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(E,E)-3-Methyl-2,5-bis(4-methylbenzylidene)cyclopentanone: synthesis, characterization, Hirshfeld surface analysis and antibacterial activity

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The title compound, (E,E)-3-methyl-2,5-bis(4-methylbenzylidene)cyclopentanone (MBMCP), C22H22O, was obtained by Claisen–Schmidt condensation of 4-methylbenzaldehyde with 3-methylcyclopentanone in good yield. The structure of MBMCP was studied using UV, FT–IR and Raman spectroscopy, single-crystal X-ray diffraction (XRD) measurements, and 1H and 13C nuclear magnetic resonance (NMR) spectroscopy. The molecular structure of MBMCP is fully extended in the E,E configuration. C—H · · · H stacking interactions play a significant role in the stabilization of the molecular packing. Hirshfeld surface analysis was used to quantify the non-covalent interactions in the crystal lattice. Microbiological studies were performed to investigate the antimicrobial activity of this new product.

1. Chemical context

The Claisen–Schmidt reaction has great importance in the synthesis of organic compounds (Rajput & Kaur, 2012), in particular in the synthesis of bis(substituted-benzylidene)cycloalkanones. This reaction is catalysed using strong acids (Dhar & Barton, 1981; Gall et al., 1999) and base with or without solvents (Geissman & Clinton, 1946; Shan et al., 2010). Recently, animal bone meal was used as a catalyst for crossed-aldol condensation (Riadi et al., 2010). The preparation of β-chloro, β-bromo and α,β-unsaturated ketones from β-diketones has been carried out using Vilsmeier reagents (Mewshaw et al., 1989). Numerous α,α'-bis(substituted-benzylidene)cycloalkanones exhibit biological activities (Robinson et al., 2005; Piantadosi et al., 1973). Furthermore, they are used as precursors for the preparation of biologically active heterocyclic compounds, such as pyrimidines (Deli et al., 1984; Guilford et al., 1999) and pyrazolines (Ziani et al., 2013). These compounds have received a lot of attention because of their uses as perfume intermediates, pharmaceutical, agrochemical and liquid-crystal polymer units (Artico et al., 1998; Amoozadeh et al., 2010). α,α'-Bis(substituted-benzylidene)cycloalkanones are also essential pharmacophores of various natural products (Shetty et al., 2015). An example of permitted therapeutic agents including this molecular framework is coumarin-chalcone (anticancer agents).

In the present work, we have synthesized, in one-step, (E,E)-3-methyl-2,5-bis(4-methylbenzylidene)cyclopentanone (MBMCP) by NaOH-catalysed Claisen–Schmidt condensation of 4-methyl benzaldehyde with 3-methyl cyclopentanone.
(see scheme). The structure of MBMCP was investigated by UV, FT–IR and Raman spectroscopy, single crystal X-ray diffraction (XRD) measurements and $^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectroscopy.

Several studies on the biological activity of unsaturated carbonyl compounds have been carried out. As an example, a series of chalcone derivatives that mimic the essential properties of cationic antimicrobial peptides were designed and synthesized by Chu et al. (2018). The antibacterial activities of these chalcones against drug-sensitive bacteria, including Staphylococcus aureus, Enterococcus faecalis, Escherichia coli and Salmonella enterica indicate that these compounds have potential therapeutic effects against bacterial infections. The phenyl group and the fluoride atom in these compounds were found to play an important role in their antibacterial and hemolytic activities. The above findings prompted us to evaluate the antibacterial activity of MBMCP in vitro against four bacterial strains.

2. Structural commentary

The structure of MBMCP was confirmed using single X-ray diffraction. The asymmetric unit comprised a single molecule, illustrated in Fig. 1 with the atom-numbering scheme. The cyclopentanone ring adopts a half-chair form, with deviations of $-0.146$ (2) and $0.160$ (2) Å from the mean plane of the ring for C13 and C14, respectively. The torsion angles within the five-membered ring are $4.7$ (2) (C9—C10—C12—C13), $-19.5$ (2) (C10—C12—C13—C14) and $26.3$ (2) (C12—C13—C14—C9), confirming the non-planarity of the central ring. The C15 methyl group in MBMCP lies practically perpendicular to the plane of its attached cyclopentanone ring, with torsion angle C12—C13—C14—C15 of $-91.4$ (2). The mean planes of the phenyl rings at either end of the molecule are twisted with respect to one another by $41.3$ (1)°.

The C8=C9 and C12=C16 bond lengths are $1.344$ (3) and $1.335$ (3) Å, respectively, and those for C8—C5 and C16—C17 are $1.464$ (3) and $1.462$ (3) Å, respectively. These values are in between the normal values for single and double bonds (1.54 and 1.33 Å, respectively), which is consistent with a delocalized π-bonding system.

The molecular structure of MBMCP is fully extended in the E,E configuration stabilized by two short intramolecular contacts, H8⋯O11 and H16⋯O11 (2.55 and 2.53 Å, respectively).

3. Spectroscopic results

The FT–IR spectrum of MBMCP shows the strong band of a conjugated carbonyl group at 1670 cm$^{-1}$ and two bands at 1616 and at 1596 cm$^{-1}$ for the two non-equivalent exo-cyclic C=O bonds. The Raman spectrum shows two characteristic bands in the 1720–1670 and 1620–1590 cm$^{-1}$ regions, which indicate the presence of carbonyl groups conjugated with the double bonds.
The above result is also confirmed using the chemical shifts in the $^{13}$C NMR spectrum for the carbonyl groups (196.46 ppm) and of the C=O group at (139.7 and 139.8 ppm). The dienone of cyclic ketone derivatives occur in E,E, Z,Z, or Z,E configurations (Vatsadze et al., 2006) and we have obtained the E,E isomer. The $^1$H NMR spectrum shows the signals of CH protons at a greater field than 7.2 ppm ($\delta = 7.51–7.53$ ppm), which is in agreement with the E isomers, whereas the signals for the Z isomers are identified using the chemical shifts at $\delta \sim 6.8$ ppm (George & Roth, 1971).

The UV spectrum of the designated compound in ethanol reveals four absorption bands at 208 nm ($\varepsilon = 3.215$ L mol$^{-1}$cm$^{-1}$), 237 nm ($\varepsilon = 1.984$ L mol$^{-1}$cm$^{-1}$), 364 nm ($\varepsilon = 3.215$ L mol$^{-1}$cm$^{-1}$) and 376 nm ($\varepsilon = 2.436$ L mol$^{-1}$cm$^{-1}$) assigned to n-\(\pi\), \(\pi\)-\(\pi^*\) transitions.

4. Supramolecular features

Molecules of MBMCP pack with no classical hydrogen bonds. However, C18–H18· · · O11(1 – x, –y, 1 – z) and C23–H23B· · · O11(1/2 + x, 1/2 – y, 1/2 + z) short contacts occur, where the oxygen atom of the carbonyl group works as an acceptor with O11· · · H distances of 2.61 and 2.66 Å, respectively. These interactions are neglected as the H· · · O van der Waals distance is 2.60 Å and C–H· · · O contacts frequently have H· · · O separations shorter than 2.4 Å (Taylor & Kennard, 1982). On the other hand, even though the carbonyl group is a strong acceptor, the O atom acts as a multiple acceptor. This condition corresponds to an important argument for the structural importance of the C–H· · · O hydrogen bond (Steiner, 1996).

Molecular chains of MBMCP propagate along the [101] direction through a C–H· · · \(\pi\) interaction (Table 1) involving the C4–H4 group of the C2–C7 phenyl ring pointing towards the \(\pi\) cloud on an adjacent C17–C22 ring, as shown in Fig. 2. The contact distances are consistent with those of the C–H· · · \(\pi\) edge-to-face interactions observed in the crystal structure of benzene (Bacon et al., 1964).

The molecules of MBMCP stack in waves along the a-axis direction, as shown in Fig. 3. The methyl carbon (C1) makes an important contribution to the stability of this stacking arrangement via the establishment of a C–H· · · \(\pi\) interaction with the centroid of a neighboring aryl ring.

5. Hirshfeld surface analysis

The intermolecular interactions were quantified using Hirshfeld surface analysis (Fig. 4). The Hirshfeld surfaces of MBMCP, their associated two-dimensional fingerprint plots and relative contributions to the Hirshfeld surface area from the various close intermolecular contacts were calculated using CrystalExplorer software (Wolff et al., 2007). The analysis of intermolecular interactions through the mapping of $d_{norm}$ compares the contact distances $d_l$ and $d_s$ from the Hirshfeld surface to the nearest atom inside and outside, respectively, with their respective van der Waals radii. The red
regions represent contacts shorter than the sum of van der Waals radii, white regions represent intermolecular distances equal to van der Waals contacts and blue regions represent contacts longer than van der Waals radii.

As expected in organic compounds, the shortest and most abundant contacts for MBMCP are the H⋯H intermolecular interactions with a contribution to the Hirshfeld surface of 58%. The C⋯H contacts, which refer to the C—H⋯π interactions described previously, contribute 32.2% of the Hirshfeld surfaces. On the shape-index surface, the C⋯H⋯π interactions are clearly observed as red regions over the aromatic rings. The shape-index is in agreement with the 2D fingerprint plot, in which these interactions appear as two broad spikes both having $d_i + d_f \approx 2.7$ Å (Fig. 5). The large flat region, delineated by a blue outline on the curvedness of MBMCP reveals that π⋯π stacking interactions are absent.

6. Antibacterial activity

The antibacterial activity of MBMCP was assayed in vitro against *Escherchia coli*, *Staphylococcus aureus*, *Salmonella typhi* and *Bacillus subtilis* via an agar cup-plate diffusion method (Barry, 1976; Ponce et al., 2003). The bacteria tests were sub-cultured in Mueller–Hinton broth, from which 1 mL of cell suspension was taken and the optical density was adjusted to 0.5. The suspension was then spread as a thin film over the Mueller–Hinton agar plates. The synthetic compound was loaded onto discs with concentrations of 0.2, 0.3, 0.4 and 0.5 μg mL$^{-1}$ and air-dried. The dry discs were placed on the inoculated Mueller–Hinton agar plates and incubated at 310 K for 48 h. A penicillin disc (10 μg per disc) was used as the standard. A disc of 150 μL of DMSO served as the control. After incubation, the zone of inhibition (in mm) was measured and compared with that of penicillin for each concentration.

The antibacterial screening results are collected in Table 2. They reveal that the produced compound shows an antibacterial activity at MIC = 0.5 μg mL$^{-1}$ towards all the bacterial strains, but differs from one strain to another when comparing the zones of inhibition (mm). It exhibits moderate and promising activities against *Staphylococcus aureus* (27 mm) and *Bacillus subtilis* (14 mm). However, it shows low activities against *Escherchia coli* (7 mm) and *Salmonella typhi* (12 mm), which probably demonstrate that the produced compound exhibits a specific effect on those microorganisms.

7. Database survey

A search of the Cambridge Structural Database, CSD (Version 5.38; ConQuest 1.19; Groom et al., 2016) revealed 20 derivatives of bis(benzylidene)cyclopentanone. The variety of compounds reported in the literature (Kawamata et al., 1998; Nakhaei et al., 2017) is due to substitution on the phenyl rings and/or on the cyclopentanone by different functional groups, such as hydroxy, methoxy, chlorine, fluorine etc., and also by radicals. Cyclic conjugated bis(benzylidene)ketones have been reported to exhibit potent anti-inflammatory, antibacterial and antioxidant activity (Shetty et al., 2015). *E,E*-2,5-dibenzylidene-3-methylocyclopentanone (DBMCP) is the nearest analogue to MBMCP. This molecule, like that of the title compound, exhibits a twisted five-membered ring, conveying modest non-planarity to the overall molecular shape with a maximum deviation from the mean plane of 0.44 Å (Theocharitis et al., 1984). The basic skeleton of this compound family, *E,E*-2,5-dibenzylidencyclopentanone (DBCP), has been isolated in two polymorphic forms, exhibiting two different but nearly superimposable conformations (Arshad et al., 2014). The previously reported polymorph I crystallizes in the orthorhombic $C222_1$ space group (Theocharitis et al., 1984), while the second form crystallizes in the monoclinic $P2_1$ space.
group. Both forms pack as supramolecular chains mainly stabilized by C—H···O, π–π and C—H···π interactions and forming sheet-like multilayered structures.

8. Synthesis and crystallization

A mixture of 4-methylbenzaldehyde (20 mmol, 2 eq.) and 3-methylcyclopentanone (10 mmol, 1 eq.) was dissolved in ethanol (15 mL) into a flask (simple necked, round bottomed), and the solution was stirred for a few minutes at 273 K (ice bath). A solution of NaOH (10 mL, 40%) was added dropwise over several minutes into this mixture. The resulting mixture was stirred for 4 h approximately at room temperature. The obtained yellow precipitate was then filtered, washed with HCl (0.1 N) and cold water and then dried. The pure product was crystallized from ethanol solution at room temperature in 75% yield. Single crystals for X-ray diffraction were grown by slow solvent evaporation from a solution in ethanol.

The FT–IR spectrum of the compound was measured by the KBr pellet technique in the range of 4000–400 cm⁻¹, with a Nexus Nicolet FT–IR spectrometer at a resolution of 2 cm⁻¹. A Bruker Optik GmbH system was utilized to measure the Raman spectrum of the powder compound. A class 4 laser Raman spectrometer of 532 nm excitation from a diode laser was used. The 1H NMR (400 MHz, CDCl₃) δ (ppm): 1.23 (d, 1H, CH₃), 1.54 (s, 2H, H₂O), 2.39 (s, 6H, 2CH₃), 2.76 (dd, 1H, CH cycle), 3.18 (dd, 1H, CH cycle), 3.66 (m, 1H, CH cycle), 7.22 (d, 2H ary1), 7.25 (d, 2H ary2), 7.47 (d, 3H ary), 7.51 (s, 1H ethylenic), 7.53 (s, 1H ethylenic), and 7.66 (t, 1H ary1).

13C NMR (75.46 MHz, CDCl₃) δ (ppm): 21.03 (CH₃), 23.47 (CH₂), 23.49 (CH₃), 32.01 (CH cycle), 35.98 (CH2 cycle), 129.51 (2C—Ar), 129.62 (2C—Ar), 130.71 (2C—Ar), 130.79 (2C—Ar), 133.37 (2C—Ar), 134.38 (2C—Ar), 135.57 (CH═CH cycle), 139.57 (C cycle═CH), 139.72 (C cycle═CH), 142.51 (CH═CH cycle), and 196.46 (C═O).

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Computer programs: APEX3 (Bruker, 2015), SAINT (Bruker, 2014), SHELXT (Sheldrick, 2015), SHELXL2014 (Sheldrick, 2015)

Table 3

Experimental details.

| Characteristic | Value |
|----------------|-------|
| Crystal system, space group | Monoclinic, P2₁/n |
| a, b, c (Å) | 9.8037 (9), 8.9815 (9), 18.8946 (17) |
| µ (mm⁻¹) | 0.07 |
| Crystal size (mm) | 0.52 × 0.28 × 0.06 |
| No. of reflections | 15325, 3808, 2471 |
| Rint | 0.115 |
| R₁, wR₁, S | 0.070, 0.171, 1.12 |
| No. of parameters | 211 |
| H-atom treatment | H-atom parameters constrained |
| Δρmax, Δρmin (e Å⁻³) | 0.30, −0.26 |

1. Synthesis

A mixture of 4-methylbenzaldehyde (20 mmol, 2 eq.) and 3-methylcyclopentanone (10 mmol, 1 eq.) was dissolved in ethanol (15 mL) into a flask (simple necked, round bottomed), and the solution was stirred for a few minutes at 273 K (ice bath). A solution of NaOH (10 mL, 40%) was added dropwise over several minutes into this mixture. The resulting mixture was stirred for 4 h approximately at room temperature. The obtained yellow precipitate was then filtered, washed with HCl (0.1 N) and cold water and then dried. The pure product was crystallized from ethanol solution at room temperature in 75% yield. Single crystals for X-ray diffraction were grown by slow solvent evaporation from a solution in ethanol.

The FT–IR spectrum of the compound was measured by the KBr pellet technique in the range of 4000–400 cm⁻¹, with a Nexus Nicolet FT–IR spectrometer at a resolution of 2 cm⁻¹. A Bruker Optik GmbH system was utilized to measure the Raman spectrum of the powder compound. A class 4 laser Raman spectrometer of 532 nm excitation from a diode laser (3B) was used with 2 cm⁻¹ resolution within the spectral range 3500–0 cm⁻¹. 1H and 13C NMR spectra were quantified with CDCl₃ using a (400.13 MHz in 1H) Avance 400 Bruker spectrometer with TMS as internal standard.
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(E,E)-3-Methyl-2,5-bis(4-methylbenzylidene)cyclopentanone: synthesis, characterization, Hirshfeld surface analysis and antibacterial activity

Fatiha Mahdi, Assia Sid, Rafika Bouchene, Paul Mosset and Thierry Roisnel

Computing details

Data collection: SAINT (Bruker, 2014); cell refinement: APEX3 (Bruker, 2015) and SAINT (Bruker, 2014); data reduction: SAINT (Bruker, 2014); program(s) used to solve structure: SHELXT (Sheldrick, 2015a); program(s) used to refine structure: SHELXL2014 (Sheldrick, 2015b); molecular graphics: ORTEP-3 for Windows (Farrugia, 2012) and DIAMOND (Brandenburg & Berndt, 2001); software used to prepare material for publication: CRYSCALc (T. Roisnel, local program, version of 2015).

(E,E)-3-Methyl-2,5-bis(4-methylbenzylidene)cyclopentanone

Crystal data

C_{22}H_{22}O  
Mr = 302.39
Monoclinic, P_2_1/\(hn\)
\(a = 9.8037\) (9) Å
\(b = 8.9815\) (9) Å
\(c = 18.8946\) (17) Å
\(\beta = 90.985\) (4)°
\(V = 1663.5\) (3) Å³
\(Z = 4\)

Data collection

Bruker D8 VENTURE diffractometer  
Radiation source: Incoatec microfocus sealed tube
Multilayer monochromator  
rotation images scans  
(SADABS; Bruker, 2014)
\(T_{\text{min}} = 0.735, T_{\text{max}} = 0.996\)

Refinement

Refinement on \(F^2\)
Least-squares matrix: full  
\(R[F^2 > 2\sigma(F^2)] = 0.070\)  
w\(R(F^2) = 0.171\)  
\(S = 1.12\)
3808 reflections  
211 parameters  
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained

\[ w = 1/[\sigma^2(F_o^2) + (0.0652P)^2 + 0.431P] \]

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

\( (\Delta/\sigma)_{\text{max}} = 0.005 \)

\( \Delta \rho_{\text{max}} = 0.30 \text{ e Å}^{-3} \)

\( \Delta \rho_{\text{min}} = -0.26 \text{ e Å}^{-3} \)

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.** Refinement of \( F^2 \) against ALL reflections. The weighted R-factor \( wR \) and goodness of fit \( S \) are based on \( F^2 \), conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of \( F^2 > 2\sigma(F^2) \) is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on \( F^2 \) are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

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

|      | x      | y      | z      | \( U_{\text{iso}}^*/U_{\text{eq}} \) |
|------|--------|--------|--------|------------------------------------|
| C1   | 0.6385 (3) | 0.4045 (3) | −0.09361 (12) | 0.0385 (6) |
| H1A  | 0.6054 | 0.3291 | −0.1273 | 0.058* |
| H1B  | 0.7347 | 0.4259 | −0.1025 | 0.058* |
| H1C  | 0.5848 | 0.4958 | −0.0994 | 0.058* |
| C2   | 0.6242 (2) | 0.3472 (3) | −0.01957 (12) | 0.0274 (5) |
| C3   | 0.5158 (2) | 0.2568 (3) | −0.00074 (13) | 0.0357 (6) |
| H3   | 0.4503 | 0.2287 | −0.0359 | 0.043* |
| C4   | 0.5009 (2) | 0.2070 (3) | 0.06766 (12) | 0.0316 (6) |
| H4   | 0.4260 | 0.1443 | 0.0785 | 0.038* |
| C5   | 0.5940 (2) | 0.2468 (2) | 0.12164 (11) | 0.0227 (5) |
| C6   | 0.7056 (2) | 0.3345 (3) | 0.10266 (12) | 0.0286 (5) |
| H6   | 0.7722 | 0.3611 | 0.1375 | 0.034* |
| C7   | 0.7195 (2) | 0.3824 (3) | 0.03386 (12) | 0.0308 (6) |
| H7   | 0.7964 | 0.4414 | 0.0223 | 0.037* |
| C8   | 0.5659 (2) | 0.1961 (3) | 0.19360 (12) | 0.0242 (5) |
| H8   | 0.4994 | 0.1195 | 0.1962 | 0.029* |
| C9   | 0.6180 (2) | 0.2391 (2) | 0.25660 (12) | 0.0226 (5) |
| C10  | 0.5636 (2) | 0.1772 (2) | 0.32316 (12) | 0.0232 (5) |
| O11  | 0.49025 (16) | 0.06702 (19) | 0.32852 (8) | 0.0328 (4) |
| C12  | 0.6133 (2) | 0.2716 (2) | 0.38293 (12) | 0.0228 (5) |
| C13  | 0.6898 (2) | 0.4010 (2) | 0.35203 (11) | 0.0244 (5) |
| H13A | 0.7731 | 0.4227 | 0.3805 | 0.029* |
| H13B | 0.6318 | 0.4913 | 0.3506 | 0.029* |
| C14  | 0.7269 (2) | 0.3520 (2) | 0.27653 (12) | 0.0235 (5) |
| H14  | 0.7247 | 0.4386 | 0.2433 | 0.028* |
| C15  | 0.8679 (2) | 0.2773 (3) | 0.27741 (13) | 0.0315 (6) |
| H15A | 0.8700 | 0.1980 | 0.3130 | 0.047* |
| H15B | 0.9381 | 0.3515 | 0.2891 | 0.047* |
| H15C | 0.8856 | 0.2349 | 0.2307 | 0.047* |
| C16  | 0.5869 (2) | 0.2357 (2) | 0.44987 (11) | 0.0236 (5) |
| H16  | 0.5378 | 0.1453 | 0.4553 | 0.028* |
| C17  | 0.6207 (2) | 0.3119 (2) | 0.51624 (11) | 0.0230 (5) |
C18  0.6069 (2)  0.2345 (3)  0.57982 (12)  0.0262 (5)  
H18  0.5783  0.1335  0.5787  0.031*  
C19  0.6338 (2)  0.3014 (3)  0.64411 (12)  0.0288 (6)  
H19  0.6255  0.2451  0.5866  0.033*  
C20  0.6730 (2)  0.4508 (3)  0.64823 (12)  0.0269 (5)  
H20  0.6255  0.2451  0.5866  0.033*  
C21  0.6866 (2)  0.5284 (3)  0.58517 (12)  0.0274 (5)  
H21  0.7138  0.6299  0.5866  0.033*  
C22  0.6614 (2)  0.4612 (3)  0.52014 (12)  0.0247 (5)  
H22  0.6718  0.5170  0.4779  0.030*  
C23  0.6981 (3)  0.5255 (3)  0.71853 (13)  0.0394 (7)  
   
Atomic displacement parameters (Å²)  

|    | U¹¹  | U¹²  | U¹³  | U²²  | U²³  | U³³  |
|----|------|------|------|------|------|------|
| C1 | 0.0416 (15) | 0.0411 (16) | 0.0330 (14) | −0.0006 (12) | 0.0010 (11) | 0.0032 (12) |
| C2 | 0.0267 (12) | 0.0281 (13) | 0.0273 (12) | 0.0035 (10) | 0.0014 (10) | −0.0004 (10) |
| C3 | 0.0260 (12) | 0.0494 (17) | 0.0314 (14) | −0.0082 (11) | −0.0056 (10) | −0.0007 (12) |
| C4 | 0.0218 (12) | 0.0392 (15) | 0.0338 (14) | −0.0112 (10) | 0.0002 (10) | −0.0009 (11) |
| C5 | 0.0189 (10) | 0.0199 (11) | 0.0293 (12) | 0.0013 (9) | 0.0013 (9) | 0.0003 (9) |
| C6 | 0.0218 (11) | 0.0329 (14) | 0.0309 (13) | −0.0075 (10) | −0.0032 (9) | −0.0017 (11) |
| C7 | 0.0279 (12) | 0.0310 (14) | 0.0337 (13) | −0.0112 (10) | 0.0049 (10) | 0.0000 (11) |
| C8 | 0.0168 (10) | 0.0214 (12) | 0.0346 (13) | 0.0001 (9) | 0.0009 (9) | 0.0012 (10) |
| C9 | 0.0180 (10) | 0.0180 (11) | 0.0318 (12) | 0.0041 (8) | 0.0001 (9) | 0.0022 (10) |
| C10| 0.0198 (11) | 0.0198 (11) | 0.0299 (12) | 0.0018 (9) | −0.0011 (9) | 0.0049 (10) |
| O11| 0.0343 (9)  | 0.0284 (9)  | 0.0357 (10) | −0.0127 (8) | −0.0001 (7) | 0.0056 (8)  |
| C12| 0.0191 (10) | 0.0178 (11) | 0.0314 (12) | 0.0040 (8) | −0.0008 (9) | 0.0037 (10) |
| C13| 0.0240 (11) | 0.0192 (12) | 0.0298 (12) | −0.0016 (9) | −0.0013 (9) | 0.0019 (10) |
| C14| 0.0202 (11) | 0.0203 (12) | 0.0299 (12) | −0.0027 (9) | 0.0016 (9) | 0.0031 (10) |
| C15| 0.0212 (11) | 0.0354 (15) | 0.0380 (14) | −0.0036 (10) | −0.0009 (10) | −0.0031 (11) |
| C16| 0.0205 (11) | 0.0180 (11) | 0.0323 (13) | 0.0033 (9) | 0.0017 (9) | 0.0041 (10) |
| C17| 0.0168 (10) | 0.0234 (12) | 0.0289 (12) | 0.0040 (9) | 0.0029 (9) | 0.0053 (10) |
| C18| 0.0208 (11) | 0.0248 (13) | 0.0331 (13) | 0.0035 (9) | 0.0032 (9) | 0.0065 (10) |
| C19| 0.0222 (11) | 0.0374 (14) | 0.0271 (13) | 0.0108 (10) | 0.0050 (9) | 0.0104 (11) |
| C20| 0.0164 (10) | 0.0387 (14) | 0.0258 (12) | 0.0111 (10) | 0.0011 (9) | −0.0002 (11) |
| C21| 0.0223 (11) | 0.0247 (13) | 0.0352 (14) | 0.0049 (9) | 0.0017 (10) | 0.0018 (10) |
| C22| 0.0227 (11) | 0.0263 (13) | 0.0252 (12) | 0.0043 (9) | 0.0005 (9) | 0.0061 (10) |
| C23| 0.0380 (14) | 0.0501 (17) | 0.0302 (14) | 0.0100 (12) | 0.0005 (11) | −0.0021 (12) |

Geometric parameters (Å, °)  

| Bond | Length (Å) | Angle (°) |
|------|------------|----------|
| C1—C2| 1.499 (3) | C13—H13A | 0.9900 |
| C1—H1A | 0.9800 | C13—H13B | 0.9900 |
| C1—H1B | 0.9800 | C14—C15 | 1.536 (3) |
| C1—H1C | 0.9800 | C14—H14 | 1.0000 |
| C2—C3 | 1.388 (3) | C15—H15A | 0.9800 |
| Bond          | Length (Å) | Angle (°)       | Torsion Angle (°) |
|---------------|------------|-----------------|-------------------|
| C2—C7         | 1.400 (3)  | 109.5           | H13A—C13—H13B     |
| C3—C4         | 1.378 (3)  | 109.5           | C9—C14—C15        |
| C3—H3         | 0.9500     | 109.5           | C9—C14—C13        |
| C4—C5         | 1.404 (3)  | 109.5           | C9—C14—H14        |
| C4—H4         | 0.9500     | 109.5           | C15—C14—C13       |
| C5—C6         | 1.399 (3)  | 109.5           | C14—C15—C13       |
| C5—C8         | 1.464 (3)  | 109.5           | C14—C15—H14       |
| C6—C7         | 1.379 (3)  | 109.5           | C14—C15—H15A      |
| C6—H6         | 0.9500     | 109.5           | C14—C15—H15B      |
| C7—H7         | 0.9500     | 109.5           | C14—C15—H15C      |
| C8—C9         | 1.344 (3)  | 109.5           | C14—C15—H15C      |
| C8—H8         | 0.9500     | 109.5           | C12—C16—C17       |
| C9—C10        | 1.483 (3)  | 109.5           | C12—C16—H16       |
| C9—C14        | 1.515 (3)  | 109.5           | C12—C16—C22       |
| C10—O11       | 1.228 (3)  | 109.5           | C12—C16—C22       |
| C10—C12       | 1.488 (3)  | 109.5           | C12—C16—H16       |
| C12—C16       | 1.335 (3)  | 109.5           | C12—C16—H16       |
| C12—C13       | 1.506 (3)  | 109.5           | C12—C16—H16       |
| C13—C14       | 1.543 (3)  | 109.5           | C12—C16—H16       |

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C8—C9—C14  131.9 (2)  C22—C21—C20  121.6 (2)
C10—C9—C14  107.62 (18)  C22—C21—H21  119.2
O11—C10—C9  126.3 (2)  C20—C21—H21  119.2
O11—C10—C12  125.5 (2)  C21—C22—C17  120.6 (2)
C9—C10—C12  108.17 (19)  C21—C22—H22  119.7
C16—C12—C10  121.0 (2)  C17—C22—H22  119.7
C16—C12—C13  131.3 (2)  C20—C23—H23A  109.5
C10—C12—C13  107.73 (18)  C20—C23—H23B  109.5
C12—C13—C14  105.37 (18)  H23A—C23—H23B  109.5
C12—C13—H13A  110.7  C20—C23—H23C  109.5
C14—C13—H13A  110.7  H23A—C23—H23C  109.5
C12—C13—H13B  110.7  H23B—C23—H23C  109.5
C14—C13—H13B  110.7

C7—C2—C3—C4  1.4 (4)  C16—C12—C13—C14  160.9 (2)
C1—C2—C3—C4 −178.5 (2)  C10—C12—C13—C14 −19.5 (2)
C2—C3—C4—C5  0.8 (4)  C8—C9—C14—C15 −88.7 (3)
C3—C4—C5—C6 −2.4 (4)  C10—C9—C14—C15 93.9 (2)
C3—C4—C5—C8  176.5 (2)  C8—C9—C14—C13 153.5 (2)
C4—C5—C6—C7  1.9 (3)  C10—C9—C14—C13 −23.9 (2)
C8—C5—C6—C7 −176.9 (2)  C12—C13—C14—C9 26.3 (2)
C3—C2—C7—C6 −2.0 (4)  C12—C13—C14—C15 −91.4 (2)
C1—C2—C7—C6  178.0 (2)  C10—C12—C16—C17 −178.0 (2)
C6—C5—C8—C9  13.9 (4)  C13—C12—C16—C17 1.6 (4)
C4—C5—C8—C9 −164.9 (2)  C12—C16—C17—C18 −166.3 (2)
C5—C8—C9—C10  175.1 (2)  C12—C16—C17—C22 16.4 (4)
C5—C8—C9—C14 −2.0 (4)  C22—C17—C18—C19 −0.8 (3)
C8—C9—C10—O11  14.6 (3)  C16—C17—C22—C21 177.3 (2)
C14—C9—C10—O11 −167.6 (2)  C17—C18—C20—C21 1.5 (3)
C8—C9—C10—C12 −165.43 (19)  C18—C19—C20—C21 −1.3 (3)
C14—C9—C10—C12  123.2 (2)  C18—C19—C20—C23 178.0 (2)
O11—C10—C12—C16  4.3 (3)  C19—C20—C21—C22 0.4 (3)
C9—C10—C12—C16 −175.62 (19)  C23—C20—C21—C22 −178.8 (2)
O11—C10—C12—C13 −175.4 (2)  C20—C21—C22—C17 0.2 (3)
C9—C10—C12—C13  4.7 (2)  C18—C17—C22—C21 0.0 (3)

Hydrogen-bond geometry (Å, °)

Cg1 and Cg2 are the centroids of the C2–C7 and C17–C22 rings, respectively.

| D—H—A  | D—H  | H···A | D···A | D—H···A |
|---------|-------|-------|-------|---------|
| C1—H1C—Cg1i | 0.98  | 2.84  | 3.728 (3) | 152     |
| C4—H4—Cg2i | 0.95  | 2.75  | 3.574 (2) | 146     |

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

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