

3,5-Bis(4-methoxybenzylidene)-1-methyl-4-piperidone and 3,5-bis(4-methoxybenzylidene)-1-methyl-4-oxopiperidinium chloride: potential biophotonic materials

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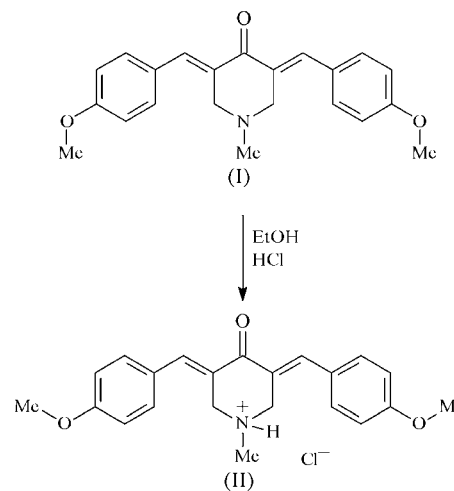
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In the title compound 3,5-bis(4-methoxybenzylidene)-1-methyl-4-piperidone, $C_{22}H_{23}NO_3$, (I), the central heterocyclic ring adopts a flattened boat conformation, while in the related salt 3,5-bis(4-methoxybenzylidene)-1-methyl-4-oxopiperidinium chloride, $C_{22}H_{24}NO_3^+ \cdot Cl^-$, (II), the ring exhibits a 'sofa' conformation in which the N atom deviates from the planar fragment. The pendant benzene rings are twisted from the heterocyclic ring planes in both molecules in the same direction, the range of dihedral angles between the ring planes being $24.5(2)$ – $32.7(2)^\circ$. The dominant packing motif in (I) involves centrosymmetric dimers bound by weak intermolecular $C-H \cdots O$ hydrogen bonds. In (II), cations and anions are linked by strong $N-H \cdots Cl$ hydrogen bonds, while weak $C-H \cdots O$ and $C-H \cdots Cl$ hydrogen bonds link the cations and anions into a three-dimensional framework.

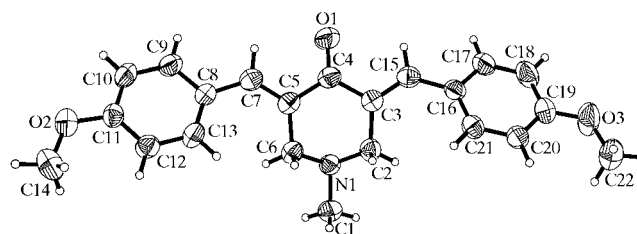
Comment

The present investigation is a continuation of our work that includes the syntheses and structural investigation of non-linear optical organic compounds with two-photon absorption properties, such compounds being potential biophotonic materials (Nesterov *et al.*, 2003; Peterson *et al.*, 2004a,b). Comparison of the structures of the investigated molecules with related compounds found in the literature that possess anticancer activities has shown that all of these compounds are very similar (Jia *et al.*, 1988, 1989; Dimmock, Arora, Duffy *et al.*, 1992; Dimmock, Arora, Semple *et al.*, 1992; Dimmock, Arora, Chen *et al.*, 1994; Dimmock, Arora, Quail *et al.*, 1994; Dimmock *et al.*, 2001). The compounds that we are investigating may find applications as agents for locating cancer cells with two-photon excited fluorescence and have potential as agents for a photodynamic treatment of cancer (Nesterov *et al.*, 2003; Peterson *et al.*, 2004a,b). The syntheses and structural

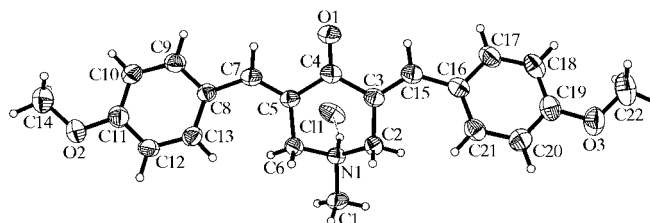
investigations of 3,5-bis(4-methoxybenzylidene)-1-methyl-4-piperidone, (I) (Fig. 1), and the chloride salt, (II) (Fig. 2), are presented here. Details of their two-photon absorption properties and fluorescence activity will be published elsewhere.



Both compounds contain two *p*-methoxyphenyl donor groups connected to the central acceptor heterocyclic ring *via* conjugated bridges, but the compounds have slightly different structures. In (I), the heterocyclic ring adopts a flattened boat conformation; atoms N1 and C4 lie $-0.714(3)$ and $-0.190(3)$ Å, respectively, out of the C2/C3/C5/C6 plane [planar within $0.027(3)$ Å]. In (II), the conformation of this ring can be described as sofa; atom N1 lies $0.686(3)$ Å out of the C2–C6 plane [planar within $0.013(3)$ Å]. We have previously described a similar conformation of the heterocyclic ring in related compounds (Nesterov *et al.*, 2003). As seen in Figs. 1 and 2, the methyl substituents of the methoxy


Figure 1

A view of (I), showing the atom numbering used. Non-H atoms are shown with displacement ellipsoids drawn at the 50% probability level.


Figure 2

A view of (II), showing the atom numbering used. Non-H atoms are shown with displacement ellipsoids drawn at the 50% probability level.

groups have different orientations relative to the phenyl rings. In both cases, these substituents almost lie in the planes of the aromatic rings [C10—C11—O2—C14 = $-175.8(3)$ and $-7.8(5)^\circ$, and C18—C19—O3—C22 = $174.0(3)$ and $3.0(5)^\circ$, in (I) and (II), respectively], with geometric parameters in good agreement with the literature data (Gallagher *et al.*, 2001). According to these results, it is possible to predict the existence of other polymorphic modifications of (I) and (II) corresponding to other orientations of these flexible substituents.

Both molecules are non-planar; the dihedral angles between the flat part of the heterocycle and the two almost flat fragments that include the phenyl ring and the bridging atom are $24.5(2)$ and $32.7(2)^\circ$ in (I), and $25.1(2)$ and $31.0(2)^\circ$ in (II). The differences in mutual orientation of these fragments and the flatness of the heterocyclic rings [especially in (II)] lead to intramolecular H···H steric interactions [H2A···H21A = 2.32 and 2.23 Å, and H6B···H13A = 2.32 and 2.09 Å, in (I) and (II), respectively]. These contacts are very close to or shorter than the sum of the van der Waals radii of H atoms (Rowland & Taylor, 1996). Nevertheless, it is possible to predict conjugation between the donor and acceptor parts of the molecules. The bond-length distributions in the bridges show a small alternation of single C—C and double C=C bond lengths (Tables 1 and 3) around standard distances (Allen *et al.*, 1987). Most of the geometric parameters in the investigated molecules are very similar to those reported in our previous studies (Nesterov *et al.*, 2003).

In the crystal structure of (I), there is an intermolecular steric contact (H22C···O1 = 2.51 Å) that, according to literature data (Desiraju & Steiner, 1999), can be considered as a weak hydrogen bond. Such hydrogen bonds link the

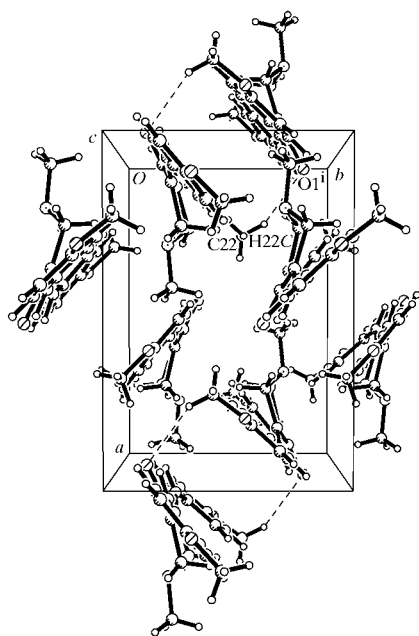


Figure 3
A projection of the crystal packing of (I) along the *c* axis. Dashed lines indicate the intermolecular C—H···O hydrogen bonds (see Table 2).

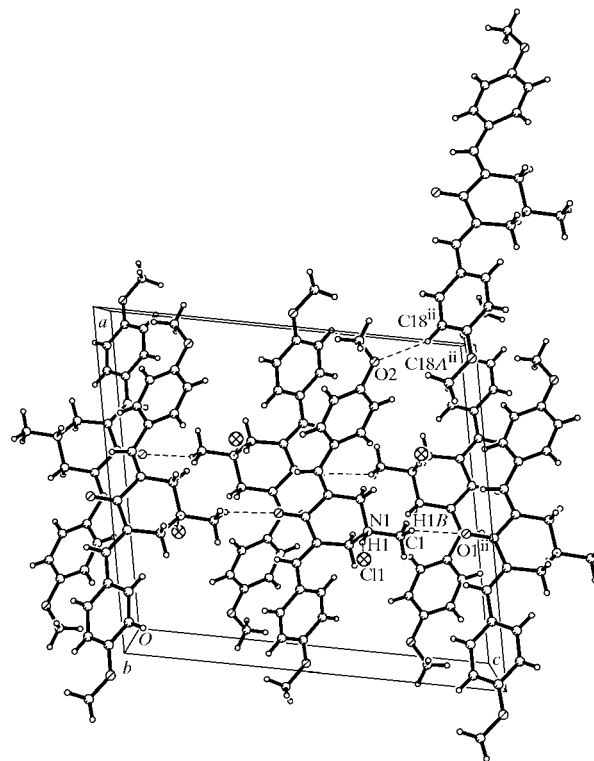


Figure 4
A projection of the crystal packing of (II) along the *b* axis. Dashed lines indicate the intermolecular N—H···Cl and C—H···O hydrogen bonds (see Table 4).

molecules into centrosymmetric dimers (Fig. 3 and Table 2). In the crystal structure of (II), the cations and anions are linked by strong N1—H1···Cl1 hydrogen bonds. In addition, weak H1B···O1 (2.45 Å) and H18A···O2 (2.52 Å) intermolecular hydrogen bonds link the cations into layers parallel to the *ac* plane (Fig. 4). Moreover, the Cl[−] anions form very weak intermolecular contacts with the cations (Cl1···H13A = 2.83 Å and Cl1···H21A = 2.89 Å), thus completing a three-dimensional framework (Table 4). In salt (II), there are also intermolecular steric contacts between C atoms that are less than the sum of the van der Waals radii of C atoms (Rowland & Taylor, 1996) [C4···C4(1 − *x*, 1 − *y*, 1 − *z*) = $3.228(4)$ Å and C7···C15(1 − *x*, 1 − *y*, 1 − *z*) = $3.376(4)$ Å]. The remaining geometric parameters in the investigated molecules have normal values (Allen *et al.*, 1987).

Experimental

Compound (I) was obtained according to the procedure described by Nesterov *et al.* (2003). The precipitate was isolated and recrystallized from tetrahydrofuran (m.p. 477 K, yield 76%). Compound (II) was synthesized from (I). A 50 ml round-bottomed flask was charged with (I) (0.70 g, 2.0 mmol), ethanol (20 ml) and concentrated HCl (1 ml). The mixture was stirred for 3 h and allowed to stand overnight. The precipitate was filtered off, washed with ethanol and recrystallized from ethanol (m.p. 484 K; yield 0.70 g, 91%). Crystals of the two compounds were grown by isothermal evaporation of acetonitrile and ethanol solutions of (I) and (II), respectively. The compounds were characterized by ¹H and ¹³C NMR spectroscopy.

Compound (I)

Crystal data

C₂₂H₂₃NO₃ D_x = 1.279 Mg m⁻³
 M_r = 349.41 Mo K α radiation
 Monoclinic, P₂₁/n Cell parameters from 24 reflections
 a = 11.315 (2) Å θ = 10–11°
 b = 7.8910 (16) Å μ = 0.09 mm⁻¹
 c = 20.356 (4) Å T = 295 (2) K
 β = 92.87 (3)° Needle, yellow
 V = 1815.2 (6) Å³ 0.50 × 0.20 × 0.10 mm
 Z = 4

Data collection

Enraf–Nonius CAD-4 θ_{\max} = 25.0°
 diffractometer h = 0 → 13
 $\theta/2\theta$ scans k = 0 → 9
 3340 measured reflections l = -24 → 24
 3167 independent reflections 3 standard reflections
 1398 reflections with I > 2 σ (I) every 97 reflections
 R_{int} = 0.073 intensity decay: 3%

Refinement

Refinement on F² H-atom parameters constrained
 R[F² > 2 σ (F²)] = 0.048 w = 1/[σ^2 (F_o²) + (0.05P)²]
 wR(F²) = 0.128 where P = (F_o² + 2F_c²)/3
 S = 1.03 (Δ/σ)_{max} < 0.001
 3167 reflections $\Delta\rho_{\max}$ = 0.16 e Å⁻³
 238 parameters $\Delta\rho_{\min}$ = -0.20 e Å⁻³

Table 1 Selected geometric parameters (Å, °) for (I).

O1–C4	1.223 (3)	C4–C5	1.488 (4)
O2–C11	1.363 (3)	C5–C7	1.351 (4)
O3–C19	1.363 (4)	C7–C8	1.455 (4)
C3–C15	1.331 (4)	C15–C16	1.458 (4)
C3–C4	1.482 (4)		
C11–O2–C14	118.0 (2)	C3–C4–C5	117.5 (3)
C19–O3–C22	118.8 (3)	C7–C5–C4	117.1 (3)
C15–C3–C4	118.1 (3)	C7–C5–C6	125.3 (3)
C15–C3–C2	125.3 (3)	C4–C5–C6	117.5 (2)
C4–C3–C2	116.5 (2)	C5–C7–C8	130.8 (3)
O1–C4–C3	121.5 (3)	C3–C15–C16	130.9 (3)
O1–C4–C5	121.0 (3)		
C4–C5–C7–C8	-179.5 (3)	C4–C3–C15–C16	177.8 (3)
C5–C7–C8–C9	-158.3 (3)	C3–C15–C16–C17	154.0 (3)
C14–O2–C11–C10	-175.8 (3)	C22–O3–C19–C18	174.0 (3)

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

D–H...A	D–H	H...A	D...A	D–H...A
C22–H22C...O1 ⁱ	0.96	2.51	3.394 (4)	153

Symmetry code: (i) -x, 1 - y, 1 - z.

Compound (II)

Crystal data

C₂₂H₂₄NO₃⁺.Cl⁻ D_x = 1.308 Mg m⁻³
 M_r = 385.87 Mo K α radiation
 Monoclinic, P₂₁/c Cell parameters from 24 reflections
 a = 15.030 (3) Å θ = 11–12°
 b = 8.0020 (16) Å μ = 0.22 mm⁻¹
 c = 16.585 (3) Å T = 295 (2) K
 β = 100.81 (3)° Prism, yellow
 V = 1959.3 (7) Å³ 0.50 × 0.35 × 0.25 mm
 Z = 4

Data collection

Enraf–Nonius CAD-4 θ_{\max} = 26.0°
 diffractometer h = 0 → 18
 $\theta/2\theta$ scans k = 0 → 9
 3962 measured reflections l = -20 → 20
 3811 independent reflections 3 standard reflections
 2057 reflections with I > 2 σ (I) every 97 reflections
 R_{int} = 0.047 intensity decay: 3%

Refinement

Refinement on F² w = 1/[σ^2 (F_o²) + (0.067P)²
 R[F² > 2 σ (F²)] = 0.049 + 0.05P]
 wR(F²) = 0.136 where P = (F_o² + 2F_c²)/3
 S = 1.01 (Δ/σ)_{max} < 0.001
 3811 reflections $\Delta\rho_{\max}$ = 0.27 e Å⁻³
 251 parameters $\Delta\rho_{\min}$ = -0.24 e Å⁻³
 H atoms treated by a mixture of independent and constrained refinement

Table 3 Selected geometric parameters (Å, °) for (II).

O1–C4	1.218 (3)	C4–C5	1.483 (4)
O2–C11	1.368 (3)	C5–C7	1.339 (4)
O3–C19	1.368 (4)	C7–C8	1.453 (4)
C3–C15	1.342 (4)	C15–C16	1.459 (4)
C3–C4	1.487 (4)		
C11–O2–C14	117.8 (2)	C5–C4–C3	118.3 (2)
C19–O3–C22	117.9 (3)	C7–C5–C4	118.2 (2)
C15–C3–C4	117.8 (2)	C7–C5–C6	123.6 (2)
C15–C3–C2	123.4 (3)	C4–C5–C6	118.2 (2)
C4–C3–C2	118.9 (2)	C5–C7–C8	130.7 (2)
O1–C4–C5	120.9 (2)	C3–C15–C16	131.0 (3)
O1–C4–C3	120.7 (2)		
C4–C5–C7–C8	-173.6 (3)	C4–C3–C15–C16	177.9 (3)
C5–C7–C8–C9	-161.6 (3)	C3–C15–C16–C17	153.2 (3)
C14–O2–C11–C10	-7.8 (5)	C22–O3–C19–C18	3.0 (5)

Table 4 Hydrogen-bonding geometry (Å, °) for (II).

D–H...A	D–H	H...A	D...A	D–H...A
N1–H1...Cl1	0.95 (3)	2.07 (3)	2.978 (3)	160 (2)
C1–H1B...O1 ⁱⁱ	0.96	2.45	3.180 (4)	133
C18–H18A...O2 ⁱⁱⁱ	0.93	2.52	3.374 (4)	154
C13–H13A...Cl1 ^{iv}	0.93	2.84	3.657 (4)	148
C21–H21A...Cl1 ^v	0.93	2.89	3.682 (4)	144

Symmetry codes: (ii) x, $\frac{3}{2}$ - y, $\frac{1}{2}$ + z; (iii) x - 1, $\frac{3}{2}$ - y, z - $\frac{1}{2}$; (iv) 1 - x, y - $\frac{1}{2}$, $\frac{3}{2}$ - z; (v) x, y - 1, z.

For both compounds, data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *SHELXTL-Plus* (Sheldrick, 1994); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus*; software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GA1078). Services for accessing these data are described at the back of the journal.

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