

4-[(1,3-Dioxo-2,3-dihydro-1*H*-isoindol-2-yl)methyl]-
phthalonitrileXiu-Zhi Xu, Mei-Jin Lin,
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Key indicators

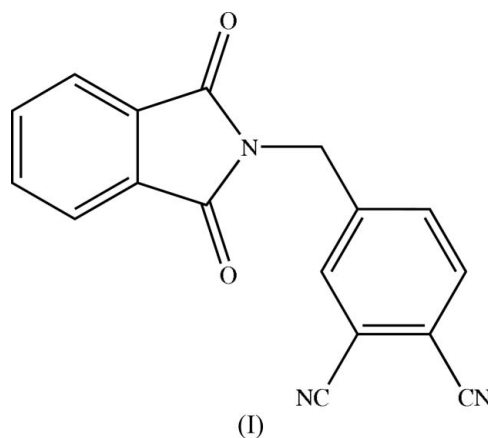
Single-crystal X-ray study
 $T = 298$ K
Mean $\sigma(\text{C}-\text{C}) = 0.003$ Å
 R factor = 0.037
 wR factor = 0.117
Data-to-parameter ratio = 13.2For details of how these key indicators were
automatically derived from the article, see
<http://journals.iucr.org/e>.

In the title compound, $\text{C}_{17}\text{H}_9\text{N}_3\text{O}_2$, the phthalonitrile group and the isoindole-1,3-dione group lie in approximately orthogonal planes and exhibit a dihedral angle of $92.76(8)^\circ$. Partial face-to-face overlap is observed between the two groups. In addition, the crystal packing is stabilized by $\text{C}-\text{H}\cdots\text{O}$ and $\text{C}-\text{H}\cdots\text{N}$ interactions.

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Comment

The title compound, (I), is a precursor for the synthesis of amphiphilic phthalocyanine, which is utilized in the photodynamic therapy (PDT) of tumors (Huang *et al.*, 2000). After phthalocyanine is formed, the phthalimide is easily converted to an amine, which is believed to have a better interaction with cell tissues. In the structure of a similar precursor (Zhu *et al.*, 2005), the two groups are connected by a flexible butoxy chain. The difference between the earlier structure and (I) is that there is no O atom linked to the phthalocyanine ring, and we are investigating if this O atom will or will not influence the yield of active $^1\text{O}_2$ in PDT (Kobayashi *et al.*, 2003).



The molecular structure of (I) is shown in Fig. 1. The cyano-group $\text{N1}-\text{C7}$ [1.130 (3) Å] and $\text{N2}-\text{C8}$ bonds [1.137 (3) Å] are short enough to indicate their triple-bond character, and agree with the values reported by Zhu *et al.* (2005). The $\text{C1}-\text{C7}$ [1.436 (3) Å] and $\text{C2}-\text{C8}$ [1.435 (3) Å] bond distances are comparable to the mean value in phthalonitrile, 1.443 (8) Å, reported by Allen *et al.* (1987). The benzene ring of the phthalonitrile group and the isoindole ring system are essentially perpendicular to each other, with an angle of $92.76(8)^\circ$.

In the crystal packing, the molecules are stacked along the short a axis with weak $\pi-\pi$ interactions due to the partial overlap of the $\text{C1}-\text{C6}$ benzene rings and the isoindole ring systems, with perpendicular distances of 3.556 and 3.150 Å,

respectively. In addition, the molecular packing is stabilized by C—H···O and C—H···N interactions (Table 1).

Experimental

4-Methylphthalic anhydride (50 g, 308 mmol) and urea (18.5 g, 308 mmol) were mixed and heated to 433 K; the mixture melted then solidified. The solid was washed with water and vacuum dried at 353 K to give 4-methylphthalimide (yield 87%, 43.5 g; m.p. 470.8–471.4 K). All of the 4-methylphthalimide obtained was suspended in methanol (800 ml) and stirred for 5–7 days at room temperature while ammonia gas was pumped into the vessel. As the reaction progressed, the suspension dissolved and then a new suspension formed. After filtering and drying at 343 K, 4-methylphthalic diamide was obtained (yield 30%, 12 g; m.p. 455.4–455.6 K). 4-Methylphthalic diamide (10 g, 56.1 mmol) was suspended in pyridine (150 ml) and POCl₃ (13 ml, 142 mmol) was added dropwise at 276–278 K. The mixture was stirred at room temperature for 3 h and then poured into ice water; the precipitate was filtered off, washed with water and dried at 353 K, and 4-methylphthalonitrile was obtained (yield 60%, 4.6 g; m.p. 391.5–391.6 K). This was suspended in CCl₄ (70 ml), and then *N*-bromosuccinimide (5.8 g, 32.6 mmol) and benzoyl peroxide (0.1–0.2 g) were added. The suspension was refluxed for 24 h, and then cooled to room temperature and filtered; the CCl₄ was evaporated and crude 4-bromomethylphthalonitrile (3.5 g) was obtained. The crude 4-bromomethylphthalonitrile (3.5 g, 15.8 mmol), phthalimide (2.4 g, 16.3 mmol) and K₂CO₃ (5 g, 36.2 mmol) were added to *N,N*-dimethylformamide (60 ml), and then stirred at 353 K for 12 h. The reaction mixture was poured into ice water (800 ml), and the precipitate was separated by centrifugation, washed with water and vacuum dried at 353 K, resulting in crude (I) (1.7 g). The crude (I) was washed with CH₃OH and recrystallized from tetrahydrofuran and CH₂Cl₂ repeatedly; colorless needle-shaped crystals of (I) were obtained (m.p. 550–551 K). MS (*m/z*, %): 287 (*M*⁺, 100); IR (KBr, cm⁻¹): 2229 (C—N), 3069 (Ar—H), 1706 (C—O), 1776, 1420 (—CH₂—), 1390, 1112 (N—H), 951 (C—H), 724; UV–vis: 227.41, 294.02 nm (CH₂Cl₂), 235.04, 284.18, 293.95 nm (THF); ¹H NMR (DMSO-*d*₆): δ 4.919 (*s*, 2H), 7.910 (*br*, 5H), 8.115 (*d*, 1H), 8.183 (*s*, 1H).

Crystal data

C ₁₇ H ₉ N ₃ O ₂	<i>D</i> _x = 1.407 Mg m ⁻³
<i>M</i> _r = 287.27	Mo <i>K</i> α radiation
Monoclinic, <i>P</i> 2 ₁ / <i>c</i>	Cell parameters from 6576 reflections
<i>a</i> = 4.9331 (3) Å	<i>θ</i> = 6.1–54.9°
<i>b</i> = 26.2490 (13) Å	<i>μ</i> = 0.10 mm ⁻¹
<i>c</i> = 10.4901 (6) Å	<i>T</i> = 298 (2) K
<i>β</i> = 93.0930 (13)°	Needle, colorless
<i>V</i> = 1356.37 (13) Å ³	0.70 × 0.10 × 0.08 mm
<i>Z</i> = 4	

Data collection

Rigaku R-Axis RAPID diffractometer	<i>R</i> _{int} = 0.044
<i>ω</i> scans	<i>θ</i> _{max} = 27.5°
11806 measured reflections	<i>h</i> = 0 → 6
3107 independent reflections	<i>k</i> = 0 → 34
1558 reflections with <i>I</i> > 2σ(<i>I</i>)	<i>l</i> = -13 → 13

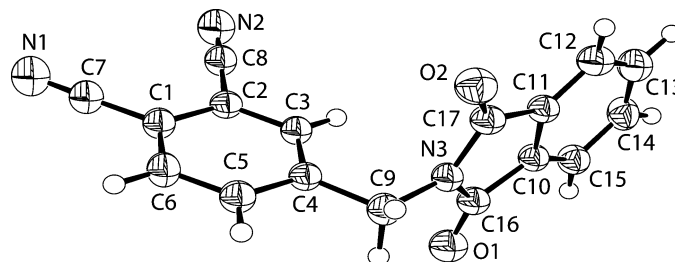


Figure 1
The structure of (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 40% probability level.

Refinement

Refinement on <i>F</i> ²	All H-atom parameters refined
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)] = 0.037	<i>w</i> = 1/[σ ² (<i>F</i> _o ²) + (0.042 <i>P</i>) ²]
<i>wR</i> (<i>F</i> ²) = 0.117	where <i>P</i> = (<i>F</i> _o ² + 2 <i>F</i> _c ²)/3
<i>S</i> = 1.00	(Δ/ <i>σ</i>) _{max} < 0.001
3107 reflections	Δ <i>ρ</i> _{max} = 0.14 e Å ⁻³
235 parameters	Δ <i>ρ</i> _{min} = -0.23 e Å ⁻³

Table 1

Hydrogen-bond geometry (Å, °).

<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>
C3—H1···O2 ⁱ	0.91 (2)	2.47 (2)	3.275 (3)	148 (2)
C6—H3···N2 ⁱⁱ	0.95 (2)	2.60 (2)	3.280 (3)	129 (2)
C15—H9···O1 ⁱⁱⁱ	0.97 (2)	2.44 (2)	3.378 (3)	161 (2)

Symmetry codes: (i) *x* - 1, *y*, *z*; (ii) *x* + 1, -*y* + ½, *z* - ½; (iii) -*x*, -*y* + 1, -*z* + 1.

All H atoms were located in a difference Fourier map and refined isotropically. The C—H distances lie in the range 0.89 (2)–1.01 (3) Å.

Data collection: *RAPID-AUTO* (Rigaku, 1998); cell refinement: *RAPID-AUTO*; data reduction: *RAPID-AUTO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEX* (McArdle, 1995); software used to prepare material for publication: *SHELXL97*.

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