

Synthesis, Spectroscopic characterization, Crystal structure of [Cd(II)] Complex of 1,10- Phenanthroline and Molecular docking studies using HEX

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ABSTRACT: cis-chloridobis(1,10-phenanthroline- π -2N,N')cadmium(II), with molecular formula $(C_{12}H_8N_2)_2CdCl_2$, has been synthesized. It is monoclinic, $P2_1/c$, $a = 9.5810(2) \text{ \AA}$, $b = 15.1388(3) \text{ \AA}$, $c = 14.6232(3) \text{ \AA}$ and $\beta = 99.486(1)^\circ$. In the title complex, the Cd(II) ion is coordinated by four N atoms of two bis-chelating 1,10-phenanthroline (phen) ligands, and two chloride ligand in a distorted octahedral environment. The dihedral angle between the two phen ligands is 90.40° . In the crystal structure, complex molecules and chloride ions are linked into centrosymmetric four-component clusters by intermolecular C-H...Cl hydrogen bonds. Both the chlorine atoms in the asymmetric unit are refined as disordered over two sites with fixed occupancies of ratios 0.55:0.45. The IR spectral data suggest the binding of cadmium atom to the 1,10-phenanthroline ligand which is in agreement with the crystal structure determination. The ligand is docked to the below said receptors using HEX; receptors and the energy values are as follows: 1AJO (-277.26), 3HS4 (-281.95), 3TYE (-237.58), 3TYZ (-274.99), 3TZF (-277.56), 3TZN (-276.10) and 3W6H (-305.29) against the title compound. Depending on the energy values we have chosen the best two drugs they are 3W6H and 3HS4.

KEYWORDS: 1,10-Phenanthroline, Intermolecular interactions, Single crystals.

I. INTRODUCTION

1,10-Phenanthroline (Phen) (Figure 1) and its various derivatives are widely used ligands in the different fields of chemical industry [1]. Heteroaromatic group on the Phen provides a binding site for different metal ions. Phen has a rigid structure and has two aromatic nitrogens which contains unshared electron pairs, that can bind metal ions [2,3]. Due to its π -electron deficiency, Phen becomes an excellent π -electron acceptor. Complexes of 1,10-phenanthroline are frequently employed for catalytic reactions. For example metal complexes functionalized with 1,10-phenanthrolines have been used as catalyst for the enantio selective hydrolysis of N-protected amino acid esters and in enantio selective reduction of acetophenone [4]. The synthesis of some phenanthroline -2,9-disubstituted compounds along with their in vitro antimicrobial properties against gram-positive and gram - negative bacteria and fungi have been reported [5]. Metal complexes of 1,10-phenanthroline have been found to be attractive species for developing new diagnostic and therapeutic agents that can recognize and cleave DNA [6,7]. Experimental evidence has been provided to prove oxovanadium complexes of dimethyl substituted phenanthroline will induce apoptosis in human cancer cells, and may be useful for the treatment of cancer [8].

International Journal of Innovative Research in Science, Engineering and Technology

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Vol. 5, Issue 5, May 2016

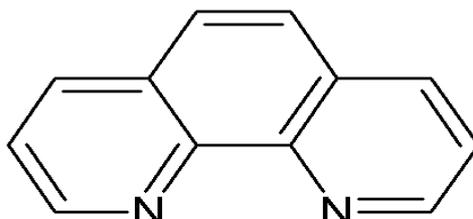


Fig. 1. 1,10-Phenanthroline

II. EXPERIMENTAL

Chemicals

1,10-Phenanthroline (Sigma, >99%), cadmium (II) chloride and all other chemicals of commercially available reagent grade are used as received.

Synthesis of the complex

The solution of cadmium chloride in distilled water is added in the solution of 1,10-Phenanthroline in 25ml methanol and the mixture is refluxed for 2 hours. A white precipitate is formed, filtered and washed with water and methanol successively and dried in a desiccator over anhydrous CaCl_2 . The yield of various preparations is around 40%. Anal. Calcd. for $(\text{C}_{12}\text{H}_8\text{N}_2)_2\text{CdCl}_2$ (%): C, 53.02; H, 2.97; N, 10.30. Found (%): C, 48.07; H, 2.66; N, 8.03. The complex is insoluble in water and in most of the common solvents, and very soluble only in DMSO and DMF. After several unsuccessful attempts, it is possible to grow a very few number of small tiny single crystals adequate for X-ray structure analysis, from DMSO.

X-ray data crystallography

Single crystal x-ray diffraction was performed using $0.40 \times 0.30 \times 0.20$ mm crystals on Bruker Kappa APEX-II CCD diffractometer with graphite monochromated $\text{MoK}\alpha$ radiation ($\lambda = 0.71703 \text{ \AA}$) at $T = 293 \text{ K}$. The intensities were collected at 293 K using φ and ω scans. The structure is solved by Patterson methods with SHELXS-97 [9] and anisotropic thermal parameters for all non-hydrogen atoms are refined by full-matrix least squares procedure against F^2 with SHELXL-97 [10]. The cell refinement and data reduction were carried out using Denzo and SAINT program []. All non-hydrogen atoms were refined anisotropically and hydrogen H atoms are positioned geometrically, with $C-H = 0.93 \text{ \AA}$ for aromatic H atoms, respectively. In addition, they are constrained to ride on their parent atoms with $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}$ (carrier atoms of CH). The program PLATON [11] and ORTEP-3 [12] within WinGX [13] are used to prepare materials for publication. Two chlorine atoms in the asymmetric unit are refined as disordered over two sites with fixed occupancies 0.55:0.45.

Physical measurements

Elemental analyses for carbon, hydrogen, and nitrogen are carried out using a Perkin-Elmer 2400-II elemental analyzer. IR spectra, in the range between 4000 and 400 cm^{-1} , are recorded on a Perkin Elmer Spectrum GX FT-IR Spectrometer using KBr pellet technique.

Docking Studies

Bioinformatics is seen as an emerging field with the potential to significantly improve how drugs are found, brought to the clinical trials and eventually released to the marketplace. Computer-Aided Drug Design (CADD) is a specialized discipline for the study of simulation of ligand-receptor interactions and is strongly dependent on bioinformatics tools, applications and databases. The structure of sulfonamide receptors are referred from different journals and retrieved from PDB (www.pdb.org/pdb). The Cd(II) complex of 1,10-Phenanthroline has been synthesized by us and three dimensional structures of this has been worked out. The corresponding CIF file of the title compound has been converted into PDB file using OBGUI software [14]. This PDB structure is used for the docking studies using Hex software [15].

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 5, Issue 5, May 2016

The parameters used for the docking process were

- Correlation type – Shape only
- FFT Mode – 3D fast lite
- Grid Dimension – 0.6
- Receptor range – 180
- Ligand Range – 180
- Twist range – 360
- Distance Range – 40

The drug and its analogues are docked with the receptor using the above parameters.

Table 1. Crystal data and refinement of $(C_{12}H_8N_2)_2CdCl_2$

| | |
|--|--|
| Empirical formula | $(C_{12}H_8N_2)_2CdCl_2$ |
| Formula weight | 543.72 |
| Temperature (K) | 293 K |
| Wavelength (Å) | 0.71073 |
| Crystal system, Space group | Monoclinic, $P2_1/c$ |
| a (Å) | 9.5810(2) |
| b (Å) | 15.1388(3) |
| c (Å) | 14.6232(3) |
| α (°) | 90.00 (0) |
| β (°) | 99.486(1) |
| γ (°) | 90.00 (0) |
| Volume (Å ³) | 2092.02(7) |
| Z | 4 |
| Calculated density (Mg m ⁻³), | 1.726 |
| Absorption coefficient (mm ⁻¹) | 1.319 |
| F(000) | 1080 |
| θ range for data collection (°) | 2 - 27.6° |
| Limiting indices | $-12 \leq h \leq 12$; $-19 \leq k \leq 19$; $-19 \leq l \leq 18$ |
| Reflections collected/unique | 4844/ 3936 |
| Absorption correction | N.A. |
| Refinement method | Full Matrix Least Square of $ F ^2$ |
| Data/restraints/parameters | 4844/0/ 300 |
| Goodness-of-fit on F^2 | 0.94 |
| Final R indices | $R_1 = 0.0272$, $wR_2 = 0.0604$ |
| R indices (all data) | $R_1 = 0.0387$, $wR_2 = 0.0657$ |
| Largest diff. peak and hole (e Å ⁻³) | 0.48 and -0.38 |

Table 2. Fractional atomic coordinates and equivalent isotropic thermal parameters (Å²)

$$U_{eq} = 1/3 \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$$

| | x | y | z | U_{eq} | Occ. (<1) |
|-------|------------|------------|------------|------------|-----------|
| Cd1 | 0.24097(2) | 0.22633(1) | 0.04889(1) | 0.0336(1) | |
| *Cl1A | 0.1836(5) | 0.1323(7) | 0.1782(5) | 0.057(2) | 0.55 (10) |
| *Cl2A | 0.0368(8) | 0.2125(9) | -0.0849(6) | 0.0449(17) | 0.45 (10) |
| *Cl1B | 0.1830(5) | 0.1278(7) | 0.1762(5) | 0.042(2) | 0.55 (10) |

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 5, Issue 5, May 2016

| | | | | | |
|-------|------------|-------------|--------------|------------|-----------|
| *Cl2B | 0.0376(11) | 0.2058(13) | -0.0812(9) | 0.054(2) | 0.45 (10) |
| N1A | 0.3870(2) | 0.13881(12) | -0.03349(13) | 0.0330(6) | |
| N1B | 0.1689(2) | 0.35904(13) | 0.11677(14) | 0.0386(6) | |
| N2A | 0.4897(2) | 0.22274(12) | 0.12914(14) | 0.0381(6) | |
| N2B | 0.3251(2) | 0.35699(12) | -0.02353(14) | 0.0392(6) | |
| C1A | 0.3368(3) | 0.09725(15) | -0.11098(17) | 0.0408(8) | |
| C1B | 0.0921(3) | 0.36003(19) | 0.18444(18) | 0.0479(9) | |
| C2A | 0.4215(3) | 0.04621(16) | -0.16043(18) | 0.0456(9) | |
| C2B | 0.0285(3) | 0.4366(2) | 0.2118(2) | 0.0586(11) | |
| C3A | 0.5618(3) | 0.03843(16) | -0.12723(18) | 0.0466(9) | |
| C3B | 0.0475(3) | 0.5140(2) | 0.1682(2) | 0.0620(11) | |
| C4A | 0.6198(3) | 0.08196(15) | -0.04460(18) | 0.0406(8) | |
| C4B | 0.1307(3) | 0.51667(17) | 0.0976(2) | 0.0506(9) | |
| C5A | 0.7662(3) | 0.07630(19) | -0.0048(2) | 0.0555(10) | |
| C5B | 0.1572(3) | 0.59589(17) | 0.0491(2) | 0.0635(10) | |
| C6A | 0.8163(3) | 0.1176(2) | 0.0749(2) | 0.0584(10) | |
| C6B | 0.2368(4) | 0.59419(18) | -0.0176(3) | 0.0658(10) | |
| C7A | 0.7260(3) | 0.16758(16) | 0.12405(19) | 0.0456(9) | |
| C7B | 0.2986(3) | 0.51442(16) | -0.0453(2) | 0.0507(9) | |
| C8A | 0.7735(3) | 0.21002(18) | 0.2087(2) | 0.0581(10) | |
| C8B | 0.3820(3) | 0.50981(19) | -0.1147(2) | 0.0598(11) | |
| C9A | 0.6810(4) | 0.25592(19) | 0.2514(2) | 0.0613(10) | |
| C9B | 0.4348(3) | 0.43090(19) | -0.1373(2) | 0.0566(10) | |
| C10A | 0.5398(3) | 0.26083(16) | 0.20932(19) | 0.0499(9) | |
| C10B | 0.4029(3) | 0.35593(18) | -0.09006(18) | 0.0475(9) | |
| C11A | 0.5811(2) | 0.17605(14) | 0.08694(17) | 0.0356(7) | |
| C11B | 0.2726(3) | 0.43501(14) | -0.00012(17) | 0.0382(8) | |
| C12A | 0.5269(2) | 0.13178(14) | 0.00061(16) | 0.0324(7) | |
| C12B | 0.1890(3) | 0.43581(15) | 0.07378(18) | 0.0399(8) | |

Table 3. Selected bond distances, bond angles and dihedral angle values (C₁₂H₈ N₂)₂CdCl₂

| Bond distances (Å) | | Bond angles (°) | | | |
|--------------------|------------|-----------------|--|--|------------|
| Cd1 -N1A | 2.3915(18) | N1A -Cd1 -N2A | | | 68.27(7) |
| Cd1 -N2A | 2.478(2) | Cl1A -Cd1 -N1A | | | 108.86(10) |
| Cd1 -Cl1A | 2.499(6) | Cl2A -Cd1 -N1A | | | 90.08(9) |
| Cd1 -Cl2A | 2.537(7) | Cl1A -Cd1 -N2A | | | 85.42(8) |
| Cd1 -N1B | 2.3924(19) | Cl2A -Cd1 -N2A | | | 156.01(8) |
| Cd1 -N2B | 2.4423(19) | Cl1A -Cd1 -Cl2A | | | 112.34(11) |
| Cd1 -Cl1B | 2.517(6) | Cl1B -Cd1 -Cl2B | | | 100.52(10) |
| Cd1 -Cl2B | 2.508(10) | Cl1B -Cd1 -N1B | | | 96.77(10) |
| | | Cl1B -Cd1 -N2B | | | 161.08(10) |
| | | Cl2B -Cd1 -N1B | | | 100.61(10) |
| | | Cl2B -Cd1 -N2B | | | 94.35(10) |
| | | N1B -Cd1 -N2B | | | 68.79(7) |

III. RESULTS AND DISCUSSION

Crystal structure of the title compound

Suitable single crystals of the complex for X-ray structure determination are grown by the slow evaporation of an equal proportion of DMF and DMSO solution. Crystal data and refinement results are summarized in Table 1. Selected

bond distances and bond angles are given in Table 2. Figure 2 is the ORTEP drawing of the title molecule with 50% probability level with the used atomic numbering scheme.

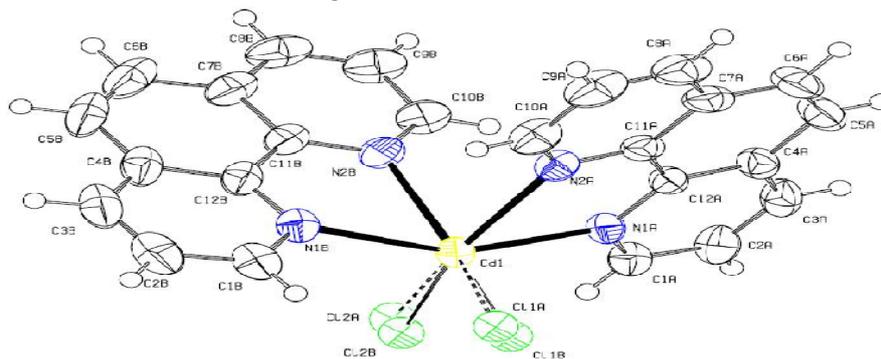


Fig. 2. Molecular structure of the cation of the title compound. Displacement ellipsoids are drawn at the 50% probability level.

The asymmetric unit contains one complex cation and two chloride anions. The Cd(II) ion is coordinated in a distorted octahedral environment by four nitrogen atoms of two 1,10-phenanthroline ligands and two chloride ions. The Cd-N bond distances are Cd1-N1A= 2.3915(18)Å, Cd1-N2A= 2.478(2)Å, Cd1-N1B= 2.3924(19)Å and Cd1-N2B= 2.4423(19)Å. The Cd-Cl bond distances are Cd1-Cl1A=2.499(6)Å, Cd1-Cl2A=2.537(7) Å, Cd1-Cl1B=2.517(6) Å, Cd1-Cl2B=2.508(10) Å. The dihedral angle between the two phen ligands is 90.40° and very similar to other reported metal complexes of it [in Co complex 84.21(3)] [16].

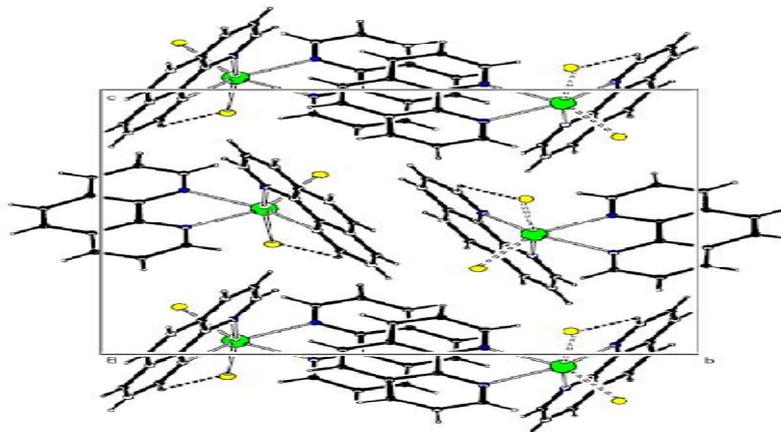


Fig.3. Packing diagram showing inter C—H...Cl hydrogen bonds as dashed lines.

Table 4. Hydrogen bond geometry and symmetry code for (C₁₂H₈N₂)₂CdCl₂

| D- H...A | D-H(Å) | H...A(Å) | D-A (Å) | ∠D-H...A(°) |
|-------------------------|--------|----------|-----------|---------------|
| C1A -- H1A ... Cl2B | 0.9300 | 2.76 | 3.437(10) | 131.00 |
| C5B -- H5B ... Cl2B (a) | 0.9300 | 2.61 | 3.530(12) | 168.00 |
| C6A -- H6A ... Cl1B (b) | 0.9300 | 2.68 | 3.601(6) | 170.00 |

(a: -x,1-y,-z; b: 1+x,y,z correspond to symmetry related molecules)

In the crystal structure, complex molecules and chloride ions are linked into centrosymmetric four component clusters by intermolecular C—H...Cl hydrogen bonds. Pair of centro symmetry related complex is connected by C-H...Halogen (Cl) interactions centering at each inversion center: C3A-H3A...Cl1B=3.437(10) Å and 131.00° (Fig.3).

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 5, Issue 5, May 2016

In the crystal structure complex molecules are linked by π - π interactions involving the centroids of centro symmetry (1-x,-y, -z) related pyridine ring (C1A/C2A/C3A/C4A/C12A/N1A) of molecule A forming a four component centrosymmetric cluster. The Cg(I)-Cg(I) distance between two centroids is 3.5390(15) Å and the slippage distance between the centroids is 1.128 Å.

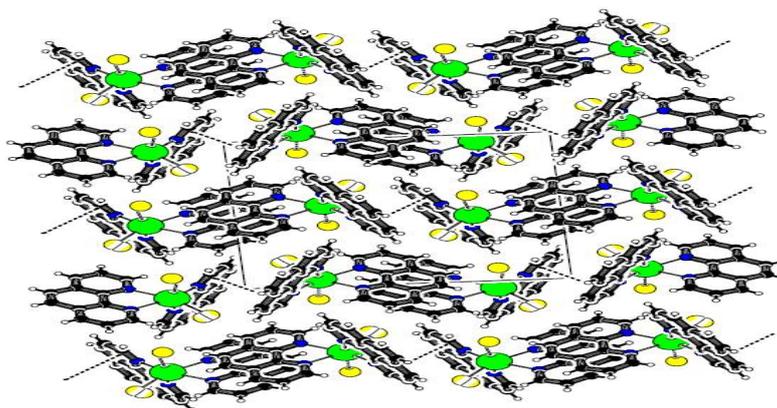


Fig.4.Packing diagram showing intra π - π stacking as dashed lines

IV. EXPERIMENTAL RESULTS

Infrared spectra

The infrared spectra of the complex which is taken in the region 4000-400 cm^{-1} is compared with those of the free ligand. Based on some general references and previous reported metal complexes of Phen, an assignment of most important bands are given in Table 5.

Table 5 Characteristics IR bands (cm^{-1}) of the spectra of 1:10 Phen. and Cd-1:10 Phen

| 1,10-Phenanthroline | Cd(1,10-Phenanthroline) | Assignment |
|---------------------|-------------------------|------------------|
| 1616 | 1620 | |
| 1503 | 1511 | Ring deformation |
| 1420 | 1424 | |
| 1343 | 1344 | |
| 1215 | 1317,1224 | ν CN |
| 778 | 768 | ρ CH |

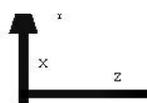
Docking studies

Docking results between the Cd-Phen and few selected receptors are tabulated in (Table 6). From the table it can be concluded that the ligand-receptor fitting (Fig. 5) is best with 3W6H (energy value -305.29).

International Journal of Innovative Research in Science, Engineering and Technology

(An ISO 3297: 2007 Certified Organization)

Vol. 5, Issue 5, May 2016



Cluster: 1 Solution: 1 Models: 0:0 H-Bonds: -1 Bumps: -1 RMS: -1.00
Etotal: -305.29 Eshape: -305.29 Eforce: 0.00 Eair: 0.00 Vshape: 0.00 Vclash: 0.00

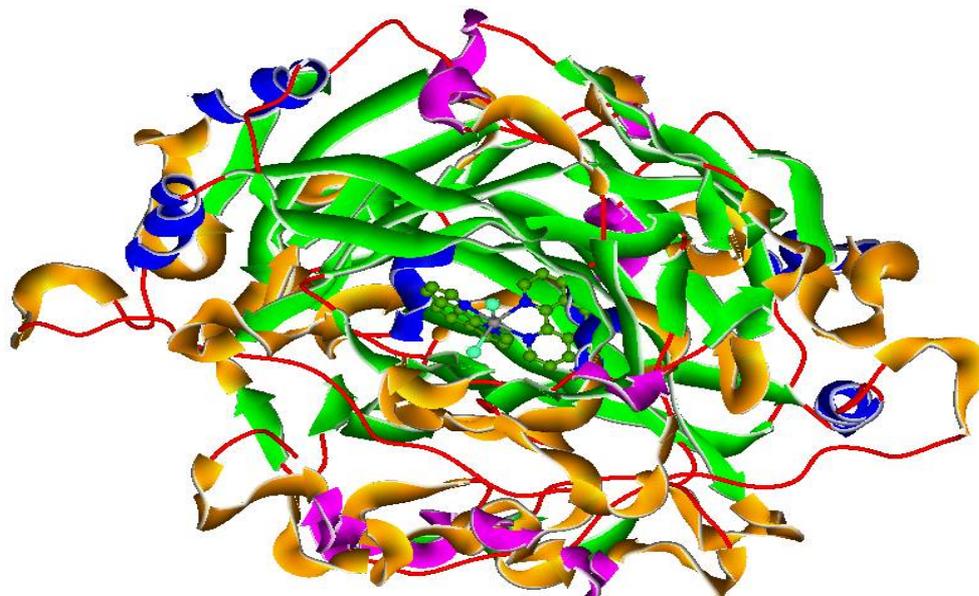


Fig.5. Interaction of Cd-Phen with 3W6H receptor

TABLE 6 Docking results of Cd-Phen and different receptors

| | Receptors | | | | | | |
|---------|-----------|---------|---------|---------|---------|---------|---------|
| | 1AJ0 | 3HS4 | 3TYE | 3TYZ | 3TZF | 3TZN | 3W6H |
| E-Value | -277.26 | -281.95 | -237.58 | -274.99 | -277.56 | -276.10 | -305.29 |

V. CONCLUSION

Cd-Phen is synthesized and characterised by elemental analysis, IR spectroscopy and structurally characterized by X-ray crystallography. The Cd(II) ion is coordinated by four N atoms of two bis-chelating 1,10-phenanthroline (Phen) ligands, and two chloride ligand in a distorted octahedral environment. The spectroscopic data are in agreement with the crystal structure. We can conclude that the Cd-Phen is having highest interaction energy with 3W6H receptor, which means that it is more compatible receptor compared to other analogous.

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Vol. 5, Issue 5, May 2016

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