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3,5-Bis{3-[4-(dimethylamino)phenyl]-prop-2-enylidene}-1-methyl-4-piperidone and 3,5-bis[3-(4-methoxyphenyl)prop-2-enylidene]-1-methyl-4-piperidone: potential biophotonic materials

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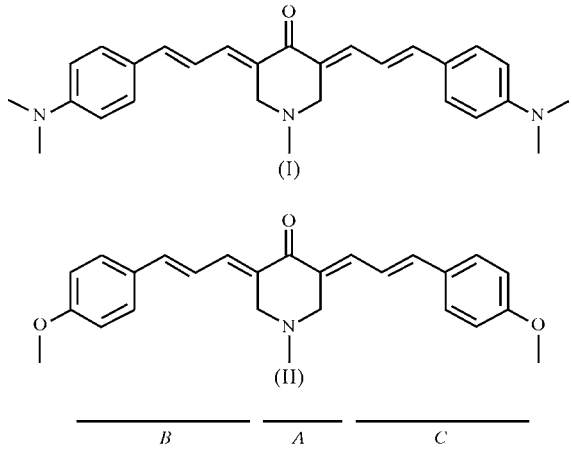
The structures of the title compounds, $C_{28}H_{33}N_3O$, (I), and $C_{26}H_{27}NO_3$, (II), together with their two-photon absorption properties and fluorescence activities are reported. Molecules of (II) reside on crystallographic mirror planes containing the piperidone C=O group and *N*-methyl H atoms. Because of the conjugation between the donor and acceptor parts, the central heterocycle in both (I) and (II) exhibits a flattened boat conformation, with deviations of the N atom and the opposite C atom from the planar fragment. The dihedral angles between the coplanar heterocyclic atoms and terminal C_6 rings are less than 20° in both (I) and (II). In (I), the *N*-methyl group of the ring occupies an equatorial position, but in (II) it is positioned in an axial site. In the crystal structure of (I), weak intermolecular C—H···π(arene) and C—H···O steric contacts link the molecules along the *a* axis. In the crystal structure of (II), molecules form stacks along the *b* axis.

Comment

There is ongoing interest in organic compounds that exhibit two-photon absorption (TPA) and two-photon excited fluorescence (TPEF). Such compounds can produce visible light when excited with IR radiation and allow penetration deep into biological tissue without absorption or causing damage. Such compounds find application as fluorescent molecular probes/markers and visualization agents in high-resolution two-photon microscopy in biomedical research and diagnostics (So *et al.*, 2003).

Continuing our investigations of these organic compounds (Nesterov, 2004; Nesterov & Nesterov, 2004; Nesterov *et al.*, 2003, 2007*a,b*; Sarkisov *et al.*, 2005), two compounds, (I) and



(II), with the general structure *D*–π–*A*–π–*D*, were synthesized and their structures, TPA properties and fluorescence activities characterized (*D* = donor and *A* = acceptor). Comparison of the two structures with 3,5-diarylidene-4-piperidone systems has shown that (I) and (II) are similar to piperidones used as anticancer agents (Jia *et al.*, 1988; Dimmock *et al.*, 2001). Combination of two such properties opens the possibility of their application as agents for localization of cancer cells with two-photon exited fluorescence and as potential agents for photodynamic treatment of cancer.

Compounds (I) and (II) (Figs. 1 and 2) contain two 4-(dimethylamino)phenyl or 4-methoxyphenyl donor groups connected to the central acceptor 1-methyl-4-piperidone ring *via* a conjugated bridge. In both molecules, the central heterocycle adopts a flattened boat conformation; atoms N1 and C4 lie 0.714 (1) and 0.055 (1) Å, respectively, out of the C2/C3/C5/C6 plane in (I), and 0.659 (1) and 0.039 (1) Å out of the C2/C3/C3*A*/C2*A* plane in (II) [the suffix *A* denotes the symmetry-related positions; the maximum deviation of one of the four atoms that make up the plane from that plane is 0.023 (1) Å for (I) and these four atoms are exactly planar in (II)].

Both molecules can be formally divided into three almost planar fragments, *viz.* the planar part of the heterocycle (*A*), and the planar fragments that consist of a benzene ring and the bridging atoms (*B* and *C*) (see scheme). In (I), the dihedral angles between plane *A* and planes *B* and *C* are 5.8 (1) and 10.2 (1)°, respectively, with similar angles in (II) of 20.0 (1)°

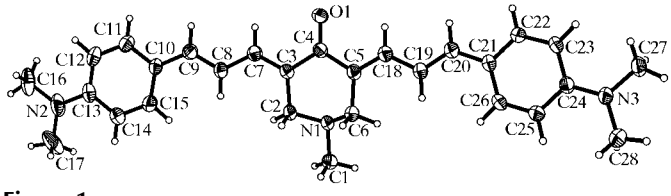


Figure 1
A view of (I), showing the atom-numbering scheme. The non-H atoms are shown with displacement ellipsoids drawn at the 50% probability level. H atoms are drawn as circles of arbitrary small radius for clarity.

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(*A*/*B*). In (I), the Me_2N– groups form different dihedral angles with the benzene rings [that between the N2/C16/C17 and C10–C15 planes is 6.0 (1)°, and that between the N3/C27/C28 and C21–C26 planes is 16.7 (1)°]. In (II), the MeO– group lies in the plane of the aromatic ring [C10—C11—O2—C14 = 178.8 (3)°] and its geometric parameters are in good agreement with literature data (Gallagher *et al.*, 2001). The nonplanarity of both compounds is caused by short intramolecular contacts [H2*B*···H8*A* = 2.16 Å, H8*A*···H15*A* = 2.21 Å, H6*A*···H19*A* = 2.21 Å and H19*A*···H26*A* = 2.32 Å in (I), and H2*A*···H6*A* = 2.28 Å and H6*A*···H13*A* = 2.34 Å in (II)] that are comparable to the sum of the van der Waals radii of H atoms (Rowland & Taylor, 1996).

In both structures, atom N1 (in the piperidone ring) has a pyramidal coordination, the sum of bond angles being 331.0 (2)° in (I) and 334.3 (2)° in (II). In (I), the methyl group on atom N1 occupies an equatorial position, while in (II) it is positioned axially. Such an unfavorable orientation of atom C1 in (II) is a reason for the presence of an intramolecular steric contact [C1···C4 = 3.282 (3) Å] equal to the sum of the van der Waals radii of the two atoms (Rowland & Taylor, 1996). The bond-length distributions in the π-conjugated bridges definitely show an alternation of single and double C—C bond lengths [especially in (I) with strong Me_2N– donor groups], with values close to the standard conjugated values (Allen *et al.*, 1987).

In (I), intermolecular C11—H11*A*···π(arene) interactions [H11*A*···*Cg*^{i} = 2.73 Å; *Cg* is the centroid of the C21–C26 ring; symmetry code: (i) $x-\frac{1}{2}, -y+\frac{1}{2}, z+\frac{1}{2}$; Fig. 3] and weak intermolecular steric contacts [C27—H27*A*···O1^{ii}, with H27*A*···O1^{ii}= 2.57 Å; symmetry code: (ii) $-x+1, -y, -z+1$] link molecules along the *a* axis. In (II), molecules form stacks along the *b* axis. Such packing is a reason for the existence of intermolecular steric contacts [N1···C4^{iii} = 2.967 (3) Å; symmetry code: (iii) $-x+1, -y, z+\frac{1}{2}$] that are shorter than the sum of the van der Waals radii of the two atoms (Rowland & Taylor, 1996).

The strong TPEF observed in (I), as opposed to a lack of TPEF in (II), is associated with the electron-donor properties of the pendant group. Thus, the Me_2N– group in (I) is a much stronger electron donor than the MeO– group in (II). In general, strong TPEF can be expected in compounds with strong electron-acceptor properties of the core, strong electron-donor properties of the pendant groups, and long π-conjugated electron bridges between the core and the pendant groups. A detailed discussion of the connection between molecular structure and TPEF was presented by Sarkisov *et al.* (2005). These results indicate that (I) can potentially be used as a two-photon fluorescent marker/molecular probe in two-photon fluorescent microscopy for biomedical research.

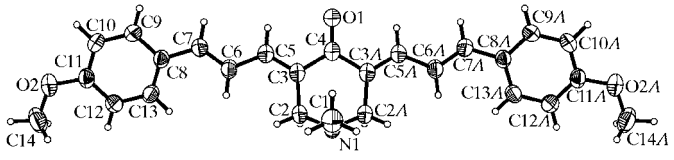

Figure 2
A view of (II), showing the atom-numbering scheme. The non-H atoms are shown with displacement ellipsoids drawn at the 50% probability level. H atoms are drawn as circles of arbitrary small radius for clarity. [Symmetry code: (*A*) $-x+1, -y, -z$.]

Experimental

The title compounds were synthesized according to literature procedures (Jia *et al.*, 1988; Nesterov *et al.*, 2003). The precipitates were isolated and recrystallized from tetrahydrofuran [(I): m.p. 471 K, yield 83%; (II): m.p. 454 K, yield 87%]. Crystals were obtained by isothermic evaporation of ethanol solutions of (I) and (II). Compounds (I) and (II) were investigated in terms of their possible fluorescence and use as TPA materials. Compound (I) demonstrated single-photon excited fluorescence (SPEF) of a red color while pumped with a UV lamp and pulsed green (532 nm) and UV (337 nm) lasers. In the case of 532 nm pumping, the SPEF was approximately 60% of that produced by reference dye Rhodamine 6G (Sarkisov *et al.*, 2005). Compound (I) also produced relatively strong red TPEF while being pumped with pulsed IR radiation at 876 nm. The TPA coefficient and molecular cross-section for (I) are 7.0 cm GW^{-1} and 2650 cm^4 s photon^{-1} molecule^{-1}, respectively, and

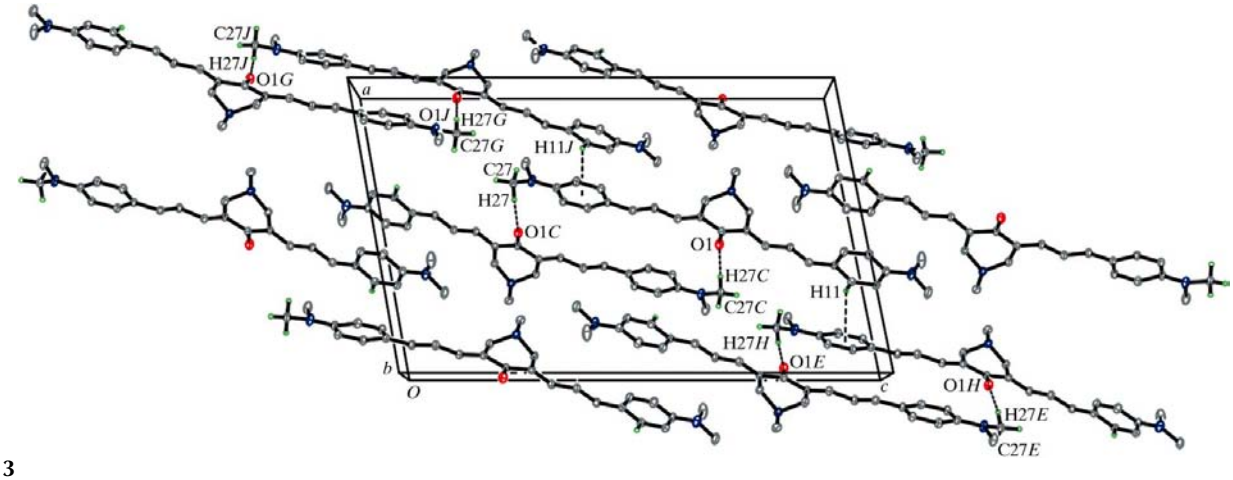

Figure 3
A projection of the crystal packing of (I) along the *b* axis. Dashed lines represent intermolecular C—H···π(arene, C21–C26) and C—H···O contacts. H atoms not involved in these interactions have been omitted for clarity. [Symmetry codes: (*C*) $-x+1, -y, -z+1$; (*E*) $-x+\frac{1}{2}, y+\frac{1}{2}, -z+\frac{1}{2}$; (*G*) $-x+\frac{3}{2}, y+\frac{1}{2}, -z+\frac{1}{2}$; (*H*) $x-\frac{1}{2}, -y+\frac{1}{2}, z+\frac{1}{2}$; (*J*) $x+\frac{1}{2}, -y+\frac{1}{2}, z-\frac{1}{2}$.]

are twice those of the benchmark reference dye Rhodamine B (Sarkisov *et al.*, 2005). The TPEF intensity was 37% of that produced by Rhodamine B. Compound (II) produced a weak orange SPEF (0.2% of that produced by Rhodamine 6G) while pumped only with a UV lamp or pulsed UV laser. There was no SPEF in the case of green pumping. This can be partially explained by the fact that the energy of green photons (2.2 eV) is way below the optical absorption band of the compound (between 2.7 and 3.4 eV). No TPEF was produced during pumping with a pulsed IR laser at 876 nm, despite the fact that the double energy of the IR photon (2.85 eV) is well inside the absorption band.

Compound (I)

Crystal data

$C_{28}H_{33}N_3O$
M_r = 427.57
Monoclinic, $P2_1/n$
a = 15.5459 (16) Å
b = 6.1017 (6) Å
c = 25.163 (3) Å
β = 100.539 (2)°
V = 2346.6 (4) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.07 mm^{-1}
T = 173 (2) K
0.34 × 0.14 × 0.06 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1995)
T_{min} = 0.905, T_{max} = 0.996
23500 measured reflections
4641 independent reflections
3393 reflections with $I > 2\sigma(I)$
R_{int} = 0.045

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.122
S = 1.01
4641 reflections
294 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.21 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

Compound (II)

Crystal data

$C_{26}H_{27}NO_3$
M_r = 401.49
Orthorhombic, $Cmc2_1$
a = 25.786 (2) Å
b = 10.0852 (8) Å
c = 8.2389 (7) Å
V = 2142.6 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.08 mm^{-1}
T = 173 (2) K
0.28 × 0.08 × 0.02 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1995)
T_{min} = 0.908, T_{max} = 0.998
15636 measured reflections
1632 independent reflections
1315 reflections with $I > 2\sigma(I)$
R_{int} = 0.042

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.097
S = 1.03
1632 reflections
151 parameters
1 restraint
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}

The absolute structure for (II) was not determined reliably; thus, for (II), Friedel pairs were merged before refinement. In (II), two H atoms of the *N*-methyl group were located from difference Fourier maps and were refined with isotropic parameters [the molecule occupies a special position in the crystal (the plane passes through atoms O1, N1, C1, C4 and H1*B*)]; the refined C—H distances are 0.99 (3) and 0.98 (5) Å. All H atoms in (I) and the remaining H atoms in (II) were placed in calculated positions (C—H = 0.95–0.99 Å) and refined in a rigid-group model [U_{iso}(H) = 1.2U_{eq}(C) and 1.5U_{eq}(C) for aromatic and methyl (AFIX 137) H atoms, respectively].

For both compounds, data collection: *SMART* (Bruker, 2004); cell refinement: *SAINT* (Bruker, 2004); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Bruker, 2005); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG3130). Services for accessing these data are described at the back of the journal.

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