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# 6-Methoxy-2-methyl-1-*m*-tolyl-1*H*-benzimidazole hemihydrate

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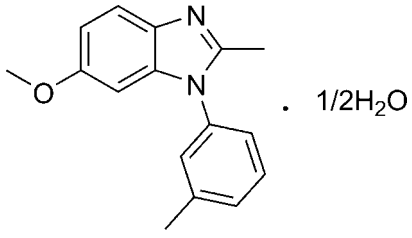
Key indicators: single-crystal X-ray study; $T$ = 293 K; mean $\sigma$(C–C) = 0.005 Å; $R$ factor = 0.081; $wR$ factor = 0.155; data-to-parameter ratio = 15.3.

The title compound, $C_{16}H_{16}N_2O\cdot0.5H_2O$, is a substituted 1-phenylbenzimidazole, which belongs to the class of ATP-site inhibitors of the platelet-derived growth-factor receptor. In the crystal, the components are linked by an O—H···N hydrogen bond.

## Related literature

For related structures, see: Zhong (2004). For medicinal background, see: Palmer (1998).




## Experimental

### Crystal data

$C_{16}H_{16}N_2O\cdot0.5H_2O$ $M_r$ = 261.32
Orthorhombic, *Pbcn*
$a$ = 16.0752 (16) Å
$b$ = 13.9140 (14) Å
$c$ = 12.6450 (13) Å
$V$ = 2828.3 (5) Å$^3$
$Z$ = 8
Mo $K\alpha$ radiation
$\mu$ = 0.08 mm$^{-1}$
$T$ = 293 K
0.25 × 0.23 × 0.21 mm

### Data collection

Bruker APEX CCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min}$ = 0.980, $T_{max}$ = 0.983
13133 measured reflections
2720 independent reflections
2018 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.029

### Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.081
$wR(F^2)$ = 0.155
$S$ = 1.03
2720 reflections
178 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.69 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.20 e Å$^{-3}$

**Table 1**
Hydrogen-bond geometry (Å, °).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| O1$W$—H1$W$···N2 | 0.85 | 2.08 | 2.911 (3) | 166 |

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *SHELXTL*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: AA2011).

## References

Bruker (2000). *SMART* and *SAINT*. Bruker AXS Inc., Madison, Wisconsin, USA.
Palmer, B. D. (1998). *J. Med. Chem.* **41**, 5457–5465.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Zhong, C.-L. (2004). *Bioorg. Med. Chem.* **12**, 4009–4015.

# supplementary materials

*Acta Cryst.* (2011). E**67**, o2263 [ **doi:10.1107/S1600536811031060** ]

# 6-Methoxy-2-methyl-1-*m*-tolyl-1*H*-benzimidazole hemihydrate

**X.-B. Fang, L. Fang and X.-Y. Liu**

## Comment

1-Phenylbenzimidazoles are shown to be a new class of ATP-site inhibitors of the platelet derived growth factor receptor (PDGFR), with clear evidence of the relationship between their molecular features and their inhibitory activity (Palmer, 1998). However, few structure-activity relationship studies involving 1-phenylbenzimidazoles have been published and the QSAR models reported were not completely satisfactory (Zhong, 2004). The synthesis of these compounds is relatively uncomplicated, many methods have been proposed in the past years. We have successfully synthesized the title compound as a key analogue of 1-phenylbenzimidazole.

## Experimental

*N*-(2-amino-5-methoxyphenyl)-*N*-*m*-tolylacetamide (1 g, 3.70 mmol) was dissolved in 40 ml of 18% hydrochloric acid, and the solution was cooled to 0°C. A solution of $NaNO_2$ (0.28 g, 4.07 mmol) in 1 ml of water was added under stirring, and the mixture was stirred for 10 min. Copper powder (1 g) was then added, and the mixture was stirred for 30 min at room temperature. The reaction solution was heated to 70°C and stirred for 3 h. The mixture was extracted with ethyl acetate (2×50 ml), and the extract was washed with a 3% aqueous solution of $NaHCO_3$ and water, respectively. The organic phase was dried over $Na_2SO_4$ and evaporated. The residue was purified by column chromatography. Yield 0.46 g (49%).

## Refinement

The H atoms were positioned geometrically and allowed to ride on their parent atoms, with C—H = 0.93–0.96 Å, and $U_{iso}$ =1.2 or 1.5$U_{eq}$(parent atom). The maximum residual electron density, 0.685 e/Å$^3$, is located at 0.7013, 0.6556, 0.0873 (1.319 Å from C2 atom). This can be explained by a little disorder of the C7 methyl group.

## Figures

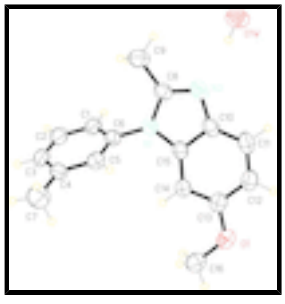

Fig. 1. The asymmetric unit of the title compound. Displacement ellipsoids are drawn at the 30% probability level.

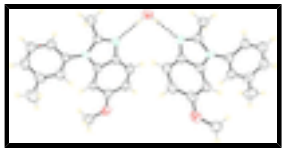

Fig. 2. The dimeric structure of the title compound is built *via* O—H···N hydrogen bonding between water molecule and N atoms of imidazole rings.

### 6-Methoxy-2-methyl-1-*m*-tolyl-1*H*-benzimidazole hemihydrate

*Crystal data*

| | |
|---|---|
| $C_{16}H_{16}N_2O{\cdot}0.5H_2O$ | $F(000) = 1112$ |
| $M_r = 261.32$ | $D_x = 1.227$ Mg m$^{-3}$ |
| Orthorhombic, *Pbcn* | Mo *K*α radiation, λ = 0.71073 Å |
| Hall symbol: -P 2n 2ab | Cell parameters from 2720 reflections |
| $a = 16.0752$ (16) Å | θ = 2.4–28.0° |
| $b = 13.9140$ (14) Å | μ = 0.08 mm$^{-1}$ |
| $c = 12.6450$ (13) Å | $T = 293$ K |
| $V = 2828.3$ (5) Å$^3$ | Plate-like, colourless |
| $Z = 8$ | 0.25 × 0.23 × 0.21 mm |

*Data collection*

| | |
|---|---|
| Bruker APEX CCD diffractometer | 2720 independent reflections |
| Radiation source: fine-focus sealed tube | 2018 reflections with $I > 2\sigma(I)$ |
| graphite | $R_{int} = 0.029$ |
| φ and ω scans | $\theta_{max} = 26.0°$, $\theta_{min} = 2.5°$ |
| Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996) | $h = -17\rightarrow19$ |
| $T_{min} = 0.980$, $T_{max} = 0.983$ | $k = -17\rightarrow17$ |
| 13133 measured reflections | $l = -15\rightarrow14$ |

*Refinement*

| | |
|---|---|
| Refinement on $F^2$ | Secondary atom site location: difference Fourier map |
| Least-squares matrix: full | Hydrogen site location: inferred from neighbouring sites |
| $R[F^2 > 2\sigma(F^2)] = 0.081$ | H-atom parameters constrained |
| $wR(F^2) = 0.155$ | $w = 1/[\sigma^2(F_o^2) + (0.0196P)^2 + 3.0292P]$ where $P = (F_o^2 + 2F_c^2)/3$ |
| $S = 1.03$ | $(\Delta/\sigma)_{max} < 0.001$ |
| 2720 reflections | $\Delta\rho_{max} = 0.69$ e Å$^{-3}$ |
| 178 parameters | $\Delta\rho_{min} = -0.20$ e Å$^{-3}$ |
| 0 restraints | Extinction correction: *SHELXL97* (Sheldrick, 2008), $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$ |
| Primary atom site location: structure-invariant direct methods | Extinction coefficient: 0.0037 (5) |

*Special details*

**Geometry**. All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'s involving l.s. planes.

**Refinement**. Refinement of $F^2$ against ALL reflections. The weighted *R*-factor *wR* and goodness of fit *S* are based on $F^2$, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative $F^2$. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on $F^2$ are statistically about twice as large as those based on *F*, and *R*- factors based on ALL data will be even larger.

*Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å$^2$)*

| | *x* | *y* | *z* | $U_{iso}$*/$U_{eq}$ |
|---|---|---|---|---|
| C1 | 0.6204 (2) | 0.6782 (2) | 0.2566 (2) | 0.0725 (8) |
| H1A | 0.5851 | 0.6253 | 0.2539 | 0.087* |
| C2 | 0.6771 (2) | 0.6930 (3) | 0.1781 (3) | 0.0851 (10) |
| H2A | 0.6809 | 0.6497 | 0.1223 | 0.102* |
| C3 | 0.7285 (2) | 0.7711 (3) | 0.1814 (3) | 0.0863 (11) |
| H3A | 0.7671 | 0.7800 | 0.1274 | 0.104* |
| C4 | 0.72472 (19) | 0.8370 (2) | 0.2623 (3) | 0.0789 (10) |
| C5 | 0.66713 (18) | 0.8218 (2) | 0.3437 (3) | 0.0699 (8) |
| H5A | 0.6636 | 0.8650 | 0.3996 | 0.084* |
| C6 | 0.61540 (17) | 0.7422 (2) | 0.3404 (2) | 0.0624 (7) |
| C8 | 0.5560 (2) | 0.6505 (2) | 0.4939 (2) | 0.0681 (8) |
| C9 | 0.6135 (2) | 0.5667 (2) | 0.4845 (3) | 0.0848 (10) |
| H9A | 0.6020 | 0.5215 | 0.5401 | 0.127* |
| H9B | 0.6700 | 0.5884 | 0.4903 | 0.127* |
| H9C | 0.6055 | 0.5361 | 0.4172 | 0.127* |
| C10 | 0.4610 (2) | 0.7482 (2) | 0.5473 (2) | 0.0681 (8) |
| C11 | 0.3959 (2) | 0.7953 (3) | 0.5984 (3) | 0.0819 (10) |
| H11A | 0.3717 | 0.7687 | 0.6585 | 0.098* |
| C12 | 0.3683 (2) | 0.8807 (3) | 0.5596 (3) | 0.0756 (9) |
| H12A | 0.3245 | 0.9120 | 0.5932 | 0.091* |
| C13 | 0.40456 (18) | 0.9223 (2) | 0.4699 (2) | 0.0677 (8) |
| C14 | 0.46999 (17) | 0.8783 (2) | 0.4176 (2) | 0.0611 (7) |
| H14A | 0.4946 | 0.9056 | 0.3583 | 0.073* |
| C15 | 0.49675 (18) | 0.7910 (2) | 0.4588 (2) | 0.0592 (7) |
| C16 | 0.4029 (2) | 1.0538 (3) | 0.3480 (3) | 0.0863 (10) |
| H16A | 0.3731 | 1.1123 | 0.3341 | 0.129* |
| H16B | 0.3979 | 1.0116 | 0.2883 | 0.129* |
| H16C | 0.4605 | 1.0683 | 0.3601 | 0.129* |
| N1 | 0.55804 (15) | 0.72736 (17) | 0.42521 (18) | 0.0628 (6) |
| N2 | 0.49971 (19) | 0.66035 (18) | 0.5677 (2) | 0.0764 (7) |
| O1 | 0.36911 (13) | 1.00859 (17) | 0.43877 (19) | 0.0811 (7) |
| O1W | 0.5000 | 0.5327 (2) | 0.7500 | 0.0961 (11) |
| H1W | 0.4912 | 0.5668 | 0.6953 | 0.144* |

| | | | | |
|---|---|---|---|---|
| C7 | 0.7786 (3) | 0.9187 (3) | 0.2623 (4) | 0.1196 (16) |
| H7A | 0.8138 | 0.9166 | 0.2011 | 0.179* |
| H7B | 0.8123 | 0.9180 | 0.3250 | 0.179* |
| H7C | 0.7459 | 0.9764 | 0.2609 | 0.179* |

*Atomic displacement parameters (Å$^2$)*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{12}$ | $U^{13}$ | $U^{23}$ |
|---|---|---|---|---|---|---|
| C1 | 0.077 (2) | 0.076 (2) | 0.0645 (18) | 0.0169 (17) | 0.0040 (16) | 0.0042 (16) |
| C2 | 0.092 (2) | 0.093 (3) | 0.070 (2) | 0.029 (2) | 0.0057 (19) | 0.0060 (19) |
| C3 | 0.081 (2) | 0.104 (3) | 0.074 (2) | 0.038 (2) | 0.0189 (18) | 0.019 (2) |
| C4 | 0.0568 (18) | 0.074 (2) | 0.106 (3) | 0.0035 (16) | 0.0035 (18) | 0.033 (2) |
| C5 | 0.0636 (18) | 0.0701 (19) | 0.076 (2) | 0.0092 (16) | 0.0030 (15) | 0.0106 (16) |
| C6 | 0.0602 (17) | 0.0685 (18) | 0.0584 (16) | 0.0054 (15) | 0.0027 (13) | 0.0111 (14) |
| C8 | 0.083 (2) | 0.0562 (17) | 0.0649 (18) | −0.0107 (16) | 0.0003 (16) | 0.0009 (14) |
| C9 | 0.110 (3) | 0.066 (2) | 0.079 (2) | 0.0055 (19) | −0.004 (2) | 0.0036 (17) |
| C10 | 0.077 (2) | 0.0635 (18) | 0.0634 (17) | −0.0187 (16) | 0.0101 (15) | −0.0055 (14) |
| C11 | 0.083 (2) | 0.089 (2) | 0.074 (2) | −0.025 (2) | 0.0264 (18) | −0.0117 (18) |
| C12 | 0.0671 (19) | 0.079 (2) | 0.081 (2) | −0.0068 (17) | 0.0137 (17) | −0.0201 (18) |
| C13 | 0.0566 (17) | 0.075 (2) | 0.0714 (19) | −0.0066 (15) | −0.0019 (15) | −0.0158 (16) |
| C14 | 0.0597 (16) | 0.0658 (17) | 0.0579 (16) | −0.0049 (14) | 0.0025 (13) | −0.0022 (14) |
| C15 | 0.0563 (15) | 0.0632 (17) | 0.0582 (15) | −0.0087 (14) | 0.0045 (13) | −0.0069 (13) |
| C16 | 0.090 (2) | 0.081 (2) | 0.088 (2) | 0.011 (2) | −0.005 (2) | 0.0008 (19) |
| N1 | 0.0676 (15) | 0.0610 (14) | 0.0599 (13) | −0.0022 (12) | 0.0055 (12) | 0.0042 (11) |
| N2 | 0.0991 (19) | 0.0625 (15) | 0.0677 (16) | −0.0165 (15) | 0.0114 (15) | 0.0024 (13) |
| O1 | 0.0725 (13) | 0.0838 (15) | 0.0870 (16) | 0.0143 (12) | −0.0013 (12) | −0.0094 (13) |
| O1W | 0.144 (3) | 0.0619 (19) | 0.082 (2) | 0.000 | 0.002 (2) | 0.000 |
| C7 | 0.100 (3) | 0.097 (3) | 0.163 (4) | −0.008 (2) | 0.008 (3) | 0.013 (3) |

*Geometric parameters (Å, °)*

| | | | |
|---|---|---|---|
| C1—C2 | 1.363 (5) | C10—C11 | 1.394 (4) |
| C1—C6 | 1.387 (4) | C10—N2 | 1.395 (4) |
| C1—H1A | 0.9300 | C11—C12 | 1.359 (5) |
| C2—C3 | 1.366 (5) | C11—H11A | 0.9300 |
| C2—H2A | 0.9300 | C12—C13 | 1.401 (4) |
| C3—C4 | 1.375 (5) | C12—H12A | 0.9300 |
| C3—H3A | 0.9300 | C13—C14 | 1.385 (4) |
| C4—C5 | 1.400 (4) | C13—O1 | 1.386 (4) |
| C4—C7 | 1.429 (5) | C14—C15 | 1.389 (4) |
| C5—C6 | 1.385 (4) | C14—H14A | 0.9300 |
| C5—H5A | 0.9300 | C15—N1 | 1.391 (4) |
| C6—N1 | 1.429 (3) | C16—O1 | 1.417 (4) |
| C8—N2 | 1.307 (4) | C16—H16A | 0.9600 |
| C8—N1 | 1.378 (4) | C16—H16B | 0.9600 |
| C8—C9 | 1.492 (4) | C16—H16C | 0.9600 |
| C9—H9A | 0.9600 | O1W—H1W | 0.8500 |
| C9—H9B | 0.9600 | C7—H7A | 0.9600 |
| C9—H9C | 0.9600 | C7—H7B | 0.9600 |

| | | | |
|---|---|---|---|
| C10—C15 | 1.392 (4) | C7—H7C | 0.9600 |
| C2—C1—C6 | 119.9 (3) | C12—C11—H11A | 120.4 |
| C2—C1—H1A | 120.1 | C10—C11—H11A | 120.4 |
| C6—C1—H1A | 120.1 | C11—C12—C13 | 121.2 (3) |
| C1—C2—C3 | 120.2 (4) | C11—C12—H12A | 119.4 |
| C1—C2—H2A | 119.9 | C13—C12—H12A | 119.4 |
| C3—C2—H2A | 119.9 | C14—C13—O1 | 124.1 (3) |
| C2—C3—C4 | 121.7 (3) | C14—C13—C12 | 121.3 (3) |
| C2—C3—H3A | 119.1 | O1—C13—C12 | 114.7 (3) |
| C4—C3—H3A | 119.1 | C13—C14—C15 | 116.3 (3) |
| C3—C4—C5 | 118.4 (3) | C13—C14—H14A | 121.9 |
| C3—C4—C7 | 120.2 (4) | C15—C14—H14A | 121.9 |
| C5—C4—C7 | 121.4 (4) | C14—C15—N1 | 131.4 (3) |
| C6—C5—C4 | 119.7 (3) | C14—C15—C10 | 123.2 (3) |
| C6—C5—H5A | 120.1 | N1—C15—C10 | 105.4 (3) |
| C4—C5—H5A | 120.1 | O1—C16—H16A | 109.5 |
| C5—C6—C1 | 120.1 (3) | O1—C16—H16B | 109.5 |
| C5—C6—N1 | 118.8 (3) | H16A—C16—H16B | 109.5 |
| C1—C6—N1 | 121.2 (3) | O1—C16—H16C | 109.5 |
| N2—C8—N1 | 112.6 (3) | H16A—C16—H16C | 109.5 |
| N2—C8—C9 | 124.6 (3) | H16B—C16—H16C | 109.5 |
| N1—C8—C9 | 122.8 (3) | C8—N1—C15 | 106.6 (2) |
| C8—C9—H9A | 109.5 | C8—N1—C6 | 126.9 (3) |
| C8—C9—H9B | 109.5 | C15—N1—C6 | 126.4 (2) |
| H9A—C9—H9B | 109.5 | C8—N2—C10 | 105.7 (3) |
| C8—C9—H9C | 109.5 | C13—O1—C16 | 117.2 (2) |
| H9A—C9—H9C | 109.5 | C4—C7—H7A | 109.5 |
| H9B—C9—H9C | 109.5 | C4—C7—H7B | 109.5 |
| C15—C10—C11 | 118.8 (3) | H7A—C7—H7B | 109.5 |
| C15—C10—N2 | 109.8 (3) | C4—C7—H7C | 109.5 |
| C11—C10—N2 | 131.4 (3) | H7A—C7—H7C | 109.5 |
| C12—C11—C10 | 119.2 (3) | H7B—C7—H7C | 109.5 |

*Hydrogen-bond geometry (Å, °)*

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O1W—H1W···N2 | 0.85 | 2.08 | 2.911 (3) | 166. |

**Fig. 1**

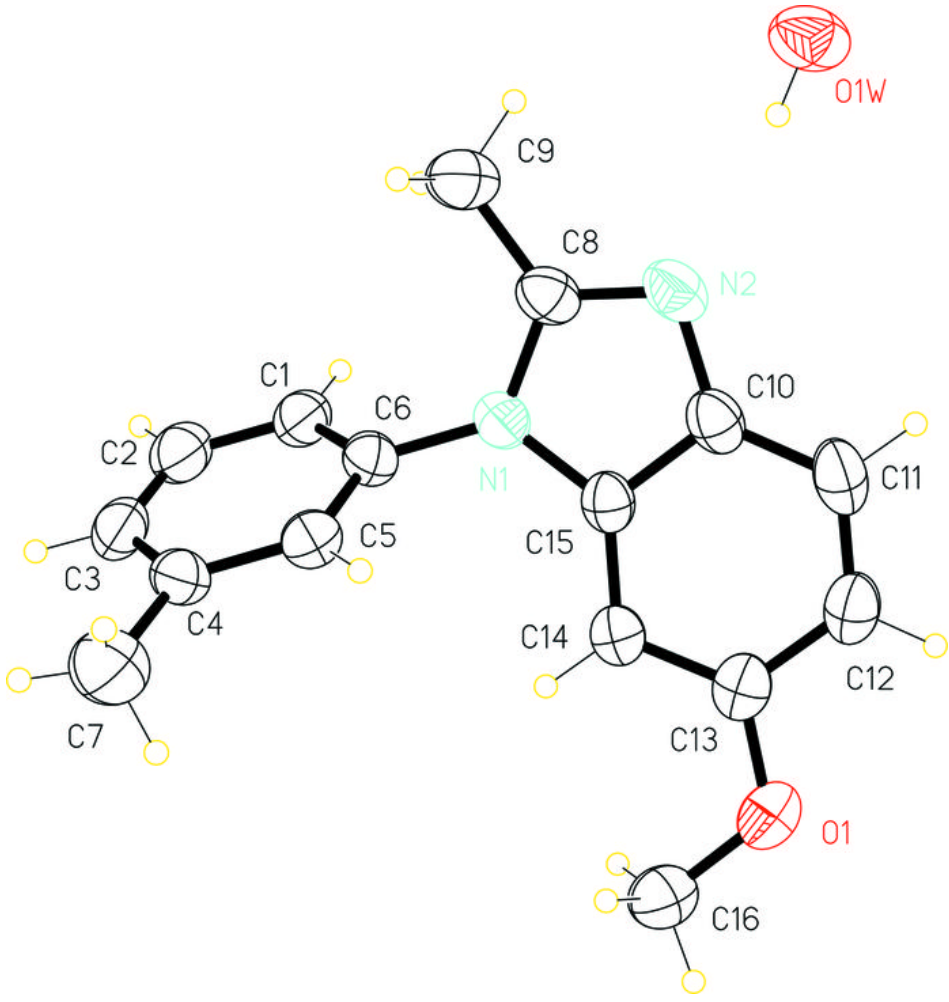

**Fig. 2**