

9-(Thio-2'-methyl-4'-nitrophenyl) acridine

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Key indicators

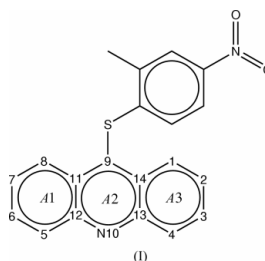
Single-crystal X-ray study
 T = 293 K
 Mean $\sigma(\text{C}-\text{C}) = 0.006 \text{ \AA}$
 R factor = 0.058
 wR factor = 0.166
 Data-to-parameter ratio = 10.8

For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

All interatomic distances in the title compound, $\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$, (I), are normal. The molecule consists of two cyclic moieties, an acridine and a substituted phenyl ring. The two rings are joined *via* a sulfur bridge [S—C = 1.782 (3) and 1.764 (4) Å]. The substituted phenyl ring in (I) is nearly perpendicular to the acridine moiety, with a dihedral angle of 75.01 (7)°. The acridine skeleton is slightly bent, with dihedral angles between the two terminal carbocyclic rings and the central heterocycle of 1.2 (1) and 0.5 (1)°. The molecules of the title compound stack head-to-tail along the *b* axis, with a distance between molecules of about 4.381 Å. In order to investigate quantitatively the aromaticity in acridines, we calculated the HOMA index [Krygowski (1993). *J. Chem. Inf. Comput. Sci.* **33**, 70.] for each of the acridine rings; values were 0.568 and 0.524 for the carbocyclic rings and 0.816 for the heterocycle.

Comment

Acridine derivatives are currently delivered to animals as antihelminthics agents (Durchheimer *et al.*, 1980). In addition, acridine derivatives have shown *in vitro* activity against protozoan-like *Trypanosoma cruzi* (Ngadi *et al.*, 1993) and *Leishmania donovani* (Mesa-Valle *et al.*, 1996). This work has been undertaken in the context of our studies on acridine derivatives with potential pharmacological properties (Karolak-Wojciechowska *et al.*, 1996; Karolak-Wojciechowska *et al.*, 1998). It was especially important to perform an X-ray analysis on single crystals of 9-(thio-2-methyl-4-nitrophenyl) acridine, (I), to obtain atomic coordinates which could be used as a starting point for further molecular modelling.



The molecular structure of (I) is presented in Fig. 1. The molecule consists of two cyclic moieties, an acridine and a substituted phenyl ring. The rings are joined *via* a sulfur bridge at C9 (S1—C9 = 1.782 (3) and S1—C1' = 1.764 (4) Å). The substituted phenyl ring in (I) is nearly perpendicular to the acridine moiety, with a dihedral angle of 75.01 (7)°. The molecules of (I) stack head-to-tail along the *b* axis, with a distance between molecules of about 4.381 Å. All bond distances and angles have normal values. The acridine

Received 26 July 2002
 Accepted 2 September 2002
 Online 13 September 2002

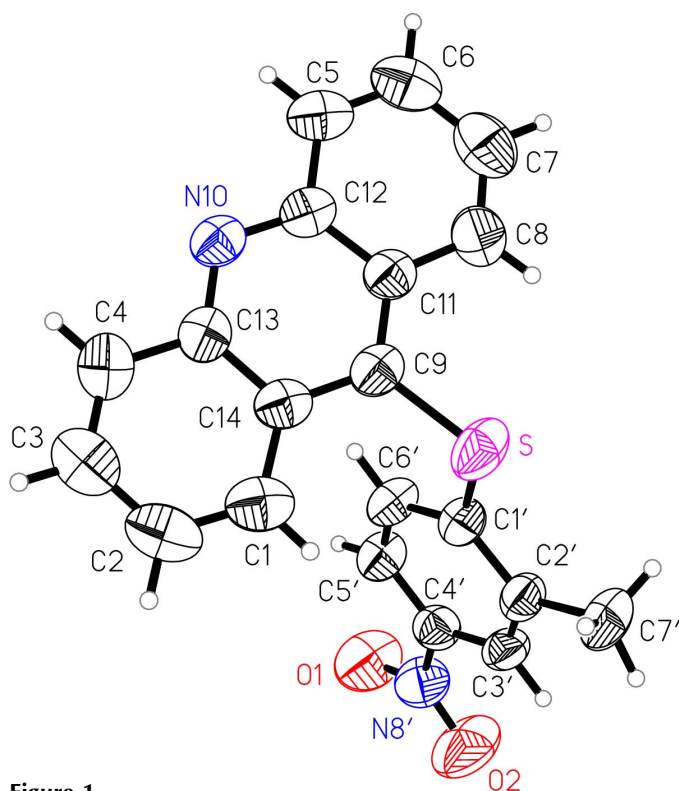


Figure 1
Molecular structure of (I). Displacement ellipsoids are drawn at the 50% probability level.

skeleton is slightly bent, with dihedral angles between the two terminal carbocyclic rings, A1 and A3, and the heterocycle A2 of 1.2 (1) and 0.5 (1)°, respectively. As has been shown for various hydrocarbon systems, such small deviations from planarity of an aromatic species do not affect the aromaticity significantly (Krygowski *et al.*, 2000; Krygowski & Cyranski, 2001). It should also be noted that such a slight deformation of the acridine skeleton is in accordance with data for 34 C9-substituted acridines retrieved from the Cambridge Structural Database (Version of November 2001; Allen & Kennard, 1993). Most of these molecules include an acridine moiety with a very slight boat conformation. Only two structures found in the CSD contain acridine in a chair conformation. The average value of the dihedral angles between the terminal and central rings for the 34 molecules is 1.5°. On account of the interest in hydrocarbons and the aromaticity of their aza analogues (Krygowski *et al.*, 2000; Krygowski & Cyranski, 2001), we decided to investigate quantitatively the aromaticity in acridines (Mrozek, Karolak-Wojciechowska, Amiel & Barbe, 2000*a,b*) by calculating the HOMA index (Krygowski, 1993) for each acridine ring in (I); its values are 0.568 and 0.524 for the carbocyclic rings, and 0.816 for the heterocycle. To confirm these results, calculations of the HOMA index were performed for all 34 C9-substituted acridines found in the CSD (Set 1, $\text{HOMA}_{\text{AV}} = 0.744$ and $\text{HOMA}_{\text{A2}} = 0.510$), and as, an extension of our statistical research, for 18 unsubstituted acridines (Set 2; $\text{HOMA}_{\text{AV}} = 0.810$ and $\text{HOMA}_{\text{A2}} = 0.601$) also found in the CSD. For the terminal rings A1 and A3, the results of the HOMA calculations are given as an averaged

HOMA index (HOMA_{AV}), whereas HOMA_{A2} is the value of the HOMA index for the central heterocyclic ring A2. The aromaticity of the central heterocycle is notably higher than for the terminal carbocyclic rings. A similar effect is observed, not only for the acridine parent molecule anthracene, where the HOMA index values are 0.638 for the terminal rings and 0.763 for the central one, but also for different aza-substituted benzenoids (Krygowski *et al.*, 2000; Krygowski & Cyranski, 2001; Cyranski & Krygowski, 1996). Moreover, the replacement of CH by N usually leads to an increase in the aromaticity of the system. This conclusion is confirmed by the fact that the HOMA indices for the central acridine ring are higher or, at least comparable to, those for anthracene.

Experimental

The title compound was synthesized according to the method of Mrozek, Karolak-Wojciechowska, Bsiri & Barbe (2000).

Crystal data

$\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$
 $M_r = 346.39$
 Monoclinic, $P2_1/n$
 $a = 9.826$ (2) Å
 $b = 7.171$ (1) Å
 $c = 23.941$ (5) Å
 $\beta = 101.57$ (3)°
 $V = 1652.7$ (5) Å³
 $Z = 4$

$D_x = 1.392$ Mg m⁻³
 Cu $K\alpha$ radiation
 Cell parameters from 25 reflections
 $\theta = 10\text{--}35^\circ$
 $\mu = 1.87$ mm⁻¹
 $T = 293$ (2) K
 Needle, colourless
 $0.5 \times 0.2 \times 0.1$ mm

Data collection

Kuma KM4 diffractometer
 ω -2 θ scans
 Absorption correction: numerical
 (*X-RED*; Stoe & Cie, 1999)
 $T_{\text{min}} = 0.421$, $T_{\text{max}} = 0.872$
 2670 measured reflections
 2469 independent reflections
 1802 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.063$
 $\theta_{\text{max}} = 80.9^\circ$
 $h = -8 \rightarrow 0$
 $k = -9 \rightarrow 0$
 $l = -27 \rightarrow 30$
 2 standard reflections
 every 100 reflections
 intensity decay: 2%

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.058$
 $wR(F^2) = 0.166$
 $S = 1.11$
 2469 reflections
 228 parameters
 H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0874P)^2]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} < 0.001$
 $\Delta\rho_{\text{max}} = 0.38$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.40$ e Å⁻³
 Extinction correction: *SHELXL*
 Extinction coefficient: 0.0118 (10)

Table 1

Selected geometric parameters (Å).

C9—C11	1.392 (5)	C12—N10	1.342 (4)
C9—C14	1.408 (5)	N10—C13	1.339 (5)
C11—C8	1.421 (5)	C13—C14	1.428 (5)
C11—C12	1.431 (5)	C13—C4	1.434 (5)
C8—C7	1.342 (6)	C4—C3	1.342 (5)
C7—C6	1.418 (6)	C3—C2	1.408 (6)
C6—C5	1.349 (5)	C2—C1	1.359 (5)
C5—C12	1.424 (5)	C1—C14	1.429 (5)

As the collected data were relatively weak, there was a large proportion of reflections with low intensities, and thus some of the reflections were marked as unobserved. This affects the fraction of unique reflections observed (to $\theta = 80.91^\circ$), which is equal to 62.6%.

All H atoms were placed in calculated positions and treated as riding on the adjacent C atom. The methyl group was allowed to rotate about its local threefold axis.

Data collection: *KM4 Software* (Kuma, 1993); cell refinement: *KM4 Software*; data reduction: *DATAPROC* (Galdecki *et al.*, 1998); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990a); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *XP* in *SHELXTL/PC* (Sheldrick, 1990b) *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

References

- Allen, F. R. & Kennard, O. (1993). *Chem. Des. Autom. News*, **8**, 1, 31–37.
- Cyranski, M. & Krygowski, T. M. (1996). *Tetrahedron*, **52**, 13795–13802.
- Durchheimer, W., Raether, W., Seliger, H. & Seidenath, H. (1980). *Arzneim. Forsch. Drug. Res.* **30**, 1041–1046.
- Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
- Galdecki, Z., Kowalski, A. & Uszynski, I. (1998). *DATAPROC*. Version 10.0.4. Kuma Diffraction, Wrocław, Poland.
- Kuma (1993). *KM4 Software*. Kuma Diffraction, Wrocław, Poland.
- Karolak-Wojciechowska, J., Mrozek, A., Amiel, P., Brouant, P. & Barbe, J. (1996). *Acta Cryst.* **C52**, 2939–2941.
- Karolak-Wojciechowska, J., Mrozek, A., Trzezwinska, B., Morel, S., Galy, J. P. & Barbe, J. (1998). *Acta Cryst.* **C54**, 1689–1690.
- Krygowski, T. M. (1993). *J. Chem. Inf. Comput. Sci.* **33**, 70.
- Krygowski, T. M., Cyranski, M., Czarnocki, Z., Hafelinger, G. & Katritzky, A. R. (2000). *Tetrahedron*, **56**, 1783–1796.
- Krygowski, T. M. & Cyranski, M. (2001). *Chem. Rev.* **101**, 1385–1419.
- Mesa-Valle, C., Castilla-Calvente, J. J. & Sanchez-Moreno, M. (1996). *Antimicrob. Agents Chemother.* **40**, 684.
- Mrozek, A., Karolak-Wojciechowska, J., Amiel, P. & Barbe, J. (2000a). *J. Mol. Struct.* **524**, 151–157.
- Mrozek, A., Karolak-Wojciechowska, J., Amiel, P. & Barbe, J. (2000b). *J. Mol. Struct.* **524**, 159–167.
- Mrozek, A., Karolak-Wojciechowska, J., Bsiri, N. & Barbe, J. (2000). *Acta Pol. Pharm. Drug. Res.*, **57**, 345–351.
- Ngadi, L., Bsiri, N., Mahamoud, A., Galy, A. M., Galy, J. P., Soyfer, J. C., Barbe, J., Placidi, M., Rodriguez-Santiago, J. J., Mesa-Valle, C., Lombardo, R., Mascaro, C. & Osuna, A. (1993). *Arzneim. Forsch. Drug. Res.* **43**, 480.
- Sheldrick, G. M. (1990a). *Acta Cryst.* **A46**, 467–473.
- Sheldrick, G. M. (1990b). *SHELXTL/PC*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
- Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.
- Stoe & Cie (1999). *X-RED*. Version 1.18. Stoe & Cie GmbH, Darmstadt, Germany.