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## Bis(*epi*-globulyloxy)(phthalocyaninato)-silicon,† a new photosensitizer for the photodynamic therapy of cancer

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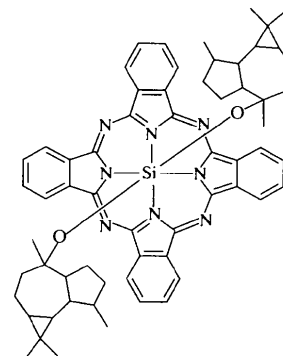
### Abstract

The structure of bis(*epi*-globulyloxy)(phthalocyaninato)-silicon, C<sub>62</sub>H<sub>66</sub>N<sub>8</sub>O<sub>2</sub>Si or [Si(C<sub>32</sub>H<sub>16</sub>N<sub>8</sub>)(C<sub>15</sub>H<sub>25</sub>O)<sub>2</sub>], has been assigned. The Si atom is coordinated to the N atoms of the phthalocyanine ring and bridges the two *epi*-globulyloxy moieties through two Si—O bonds, which are almost perpendicular to the phthalocyanine plane. The molecule displays a pseudo-centrosymmetric character relative to silicon, but the two apical ligands break the symmetry.

### Comment

In recent publications (Decréau, Chanon & Julliard, 1998, 1999), we described the binding of steroid moieties on silicon and aluminium phthalocyanines, leading to new efficient photosensitizers against human melanoma cells in the photodynamic therapy of cancer (Decréau, Verrando *et al.*, 1998). The binding of sesquiterpenoid moieties was also performed in order to reach a higher solubility, to decrease the stacking aggregation of the phthalocyanine (PHC) rings, and to increase the molecular recognition for the liposome-

delivered new photosensitizers. It was then achieved by reacting the *epi*-globulol alcoholate with dichlorosilicon phthalocyanine, (1) (Decréau, Julliard *et al.*, 1999), leading to bis(*epi*-globulyloxy)(phthalocyaninato)silicon, (2), in 65% yield. The *in vitro* photodynamic activity of (2) was higher than that of (1) (Decréau, 1998). The structure of (2) has been assigned here by X-ray crystallography analysis.



(2)

The core of photosensitizer (2) is composed of two *epi*-globulol moieties, each of which is connected to the silicon phthalocyanine *via* an Si—O bond. The Si atom lies in the middle of the phthalocyanine cavity and exhibits an octahedral geometry with the two bridging O atoms in apical positions. Each *epi*-globulol is composed of a seven-membered ring to which three- and five-membered rings are fused. The molecular structure of (2) shows that these units are related by a pseudo-twofold axis parallel to the O—Si—O direction, conferring a centrosymmetric character on the structure. However, the relative orientation of the seven- or five-membered rings breaks this symmetry; the C54—C58 and the C39—C43 cycles point in the same direction (Fig. 1). The geometrical parameters of (2) show that the PHC macrocycle is essentially planar, as previously described in the case of other metallophthalocyanines (Mooney *et al.*, 1975; Silver *et al.*, 1998; Brewis *et al.*, 1998).

The most interesting geometrical parameters involve the inner Si atom of (2). The average Si—O bond length is 1.696 (3) Å and the average Si—N distance is 1.919 (6) Å; nevertheless, two Si—N bonds are observed at 1.906 (3) and 1.934 (3) Å. The O—Si—O bridge is almost linear [175.4 (2)°], and the Si—O—C angles are 148.0 (3) and 148.4 (3)°. These parameters can be compared to those of silicon phthalocyanine (Si-PHC) bearing two trimethylsiloxy groups, (3) (Mooney *et al.*, 1975), two ferrocenylcarboxylate groups, (4) (Silver *et al.*, 1998), or two Fréchet's dendritic groups, (5) (Brewis *et al.*, 1998), or to those of compounds containing two silicon phthalocyanine moieties, (6), *e.g.* oligomerized silicon phthalocyanines (Si-PHC-O)<sub>n</sub> (*n* = 2, *x*), where the PHC units are connected to each other *via* a  $\mu$ -oxo bridge. So the Si—O and Si—N bond lengths display

† Alternative name: (1a,2,3,4,4a,5,6,7,7a,7b-decahydro-1,1,4,7-tetramethyl-1*H*-cycloprop[*e*]azulen-4-olato-*O*)(phthalocyaninato-*N*<sup>29</sup>,*N*<sup>30</sup>,-*N*<sup>31</sup>,*N*<sup>32</sup>)silicon.

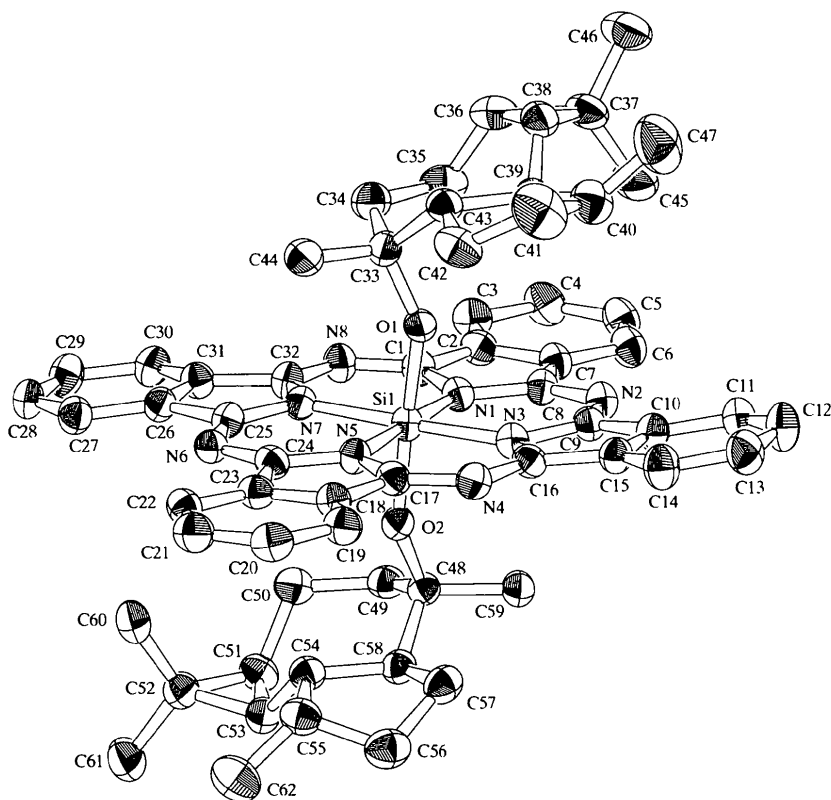


Fig. 1. An ORTEP (Johnson, 1976) view of compound (2) with displacement ellipsoids at the 20% probability level. H atoms have been omitted.

a significant difference depending on the axial ligand; the average Si—O length is 1.679 (3) Å for (3) [which is close to the average length for (2)] and is 1.750 Å for (4). This shows that, contrary to the C atoms of the ferrocenylcarboxylate groups of (4), the C atoms of the *epi*-globulol groups of (2) or the Si atoms (axial ligand) of the trimethylsilyloxy groups of (3) are less able to compete for the oxygen than the Si(PHC) atom. The average Si—O bond length is reduced to 1.673 Å for (6). It is worth comparing these data with Al-PHC-bearing nitrite groups in which the axial *M*—O bond length increases to 1.927 (2) Å (Assman & Homborg, 1996). On the other hand, the average Si—N length is 1.919 (9) Å for (3), which is closer to the value observed for (2) than the value observed for (4) (1.905 Å). The average Si—N bond length is therefore longer in (2) and (3). This may be a consequence of the shorter Si—O axial bonds which leave the Si atom not needing any electron density. This need is compensated in (4) because the Si atom bonds more strongly to the N atom in the PHC ring (Silver *et al.*, 1998). Finally, an examination of each Si—N bond length reveals that in (3) and (4), the Si atom is centered into the cavity of the PHC. On the contrary, in (2), Si is closer to the N atoms of two adjacent pyrrolic units (N1 and N3) than to the N atoms of the opposite units (N5 and N7).

The O—Si—O bridge is almost linear in (2) [175.4 (2)°], as for (3) (177.4°) and (5) (179°). The average angle around the O atom connecting the Si-PHC to the atom (*L*) of the axial ligand is 148.2 (3)° for (2) (*L* = C) and can be compared to other Si-PHC compounds where *L* = Si; the angle is 157.8 (1)° for (3) and 180° for (6) which is an oligomeric Si-PHC. In the case of other oligomeric *M*-PHC (*M* = Al, Ge, Sn, Fe, Mn), the angle around the bridging O atom is also linear (Kroenke *et al.*, 1963; Wynne, 1985; Dirk *et al.*, 1983; Ercolani *et al.*, 1983).

The shortest intramolecular distance between the core of the ligand and the ring of the phthalocyanine is 3.297 (4) Å between N3 and C59. This implies a limited interaction by comparison with the shorter 3.177 (7) Å distance measured between an indolenic N atom of Si-PHC and an axial dendritic substituent in compound (5) (Brewis *et al.*, 1998).

## Experimental

Bis(*epi*-globulyloxy)(phthalocyaninato)silicon, (2), was obtained in 65% yield from the reaction of *epi*-globulol alcoholate with dichlorosilicon phthalocyanine (Decréau, Julliard *et al.*, 1999).

*Crystal data*

C<sub>62</sub>H<sub>66</sub>N<sub>8</sub>O<sub>2</sub>Si  
*M<sub>r</sub>* = 983.33  
 Triclinic  
*P*1  
*a* = 9.608 (1) Å  
*b* = 10.742 (1) Å  
*c* = 14.468 (1) Å  
 $\alpha$  = 107.121 (1)°  
 $\beta$  = 102.757 (1)°  
 $\gamma$  = 104.349 (1)°  
*V* = 1311.1 (4) Å<sup>3</sup>  
*Z* = 1  
*D<sub>x</sub>* = 1.24 Mg m<sup>-3</sup>  
*D<sub>m</sub>* = 1.25 Mg m<sup>-3</sup>

*Data collection*

KappaCCD diffractometer  
 $\varphi$  scan  
 Absorption correction: none  
 4809 measured reflections  
 4809 independent reflections

*Refinement*

Refinement on *F*  
*R* = 0.062  
*wR* = 0.114  
*S* = 1.0181  
 3561 reflections  
 395 parameters  
 H-atom parameters not refined

Mo *K* $\alpha$  radiation  
 $\lambda$  = 0.71073 Å  
 Cell parameters from 15729 reflections  
 $\theta$  = 1–25°  
 $\mu$  = 0.098 mm<sup>-1</sup>  
*T* = 298 K  
 Thin plate  
 0.6 × 0.4 × 0.2 mm  
 Dark blue

3561 reflections with  
 $I > 2\sigma(I)$   
 $\theta_{\max}$  = 25.78°  
 $h = 0 \rightarrow 12$   
 $k = -13 \rightarrow 11$   
 $l = -18 \rightarrow 17$

$w = 1/[\sigma^2(F) + 0.03F^2]$   
 $(\Delta/\sigma)_{\max} = 0.007$   
 $\Delta\rho_{\max} = 0.23 \text{ e } \text{Å}^{-3}$   
 $\Delta\rho_{\min} = -0.22 \text{ e } \text{Å}^{-3}$   
 Extinction correction: none  
 Scattering factors from  
 Waasmaier & Kirfel  
 (1995)

Table 1. Selected geometric parameters (Å, °)

Si1—O1	1.711 (3)	Si1—N5	1.934 (3)
Si1—O2	1.682 (3)	Si1—N7	1.930 (3)
Si1—N1	1.906 (3)	O1—C33	1.416 (5)
Si1—N3	1.912 (3)	O2—C48	1.427 (4)
O1—Si1—O2	175.4 (2)	O2—Si1—N3	92.7 (2)
O1—Si1—N1	89.0 (2)	Si1—O1—C33	148.4 (3)
O1—Si1—N3	83.6 (2)	Si1—O2—C48	148.0 (3)
O2—Si1—N1	93.7 (2)		

The measurements were carried out on a Nonius area detector through a 180° scan (no Friedel pairs were required, so no complete sphere was measured, as there was no use in checking the absolute configuration) in 2°  $\varphi$  steps.

Data collection: *KappaCCD Software* (Nonius, 1997). Data reduction: *maXus* (Mackay *et al.*, 1998). Program(s) used to solve structure: *maXus*. Program(s) used to refine structure: *maXus*. Molecular graphics: *maXus*. Software used to prepare material for publication: *maXus*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1427). Services for accessing these data are described at the back of the journal.

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## Methyl $\beta$ -lactoside (methyl 4-*O*- $\beta$ -D-galactopyranosyl- $\beta$ -D-glucopyranoside) methanol solvate

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**Abstract**

The structure of the title compound, C<sub>13</sub>H<sub>24</sub>O<sub>11</sub>·CH<sub>4</sub>O, has been determined. The glycosidic torsion angles,  $\varphi$  (O5'—C1'—O4—C4) and  $\psi$  (C1'—O4—C4—C5), have values of  $-88.4(2)$  and  $-161.3(2)^\circ$ , respectively. The structure closely resembles that of methyl  $\beta$ -cellobioside (methyl 4-*O*- $\beta$ -D-glucopyranosyl- $\beta$ -D-glucopyranoside) methanol solvate, the difference being the stereochemistry at a single position (C4').