

3,5-Bis[4-(diethylamino)benzylidene]-1-methyl-4-piperidone and 3,5-bis[4-(diethylamino)cinnamylidene]-1-methyl-4-piperidone: prospective biophotonic materials

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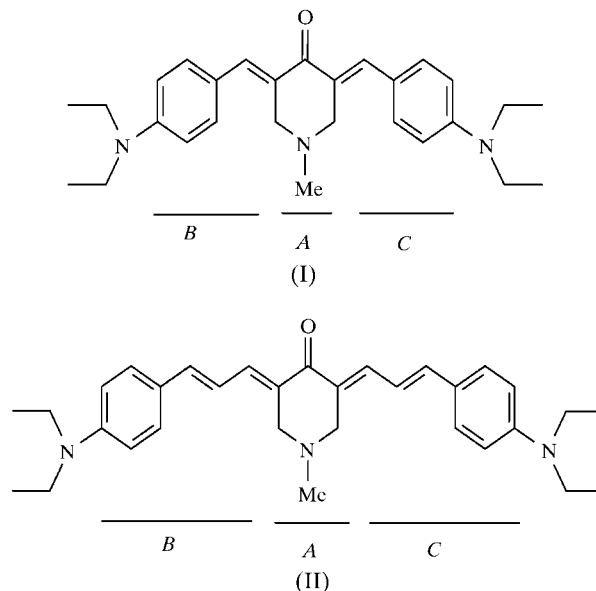
The structures of 3,5-bis[4-(diethylamino)benzylidene]-1-methyl-4-piperidone, C₂₈H₃₇N₃O, (I), and 3,5-bis[4-(diethylamino)cinnamylidene]-1-methyl-4-piperidone, C₃₂H₄₁N₃O, (II), have been characterized. Because of conjugation between donor and acceptor parts, the central heterocycles (including the carbonyl group) in (I) and (II) are flattened and exhibit a 'sofa' conformation, with a deviation of the N atom from the planar fragment. The dihedral angles between the planar part of the heterocycle and the two almost flat fragments that include a phenyl ring and bridging atoms are 23.2 (1) and 11.2 (1)° in (I), and 11.8 (1) and 8.7 (2)° in (II). One- and two-photon absorption of light and the fluorescence of (I) and (II) have also been characterized.

Comment

In the course of an investigation of non-linear optical organic compounds, in particular, those with two-photon absorption (TPA) properties, several compounds with the general structure *D*- π -*A*- π -*D* were synthesized. The structure, TPA properties and fluorescence activities of two of these compounds have been characterized. Comparison of these structures with analogous compounds found in the literature has shown that their molecules are very similar to the thoroughly investigated group of compounds used as anticancer agents (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 combination of these two

remarkable features suggests the application of these compounds as agents for localization of cancer cells with two-photon excited fluorescence and as potential agents for the photodynamic treatment of cancer.

We describe here the synthesis, structure and properties of 3,5-bis[4-(diethylamino)benzylidene]-1-methyl-4-piperidone, (I) (Fig. 1), and 3,5-bis[4-(diethylamino)cinnamylidene]-1-methyl-4-piperidone, (II) (Fig. 2), which contain two diethylaminophenyl donor groups connected to a central 1-methylpiperidone ring acceptor *via* conjugated bridges of different lengths.



In both compounds, the central heterocycle adopts a 'sofa' conformation (one atom deviates from the plane of the five other atoms). In (I), the mean deviation of atoms C2–C6 from the mean-square plane of these five atoms is 0.030 (1) Å, while the deviation of atom N1 from this plane is –0.724 (1) Å. In (II), the corresponding deviations are 0.015 (2) Å (C2–C6) and 0.681 (2) Å (N1). The positions of atoms C2–C6 in the flattened fragments in (I) and (II) are the result of conjugation of the dienone fragments with the donor groups. Atom N1 in the piperidone ring has a pyramidal coordination, with the sum of the bond angles being 331.1 (2)° for (I) and 330.8 (2)° for (II). In both compounds, the methyl group on atom N1 occupies an equatorial position. The bond-length distribution in the

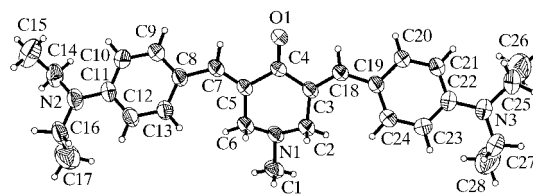
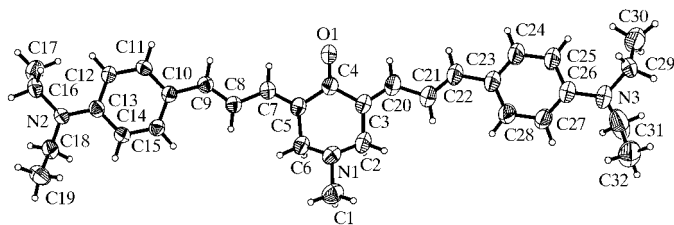


Figure 1

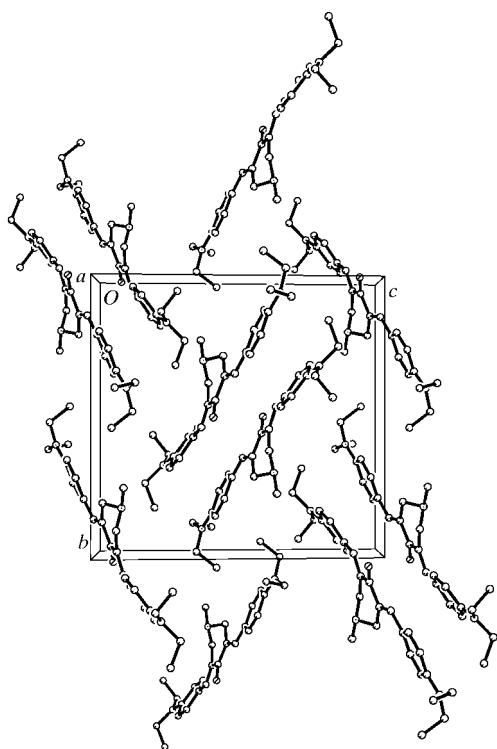
View of the molecule of (I), with the atom-numbering scheme. Non-H atoms are shown with displacement ellipsoids drawn at the 50% probability level. For clarity, H atoms are drawn as circles of arbitrary small radii. Only one set of disordered positions is shown for each of the ethyl groups.


Figure 2

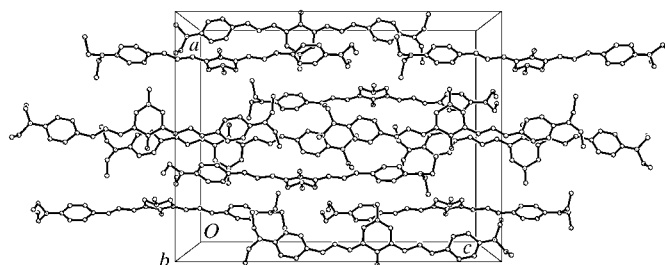
View of the molecule of (II), with the atom-numbering scheme. Non-H atoms are shown with displacement ellipsoids drawn at the 50% probability level. For clarity, H atoms are drawn as circles of arbitrary small radii. Only one set of disordered positions is shown for each of the ethyl groups.

π -conjugated bridges definitely shows an alternation of single C—C and double C=C bond lengths (Tables 1 and 2) with standard values (Allen *et al.*, 1987).

Both (I) and (II) can be formally divided into three almost planar fragments (see scheme); the first includes the planar part of the acceptor heterocycle *A*, while the almost planar fragments *B* and *C* consist of a phenyl ring and bridging atoms. In (I), the dihedral angle between fragments *A* and *B* is $23.2(1)^\circ$, and that between fragments *A* and *C* is $11.2(1)^\circ$. The corresponding angles in (II) are $11.8(1)^\circ$ (for *A/B*) and $8.7(2)^\circ$ (for *A/C*). Thus the molecule of (I) is slightly less planar than that of (II). This difference might be related to the presence in (I) of short intramolecular H2A...H24A and H6B...H13A contacts, with distances of 2.10 and 2.20 Å, respectively, which are somewhat shorter than the sums of the van der Waals radii of the H atoms (Rowland & Taylor, 1996).


Figure 3

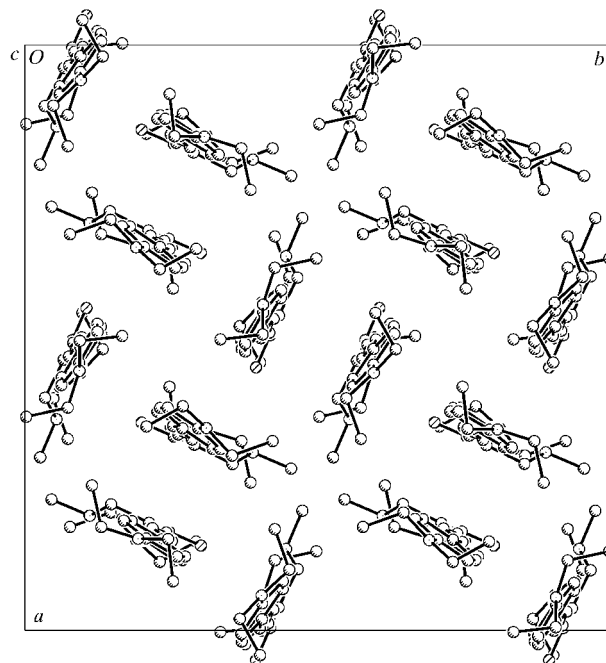
Projection of the crystal packing of (I) along the *a* axis.


Figure 4

Projection of the crystal packing of (II) along the *b* axis.

In both compounds, one of the diethylamine substituents is disordered. In the molecule of (I), only one ethyl branch of this substituent is disordered, and occupancy refinement suggests C25/C25A and C26/C26A ratios of 2:1. In (II), two branches of one diethylamine substituent are disordered, with a relative occupancy of 1:1 for atoms C29/C29A, C30/C30A, C31/C31A and C32/C32A. According to the literature, such an effect is common for many molecules bearing a diethylamine group (Suchod & Baldeck, 1995; Kliegel *et al.*, 1998).

Molecules in the crystal of (I) are organized in layers normal to the (10 $\bar{4}$) direction, and within each layer, molecules are packed in a parquet-like manner (Fig. 3). In (II), all long molecular axes are parallel to the crystallographic *c* axis (Fig. 4). On the other hand, the relative orientations of the mean molecular planes are different; in the environment of a reference molecule, three neighboring molecules are approximately parallel and four molecules are approximately perpendicular to the reference molecule (Fig. 5).


Figure 5

Projection of the crystal packing of (II) along the *c* axis.

Compound (I) demonstrated a relatively strong fluorescence, which is yellow in color, while being pumped with IR radiation. The coefficient and molecular cross-section of TPA for compound (I) are 3.9 (1) cm GW⁻¹ and 1490 (50) × 10⁻⁵⁰ cm⁴ s photon⁻¹ molecule⁻¹. Compound (II) produced a weaker fluorescence; the TPA coefficient for (II) is 6.6 (2) cm GW⁻¹ and the TPA cross-section is 2550 (70) × 10⁻⁵⁰ cm⁴ s photon⁻¹ molecule⁻¹. For both compounds, the TPA cross-sections are one order of magnitude greater than those of rhodamine B (Xu & Webb, 1996), the conventional dye used as a benchmark in the evaluation of the efficiency of TPA absorbers. Detailed results of the spectral properties and the structure–property relationships of these compounds will be published elsewhere. The present results indicate that the synthesized compounds can potentially be used as optical limiters and two-photon fluorescent labels in microscopy and bioresearch.

Experimental

Compounds (I) and (II) were obtained according to literature procedures (Dimmock, Arora, Duffy *et al.*, 1992). The precipitates were isolated and recrystallized from tetrahydrofuran [m.p. 472 K and yield 76% for (I), and m.p. 449 K and yield 71% for (II)]. Crystals were obtained by isothermic evaporation of ethanol solutions of (I) and (II).

Compound (I)

Crystal data

C₂₈H₃₇N₃O
M_r = 431.61
 Monoclinic, *P*₂₁/*c*
a = 9.2260 (18) Å
b = 16.181 (3) Å
c = 16.862 (3) Å
 β = 97.55 (3)°
V = 2495.4 (9) Å³
Z = 4

D_x = 1.149 Mg m⁻³
 Mo *K*α radiation
 Cell parameters from 24 reflections
 θ = 11–12°
 μ = 0.07 mm⁻¹
T = 298 (2) K
 Prism, orange
 0.50 × 0.40 × 0.30 mm

Table 1

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

O1–C4	1.226 (2)	C9–C10	1.377 (3)
N2–C11	1.376 (2)	C10–C11	1.396 (3)
N3–C22	1.379 (2)	C11–C12	1.403 (3)
C3–C18	1.351 (2)	C12–C13	1.367 (3)
C3–C4	1.476 (2)	C18–C19	1.450 (2)
C4–C5	1.492 (2)	C19–C24	1.386 (3)
C5–C7	1.339 (2)	C19–C20	1.404 (3)
C7–C8	1.453 (3)	C20–C21	1.372 (3)
C8–C9	1.392 (3)	C21–C22	1.389 (3)
C8–C13	1.405 (3)	C23–C24	1.374 (3)
C1–N1–C6	110.69 (15)	C3–C4–C5	117.91 (15)
C1–N1–C2	110.57 (15)	C7–C5–C4	117.20 (16)
C6–N1–C2	109.79 (14)	C7–C5–C6	125.44 (16)
C18–C3–C4	116.23 (16)	C4–C5–C6	117.29 (16)
C18–C3–C2	125.59 (16)	C5–C7–C8	131.72 (18)
C4–C3–C2	118.17 (15)	C13–C8–C7	126.06 (17)
O1–C4–C3	121.59 (16)	C3–C18–C19	131.79 (17)
O1–C4–C5	120.50 (16)	C24–C19–C18	127.58 (17)
C4–C5–C7–C8	178.84 (19)	C4–C3–C18–C19	179.44 (18)
C5–C7–C8–C9	–157.1 (2)	C3–C18–C19–C20	166.15 (19)

Data collection

Enraf–Nonius CAD-4
 diffractometer
 $\theta/2\theta$ scans
 5646 measured reflections
 5319 independent reflections
 2701 reflections with *I* > 2σ(*I*)
R_{int} = 0.020

θ_{\max} = 27.0°
h = 0 → 11
k = 0 → 20
l = –21 → 21
 3 standard reflections
 every 97 reflections
 intensity decay: 3%

Refinement

Refinement on *F*²
R [*F*² > 2σ(*F*²)] = 0.053
wR (*F*²) = 0.133
S = 1.19
 5319 reflections
 313 parameters

H-atom parameters constrained
 $w = 1/[\sigma^2(F_o^2) + (0.05P)^2]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} < 0.001$
 $\Delta\rho_{\max} = 0.14 \text{ e } \text{Å}^{-3}$
 $\Delta\rho_{\min} = -0.20 \text{ e } \text{Å}^{-3}$

Compound (II)

Crystal data

C₃₂H₄₁N₃O
M_r = 483.68
 Tetragonal, *I*₄₁/*a*
a = 20.5823 (18) Å
c = 26.794 (4) Å
V = 11351 (2) Å³
Z = 16
D_x = 1.132 Mg m⁻³

Mo *K*α radiation
 Cell parameters from 320 reflections
 θ = 4–24°
 μ = 0.07 mm⁻¹
T = 110 (2) K
 Plate, red
 0.50 × 0.40 × 0.15 mm

Data collection

Bruker SMART CCD area-detector
 diffractometer
 φ and ω scans
 22 604 measured reflections
 5553 independent reflections
 2493 reflections with *I* > 2σ(*I*)

R_{int} = 0.045
 θ_{\max} = 26.0°
h = –25 → 24
k = –19 → 25
l = –11 → 33

Table 2

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

O1–C4	1.241 (3)	C12–C13	1.410 (3)
N2–C13	1.380 (3)	C13–C14	1.400 (3)
N3–C26	1.369 (4)	C14–C15	1.372 (3)
C3–C20	1.339 (4)	C20–C21	1.434 (4)
C3–C4	1.477 (4)	C21–C22	1.326 (4)
C4–C5	1.471 (4)	C22–C23	1.451 (4)
C5–C7	1.343 (3)	C23–C28	1.352 (4)
C7–C8	1.430 (3)	C23–C24	1.375 (5)
C8–C9	1.336 (3)	C24–C25	1.368 (5)
C9–C10	1.450 (3)	C25–C26	1.369 (5)
C10–C15	1.392 (4)	C26–C27	1.352 (4)
C10–C11	1.395 (3)	C27–C28	1.380 (4)
C11–C12	1.383 (3)		
C6–N1–C2	109.8 (2)	C7–C5–C6	123.0 (2)
C6–N1–C1	110.0 (2)	C4–C5–C6	118.2 (2)
C2–N1–C1	111.0 (2)	C5–C7–C8	129.2 (3)
C20–C3–C4	119.0 (3)	C9–C8–C7	122.1 (3)
C20–C3–C2	123.2 (3)	C8–C9–C10	130.1 (3)
C4–C3–C2	117.9 (2)	C15–C10–C9	125.0 (2)
O1–C4–C5	120.8 (2)	C3–C20–C21	129.0 (3)
O1–C4–C3	121.0 (3)	C22–C21–C20	122.6 (3)
C5–C4–C3	118.2 (3)	C21–C22–C23	129.8 (3)
C7–C5–C4	118.8 (3)	C28–C23–C22	125.1 (3)
C4–C5–C7–C8	179.3 (2)	C4–C3–C20–C21	178.2 (3)
C5–C7–C8–C9	176.7 (3)	C3–C20–C21–C22	–176.6 (3)
C7–C8–C9–C10	179.5 (2)	C20–C21–C22–C23	179.2 (3)
C8–C9–C10–C11	172.9 (3)	C21–C22–C23–C24	–175.3 (5)

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.068$
 $wR(F^2) = 0.191$
 $S = 1.06$
 5553 reflections
 368 parameters
 H-atom parameters constrained

$$w = 1/[\sigma^2(F_o^2) + (0.08P)^2]$$

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

$$(\Delta/\sigma)_{\max} = 0.001$$

$$\Delta\rho_{\max} = 0.42 \text{ e } \text{Å}^{-3}$$

$$\Delta\rho_{\min} = -0.29 \text{ e } \text{Å}^{-3}$$

All H atoms were placed in geometrically calculated positions and allowed for as riding (C—H = 0.93, 0.97 and 0.96 Å for aromatic, CH₂ and methyl H atoms, respectively).

For compound (I), data collection: *CAD-4 Software* (Enraf-Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *SHELXTL-Plus* (Sheldrick, 1994). For compound (II), data collection: *SMART* (Bruker, 1998); cell refinement: *SMART*; data reduction: *SAINTE* (Bruker, 1998). For both compounds, 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*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SQ1020). Services for accessing these data are described at the back of the journal.

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