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**Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)**

|   | x     | y     | z     | Uiso #/Ueq |
|---|-------|-------|-------|------------|
| O6| 0.4659 (6) | −0.4221 (5) | −0.88303 (18) | 0.0861 (14) |
| O3| −0.9934 (5) | −0.3444 (5) | −0.61477 (18) | 0.0815 (13) |
| N2| −0.1980 (6) | −0.3968 (4) | −0.76468 (19) | 0.0658 (12) |
| O2| −1.2412 (6) | −0.2842 (6) | −0.5611 (2) | 0.0968 (15) |
| N1| −0.3161 (6) | −0.3494 (5) | −0.73078 (19) | 0.0671 (13) |
| O4| 0.7008 (8) | −0.4943 (6) | −0.9435 (2) | 0.122 (2) |
| O5| 0.8443 (9) | −0.2982 (8) | −0.9259 (3) | 0.145 (2) |
| O1| −1.3702 (7) | −0.4910 (7) | −0.5761 (2) | 0.123 (2) |
| C19| 0.0707 (7) | −0.3464 (5) | −0.61495 (2) | 0.0587 (13) |
| C8| −0.5825 (7) | −0.4041 (5) | −0.7005 (2) | 0.0590 (13) |
| C3| −1.2583 (9) | −0.4068 (9) | −0.5824 (3) | 0.090 (2) |
| C5| −0.8617 (7) | −0.3742 (6) | −0.6434 (2) | 0.0659 (15) |
| C16| 0.3406 (8) | −0.3906 (6) | −0.8529 (2) | 0.0656 (15) |
| C11| −0.4446 (7) | −0.4275 (5) | −0.7311 (2) | 0.0618 (14) |
| H11| −0.448969 | −0.504718 | −0.752671 | 0.074* |
| C9| −0.7122 (7) | −0.5040 (6) | −0.7029 (2) | 0.0689 (15) |
| H9| −0.705537 | −0.581369 | −0.724270 | 0.083* |
| C18| 0.2009 (7) | −0.2516 (5) | −0.7937 (2) | 0.0665 (15) |
| H18| 0.198036 | −0.172160 | −0.773028 | 0.079* |
| C17| 0.3358 (7) | −0.2717 (6) | −0.8230 (2) | 0.0677 (15) |
| H17| 0.421932 | −0.205814 | −0.822424 | 0.081* |
| C10| −0.8487 (7) | −0.4902 (6) | −0.6743 (2) | 0.0677 (15) |
| H10| −0.931717 | −0.558927 | −0.675966 | 0.081* |
| C22| −0.0682 (7) | −0.3205 (5) | −0.7625 (2) | 0.0617 (14) |
| H22| −0.061751 | −0.246143 | −0.739922 | 0.074* |
| C20| 0.0776 (9) | −0.4663 (5) | −0.8255 (2) | 0.0710 (16) |
| H20| −0.009621 | −0.530867 | −0.827039 | 0.085* |
| C6| −0.7324 (8) | −0.2740 (6) | −0.6404 (2) | 0.0764 (17) |
| H6| −0.739197 | −0.196246 | −0.619141 | 0.092* |
| C21| 0.2131 (8) | −0.4884 (6) | −0.8537 (2) | 0.0756 (17) |
| H21| 0.218970 | −0.569887 | −0.873361 | 0.091* |
| C4| −1.1264 (9) | −0.4449 (8) | −0.6175 (3) | 0.0857 (19) |
| H4A| −1.086821 | −0.542135 | −0.610821 | 0.103* |
| H4B| −1.171001 | −0.444297 | −0.649865 | 0.103* |
| Atom | X        | Y        | Z        | U11     | U22     | U33     |
|------|----------|----------|----------|---------|---------|---------|
| C7   | -0.5976  | -0.2901  | -0.6684  | 0.0711  |
| H7   | -0.5133  | -0.2227  | -0.6659  | 0.085*  |
| C14  | 0.7176   | -0.3829  | -0.9207  | 0.0848  |
| C15  | 0.6016   | -0.3258  | -0.8849  | 0.0785  |
| H15A | 0.6535   | -0.3200  | -0.8535  | 0.094*  |
| H15B | 0.5658   | -0.2924  | -0.8940  | 0.094*  |
| C12  | 0.9676   | -0.3616  | -0.9585  | 0.145   |
| H12A | 1.0240   | -0.4405  | -0.9424  | 0.175*  |
| H12B | 0.9145   | -0.4001  | -0.9869  | 0.175*  |
| C13  | 1.0808   | -0.2527  | -0.9718  | 0.145   |
| H13A | 1.1612   | -0.2935  | -0.9930  | 0.218*  |
| H13B | 1.0244   | -0.1752  | -0.9879  | 0.218*  |
| H13C | 1.1336   | -0.2156  | -0.9435  | 0.218*  |
| C2   | -1.3727  | -0.2480  | -0.5256  | 0.139   |
| H2A  | -1.3819  | -0.3237  | -0.5014  | 0.167*  |
| H2B  | -1.4771  | -0.2374  | -0.5416  | 0.167*  |
| C1   | -1.3215  | -0.1070  | -0.5029  | 0.139   |
| H1A  | -1.4015  | -0.0779  | -0.4795  | 0.209*  |
| H1B  | -1.2177  | -0.1193  | -0.4873  | 0.209*  |
| H1C  | -1.3123  | -0.0337  | -0.5273  | 0.209*  |

**Atomic displacement parameters (Å²)**

| Atom | U11     | U22     | U33     | U12     | U13     | U23     |
|------|---------|---------|---------|---------|---------|---------|
| O6   | 0.080   | 0.089   | 0.089   | 0.000   | 0.019   | -0.013  |
| O3   | 0.069   | 0.093   | 0.082   | -0.014  | 0.010   | -0.004  |
| N2   | 0.066   | 0.055   | 0.076   | 0.001   | -0.002  | -0.001  |
| O2   | 0.077   | 0.097   | 0.117   | 0.014   | 0.032   | 0.019   |
| N1   | 0.063   | 0.063   | 0.076   | 0.001   | 0.005   | 0.000   |
| O4   | 0.132   | 0.109   | 0.124   | 0.004   | 0.050   | -0.017  |
| O5   | 0.118   | 0.160   | 0.159   | -0.008  | 0.057   | -0.021  |
| O1   | 0.091   | 0.144   | 0.133   | -0.035  | 0.027   | 0.004   |
| C19  | 0.060   | 0.051   | 0.065   | 0.004   | -0.002  | 0.002   |
| C8   | 0.059   | 0.054   | 0.064   | 0.003   | -0.005  | 0.004   |
| C3   | 0.071   | 0.096   | 0.102   | -0.003  | -0.002  | 0.034   |
| C5   | 0.056   | 0.071   | 0.071   | 0.003   | 0.004   | 0.008   |
| C16  | 0.068   | 0.063   | 0.066   | 0.002   | 0.002   | -0.001  |
| C11  | 0.066   | 0.052   | 0.067   | 0.005   | -0.010  | 0.004   |
| C9   | 0.064   | 0.064   | 0.079   | -0.005  | -0.006  | -0.008  |
| C18  | 0.062   | 0.056   | 0.078   | 0.006   | 0.001   | -0.005  |
| C17  | 0.064   | 0.063   | 0.077   | -0.002  | -0.004  | -0.003  |
| C10  | 0.061   | 0.064   | 0.078   | -0.016  | -0.001  | -0.007  |
| C22  | 0.062   | 0.047   | 0.076   | -0.002  | -0.002  | -0.003  |
| C20  | 0.075   | 0.056   | 0.082   | -0.006  | -0.001  | -0.001  |
| C6   | 0.075   | 0.069   | 0.085   | -0.003  | 0.002   | -0.018  |
| C21  | 0.082   | 0.062   | 0.083   | -0.006  | 0.009   | -0.015  |
| C4   | 0.079   | 0.099   | 0.079   | -0.018  | 0.004   | 0.007   |
| C7   | 0.064   | 0.060   | 0.089   | -0.007  | -0.007  | -0.004  |
### Geometric parameters (Å, °)

| Bond                   | Distance   | Angle        |
|-----------------------|------------|--------------|
| O6—C16                | 1.355 (7)  | C18—H18     | 0.9300 |
| O6—C15                | 1.422 (8)  | C17—H17     | 0.9300 |
| O3—C5                 | 1.367 (7)  | C10—H10     | 0.9300 |
| O3—C4                 | 1.432 (8)  | C22—H22     | 0.9300 |
| N2—C22                | 1.275 (7)  | C20—C21     | 1.372 (9) |
| N2—N1                 | 1.419 (7)  | C20—H20     | 0.9300 |
| O2—C3                 | 1.282 (9)  | C6—C7       | 1.359 (9) |
| O2—C2                 | 1.497 (10) | C6—H6       | 0.9300 |
| N1—C11                | 1.274 (7)  | C21—H21     | 0.9300 |
| O4—C14                | 1.212 (8)  | C4—H4A      | 0.9700 |
| O5—C14                | 1.306 (9)  | C4—H4B      | 0.9700 |
| O5—C12                | 1.477 (10) | C7—H7       | 0.9300 |
| O1—C3                 | 1.213 (8)  | C14—C15     | 1.474 (9) |
| C19—C18               | 1.378 (7)  | C15—H15A    | 0.9700 |
| C19—C20               | 1.403 (8)  | C15—H15B    | 0.9700 |
| C19—C22               | 1.463 (8)  | C12—C13     | 1.415 (10) |
| C8—C7                 | 1.382 (8)  | C12—H12A    | 0.9700 |
| C8—C9                 | 1.406 (8)  | C12—H12B    | 0.9700 |
| C8—C11                | 1.431 (8)  | C13—H13A    | 0.9600 |
| C3—C4                 | 1.498 (10) | C13—H13B    | 0.9600 |
| C5—C10                | 1.375 (8)  | C13—H13C    | 0.9600 |
| C5—C6                 | 1.407 (8)  | C2—C1       | 1.502 (10) |
| C16—C17               | 1.375 (8)  | C2—H2A      | 0.9700 |
| C16—C21               | 1.379 (8)  | C2—H2B      | 0.9700 |
| C11—H11               | 0.9300     | C1—H1A      | 0.9600 |
| C9—C10                | 1.376 (8)  | C1—H1B      | 0.9600 |
| C9—H9                 | 0.9300     | C1—H1C      | 0.9600 |
| C18—C17               | 1.385 (8)  |              |        |

| Bond                   | Distance   | Angle        |
|-----------------------|------------|--------------|
| C16—O6—C15            | 118.7 (5)  | C20—C21—C16 | 120.4 (5) |
| C5—O3—C4              | 116.0 (5)  | C20—C21—H21 | 119.8   |
| C22—N2—N1             | 111.5 (5)  | C16—C21—H21 | 119.8   |
| C3—O2—C2              | 114.9 (6)  | O3—C4—C3    | 111.2 (6) |
| C11—N1—N2             | 112.6 (4)  | O3—C4—H4A   | 109.4   |
| C14—O5—C12            | 112.0 (7)  | C3—C4—H4A   | 109.4   |
| C18—C19—C20           | 118.5 (5)  | O3—C4—H4B   | 109.4   |
| C18—C19—C22           | 119.3 (5)  | C3—C4—H4B   | 109.4   |
| C20—C19—C22           | 122.2 (5)  | H4A—C4—H4B  | 108.0   |
| C7—C8—C9              | 117.4 (6)  | C6—C7—C8    | 121.6 (6) |
| Bond                     | Length (Å) | Bond                     | Length (Å) |
|--------------------------|------------|--------------------------|------------|
| C7—C8—C11                | 1.246 (5)  | C6—C7—H7                | 1.192      |
| C9—C8—C11                | 1.280 (5)  | C8—C7—H7                | 1.192      |
| O1—C3—O2                 | 1.025 (8)  | O4—C14—O5               | 1.122 (6)  |
| O1—C3—C4                 | 1.202 (8)  | O4—C14—C15              | 1.125 (7)  |
| O2—C3—C4                 | 1.154 (6)  | O5—C14—C15              | 0.1119 (6) |
| O3—C5—C10                | 1.255 (5)  | O6—C15—C14              | 1.078 (6)  |
| O3—C5—C6                 | 1.153 (5)  | O6—C15—H15A             | 1.101      |
| C10—C5—C6                | 1.192 (6)  | C14—C15—H15A            | 1.101      |
| O6—C16—C17               | 1.244 (6)  | O6—C15—H15B             | 1.101      |
| O6—C16—C21               | 1.195 (5)  | C14—C15—H15B            | 1.101      |
| C17—C16—C21              | 1.200 (6)  | H15A—C15—H15B           | 1.085      |
| N1—C11—C8                | 1.242 (5)  | C13—C12—O5              | 1.1092 (8) |
| N1—C11—H11               | 1.179      | C13—C12—H12A            | 1.098      |
| C8—C11—H11               | 1.179      | O5—C12—H12A             | 1.098      |
| C10—C9—C8                | 1.217 (5)  | C13—C12—H12B            | 1.098      |
| C10—C9—H9                | 1.191      | O5—C12—H12B             | 1.098      |
| C8—C9—H9                 | 1.191      | H12A—C12—H12B           | 1.083      |
| C19—C18—C17              | 1.216 (5)  | C12+C13—H13A            | 1.095      |
| C19—C18—H18              | 1.192      | C12+C13—H13B            | 1.095      |
| C17—C18—H18              | 1.192      | H13A—C13—H13B           | 1.095      |
| C16—C17—C18              | 1.190 (6)  | C12+C13—H13C            | 1.095      |
| C16—C17—H17              | 1.205      | H13A—C13—H13C           | 1.095      |
| C18—C17—H17              | 1.205      | H13B—C13—H13C           | 1.095      |
| C5—C10—C9                | 1.197 (5)  | O2—C2—C1                | 1.055 (8)  |
| C5—C10—H10               | 1.202      | O2—C2—H2A               | 1.106      |
| C9—C10—H10               | 1.202      | C1—C2—H2A               | 1.106      |
| N2—C22—C19               | 1.220 (5)  | O2—C2—H2B               | 1.106      |
| N2—C22—H22               | 1.190      | C1—C2—H2B               | 1.106      |
| C19—C22—H22              | 1.190      | H2A—C2—H2B              | 1.088      |
| C21—C20—C19              | 1.200 (6)  | C2—C1—H1A               | 1.095      |
| C21—C20—H20              | 1.200      | C2—C1—H1B               | 1.095      |
| C19—C20—H20              | 1.200      | H1A—C1—H1B              | 1.095      |
| C7—C6—C5                 | 1.204 (5)  | C2—C1—H1C               | 1.095      |
| C7—C6—H6                 | 1.198      | H1A—C1—H1C              | 1.095      |
| C5—C6—H6                 | 1.198      | H1B—C1—H1C              | 1.095      |

**C22—N2—N1—C11** -1.177.6 (5) **C20—C19—C22—N2** -0.075 (8)

**C2—O2—C3—O1** 0.7 (11) **C18—C19—C20—C21** 1.1 (8)

**C2—O2—C3—C4** -1.179.3 (7) **C22—C19—C20—C21** -1.177.9 (6)

**C4—O3—C5—C10** 0.8 (9) **O3—C5—C6—C7** -1.177.8 (6)

**C4—O3—C5—C6** 1.179.7 (5) **C10—C5—C6—C7** 1.12 (9)

**C15—O6—C16—C17** -1.0 (9) **C19—C20—C21—C16** -2.3 (9)

**C15—O6—C16—C21** 1.179.3 (5) **O6—C16—C21—C20** -1.178.5 (6)

**N2—N1—C11—C8** 1.179.8 (5) **C17—C16—C21—C20** 1.18 (9)

**C7—C8—C11—N1** 3.4 (9) **C5—O3—C4—C3** 1.176.2 (5)

**C9—C8—C11—N1** -1.176.4 (5) **O1—C3—C4—O3** -1.171.2 (6)

**C7—C8—C9—C10** -0.4 (8) **O2—C3—C4—O3** 8.8 (9)

**C11—C8—C9—C10** 1.179.4 (5) **C5—C6—C7—C8** 0.0 (10)
C20—C19—C18—C17 0.6 (8)  C9—C8—C7—C6  −0.4 (9)
C22—C19—C18—C17 179.6 (5)  C11—C8—C7—C6  179.8 (5)
O6—C16—C17—C18  −179.8 (5)  C12—O5—C14—O4  −5.3 (13)
C21—C16—C17—C18  −0.1 (9)  C12—O5—C14—C15  174.9 (8)
C19—C18—C17—C16  −1.1 (9)  C16—O6—C15—C14  −178.8 (5)
O3—C5—C10—C9  176.9 (6)  O4—C14—C15—O6  −1.8 (11)
C6—C5—C10—C9  −2.0 (9)  O5—C14—C15—O6  178.0 (6)
C8—C9—C10—C5  1.6 (9)  C14—O5—C12—C13  165.9 (10)
N1—N2—C22—C19  −178.9 (5)  C3—O2—C2—C1  176.1 (8)
C18—C19—C22—N2  173.6 (5)

Hydrogen-bond geometry (Å, º)

| D—H···A     | D—H | H···A | D···A | D—H···A |
|------------|------|-------|-------|--------|
| C6—H6···O4' | 0.93 | 2.57  | 3.483 (9) | 169     |
| C4—H4B···N1' | 0.97 | 2.69  | 3.618 (10) | 161     |

Symmetry codes: (i) −x, y+1/2, −z−3/2; (ii) x−1, y, z.