

(9E)-9-Benzylidene-3-methyl-2-methylsulfanyl-5-phenyl-5,6,7,8,9,10-hexahydropyrimido[4,5-*b*]quinolin-4(3H)-one: polarized molecules within hydrogen-bonded bilayersDiana Becerra,^a Braulio Insuasty,^a Justo Cobo^b and Christopher Glidewell^{c*}^aDepartamento de Química, Universidad de Valle, AA 25360 Cali, Colombia,^bDepartamento de Química Inorgánica y Orgánica, Universidad de Jaén, 23071Jaén, Spain, and ^cSchool of Chemistry, University of St Andrews, Fife KY16 9ST, Scotland

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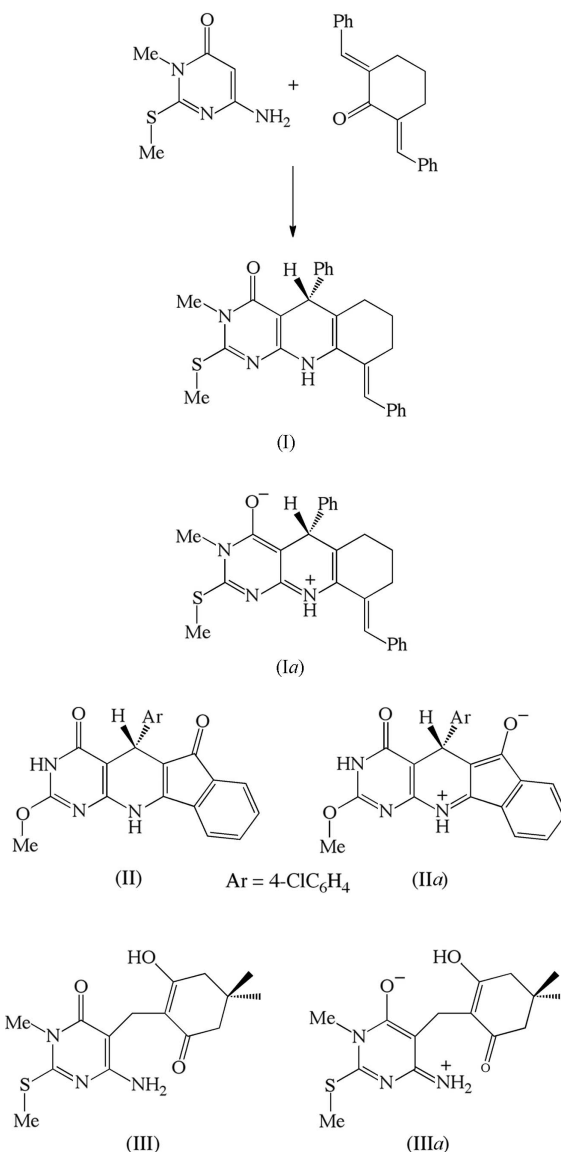
The molecules of the title compound, C₂₆H₂₅N₃OS, which was prepared by means of an acid-catalysed cyclocondensation reaction between a 6-aminopyrimidinone and 2,6-dibenzylidenecyclohexanone, exhibit a polarized electronic structure, namely (9E)-9-benzylidene-3-methyl-2-methylsulfanyl-5-phenyl-3,5,6,7,8,9-hexahydropyrimido[4,5-*b*]quinolin-10-ium-4-olate, involving charge separation in the vinylogous amide portion. Four hydrogen bonds, two each of the C—H...O and C—H... π (arene) types, link the molecules into bilayers comprising inversion-related pairs of sheets, each containing a single type of R₃³(36) ring.

Comment

In our search for new bioactive compounds based on heterocyclic frameworks, pyrimido[4,5-*b*]quinolines have emerged as interesting targets because of their structural analogy with flavones. We report here the molecular and supramolecular structure of the title compound, (I), which was prepared using an acid-catalysed cyclocondensation between (2E,6E)-2,6-dibenzylidenecyclohexanone and 6-amino-3-methyl-2-(methylsulfanyl)pyrimidin-4(3H)-one (see scheme). This synthetic procedure may be contrasted with the synthesis of the related compound, (II), which employed a multi-component cyclocondensation reaction under environmentally friendly solvent-free conditions, mediated by microwave radiation (Low, Cobo, Cisneros *et al.*, 2004).

The molecules of (I) contain a stereogenic centre at C5 (Fig. 1) and the reference molecule was selected as one having the *R* configuration at C5. However, the centrosymmetric space group accommodates equal numbers of the two enantiomorphs. In addition, the two rings which are fused at

the C5a—C9a bond (Fig. 1) are both nonplanar. The heterocyclic ring containing atom N10 adopts a boat-type conformation, with atoms C5 and N10 acting as the stem and stern of the boat, respectively. The ring-puckering parameters (Cremer & Pople, 1975) for the atom sequence N10/C9a/C5a/C5/C4a/C10a are $Q = 0.205$ (2) Å, $\theta = 103.8$ (6)° and $\varphi = 2.6$ (7)°, whereas the ideal puckering angles for a boat conformation are $\theta = 90^\circ$ and $\varphi = 60k^\circ$, where k represents an integer.



The adjacent carbocyclic ring adopts an envelope conformation, folded across the line C6...C8, with ring-puckering parameters, for the atom sequence C5a—C6—C7—C8—C9—C9a, of $Q = 0.481$ (3) Å, $\theta = 58.6$ (4)° and $\varphi = 117.6$ (4)°. The angles may be compared with the ideal values for an envelope conformation of $\theta = 54.7^\circ$ and $\varphi = 60k^\circ$, where k again represents an integer. By contrast, the pyrimidine component of the fused ring system is planar. The remainder of the molecular conformation can be specified in terms of just three torsion angles (Table 1), defining the orientation of the various substituents relative to the adjacent components of the fused ring system. While the C atom of the methylsulfanyl substiti-

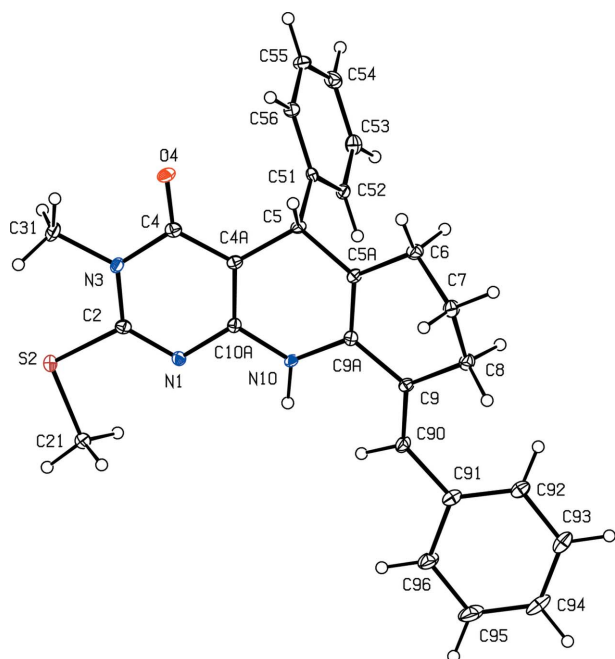


Figure 1

The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

tuent is almost coplanar with the adjacent ring, the C51–C56 aryl ring is nearly orthogonal to the mean plane of the reduced pyridine ring (Table 1), with a dihedral angle between the mean planes of 83.0 (2)°.

Within the fused heterocyclic ring system, the bond distances are fairly similar to those found in the related methylsulfanylpurimidine (III), where the polarized form (IIIa) was deduced to be important (Low, Cobo, Cruz *et al.*, 2004). In particular, in (I), the N10–C10a bond is significantly longer than the N10–C9a bond, while the C4–C4a bond is significantly shorter than the analogous C9–C9a bond. The C5a–C9a and C9–C90 bonds are localized double bonds. These observations point to a contribution to the electronic structure of (I) from the polarized form (Ia). By contrast, in (II) (Low, Cobo, Cisneros *et al.*, 2004), the polarization of the structure involves the carbonyl unit in the five-membered carbocyclic ring, rather than that in the pyrimidone ring (see scheme).

The supramolecular aggregation in (I) is determined by two C–H···O hydrogen bonds and two C–H··· π (arene) hydrogen bonds (Table 2), but the N–H group in the reduced pyridine ring plays no part in the hydrogen bonding. The only potential acceptor within plausible hydrogen-bonding distance of atom N10 in the reference molecule at (x , y , z) is the corresponding atom N10 in the molecule at ($1-x$, $1-y$, $1-z$), but the N···N distance is 3.163 (2) Å and, more significantly, the N–H···N angle is only 91°.

The two C–H···O hydrogen bonds form a simple sheet. The hydrogen bond having atom C53 as the donor links molecules related by translation into a $C(8)$ (Bernstein *et al.*, 1995) chain running parallel to the [100] direction, while the hydrogen bond having atom C94 as the donor links molecules,

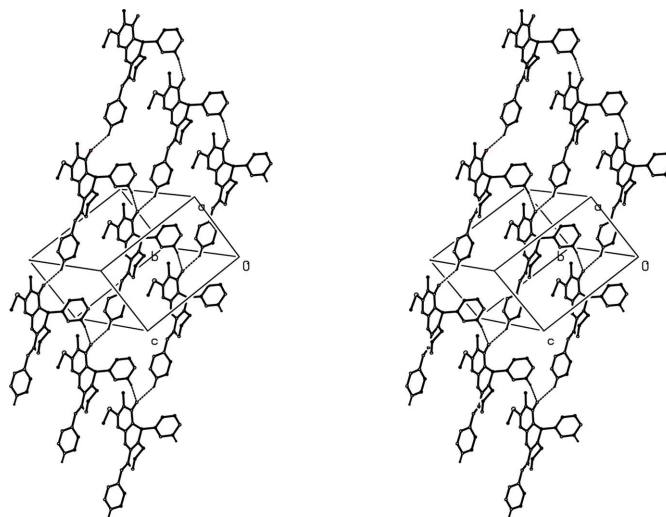


Figure 2

A stereoview of part of the crystal structure of (I), showing the formation of a hydrogen-bonded sheet of $R_4^3(36)$ rings lying parallel to (010) and built from two independent C–H···O hydrogen bonds. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

again related by translation, into a $C(13)$ chain running parallel to the [10 $\bar{1}$] direction. The combination of these two chain motifs generates a sheet lying parallel to (010) and built from a single type of $R_4^3(36)$ ring (Fig. 2). Of the two C–H··· π (arene) hydrogen bonds, that having the longer H···centroid distance lies within the (010) sheet and hence provides a modest reinforcement of the sheet formation, while the shorter of these two interactions weakly links an inversion-related pair of sheets into a bilayer parallel to (010). Aromatic π – π stacking interactions, however, are absent from the structure.

It is of interest briefly to compare the supramolecular aggregation in (I) with those in the related compounds, (II) and (III). In (II), which crystallizes as a stoichiometric 1:1 solvate with dimethylformamide (Low, Cobo, Cisneros *et al.*, 2004), inversion-related pairs of pyrimidinedione molecules are linked by pairs of N–H···O hydrogen bonds to form centrosymmetric $R_2^2(8)$ dimers, from which the dimethylformamide molecules are pendent, and these dimers are linked into chains by a single C–H··· π (arene) hydrogen bond.

By contrast, (III) crystallizes in a solvent-free form (Low, Cobo, Cruz *et al.*, 2004) and, while the structure contains three hydrogen bonds, one of the O–H···O type and two of the N–H···O type, two of them are intramolecular. The remaining N–H···O hydrogen bond links molecules related by translation into simple $C(9)$ chains, and antiparallel pairs of these chains are weakly linked by a single π – π stacking interaction involving pyrimidine rings.

Experimental

A catalytic quantity of boron trifluoride etherate was added to an ethanol solution containing equimolar quantities of (2*E*,6*E*)-2,6-dibenzylidencyclohexanone and 6-amino-3-methyl-2-(methylsulfan-

yl)pyrimidin-4(3*H*)-one, and this mixture was then stirred for 3 d at ambient temperature. The resulting solid product was collected by filtration and recrystallized from an ethanol–dimethylformamide mixture (1:1 *v/v*) to give yellow crystals of (I) suitable for single-crystal X-ray diffraction [yield 56%, m.p. 490–493 K (decomposition)]. MS (EI) *m/z*: 427 [*M*⁺] (6), 350 (100), 302 (8).

Crystal data

C ₂₆ H ₂₅ N ₃ OS	$\gamma = 76.43 (3)^\circ$
<i>M_r</i> = 427.55	<i>V</i> = 1071.1 (5) Å ³
Triclinic, <i>P</i> $\bar{1}$	<i>Z</i> = 2
<i>a</i> = 8.382 (2) Å	Mo <i>K</i> α radiation
<i>b</i> = 10.777 (3) Å	$\mu = 0.18 \text{ mm}^{-1}$
<i>c</i> = 12.745 (4) Å	<i>T</i> = 120 K
$\alpha = 73.18 (3)^\circ$	0.27 × 0.20 × 0.10 mm
$\beta = 85.13 (4)^\circ$	

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer	22289 measured reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	3983 independent reflections
<i>T</i> _{min} = 0.942, <i>T</i> _{max} = 0.983	2998 reflections with <i>I</i> > 2σ(<i>I</i>)
	<i>R</i> _{int} = 0.060

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.053$	282 parameters
$wR(F^2) = 0.104$	H-atom parameters constrained
<i>S</i> = 1.10	$\Delta\rho_{\text{max}} = 0.25 \text{ e } \text{Å}^{-3}$
3983 reflections	$\Delta\rho_{\text{min}} = -0.33 \text{ e } \text{Å}^{-3}$

Table 1

Selected geometric parameters (Å, °).

N1–C2	1.296 (3)	C4–O4	1.228 (3)
C2–N3	1.362 (3)	C9–C90	1.339 (3)
N3–C4	1.408 (3)	C5a–C9a	1.341 (3)
C4–C4a	1.417 (3)	C9–C9a	1.467 (3)
C4a–C10a	1.355 (3)	C9a–N10	1.401 (3)
C10a–N1	1.361 (3)	N10–C10a	1.357 (3)
<hr/>			
N1–C2–S2–C21	1.6 (2)	C4a–C5–C51–C52	−84.5 (3)
C9–C90–C91–C92	−23.7 (4)		

Table 2

Hydrogen-bond geometry (Å, °).

Cg1 and Cg2 are the centroids of the C51–C56 and C91–C96 rings, respectively.

<i>D</i> –H... <i>A</i>	<i>D</i> –H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> –H... <i>A</i>
C53–H53...O4 ⁱ	0.95	2.50	3.440 (3)	170
C94–H94...O4 ⁱⁱ	0.95	2.48	3.325 (3)	148
C54–H54...Cg2 ⁱⁱⁱ	0.95	2.93	3.772 (3)	149
C96–H96...Cg1 ^{iv}	0.95	2.89	3.765 (3)	154

Symmetry codes: (i) *x* − 1, *y*, *z*; (ii) *x* − 1, *y*, *z* + 1; (iii) *x*, *y*, *z* − 1; (iv) −*x* + 1, −*y* + 1, −*z* + 1.

All H atoms were located in difference maps. H atoms bonded to C were then treated as riding in geometrically idealized positions,

with C–H = 0.95 (aromatic and alkenyl), 0.98 (CH₃), 0.99 (CH₂) or 1.00 Å (aliphatic CH), and with $U_{\text{iso}}(\text{H}) = kU_{\text{eq}}(\text{C})$, where *k* = 1.5 for the methyl groups, which were permitted to rotate but not to tilt, and 1.2 for all other H atoms bonded to C atoms. The H atom bonded to atom N10 was permitted to ride at the position found in a difference map, with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{N})$, giving an N–H distance of 0.92 Å and a sum of the bond angles at atom N10 of 359°. There is a short (1.80 Å) nonbonded intramolecular contact between atoms H10 and H90, but the mutual disposition of the carrier atoms N10 and C90 is determined by the rigidity imposed on this part of the molecular skeleton by the π-system (see scheme). PLATON (Spek, 2009) reports a void volume of 54.3 Å³ centred at the origin, but none of the maxima in the final difference map is particularly close to the origin, while the SQUEEZE option in PLATON reported only one additional electron per unit cell. We conclude that there is no significant electron density within this void volume.

Data collection: COLLECT (Nonius, 1999); cell refinement: DIRAX/LSQ (Duisenberg *et al.*, 2000); data reduction: EVALCCD (Duisenberg *et al.*, 2003); program(s) used to solve structure: SIR2004 (Burla *et al.*, 2005); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: PLATON (Spek, 2009); software used to prepare material for publication: SHELXL97 and PLATON.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3376). Services for accessing these data are described at the back of the journal.

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