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Syntheses and Characterization of Anti-Inflammatory Cupper II Complex.

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SYNTHESES AND CHARACTERIZATION OF ANTI-INFLAMMATORY CUPPER II COMPLEX

تخليق و دراسة متراكب النحاس الثنائي مع مضاد الالتهاب

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ملخص

دراسة البلورة والتركيب الجزيئي لل $Dic_4(DMF)_2Cu_2$ ($C_{62}H_{54}C_{18}Cu_2N_6O_{10}$) والتي تحددها الطريقة المباشرة وتقنيات فوريه .وقد تم معرفة هيكل كامل من مصفوفة المربعات الأقل إلى عامل مرجح R يساوي ٠,٠٧٠٥ .المركب تم تحديده بثنائي النواة حيث يتم اتصال ذرتين من النحاس(الثنائي) مع أربع ذرات أكسجين من مجموعات الكربوكسيل ، في حين يتصل من أعلي و أسفل جزيئين من DMF ووجد ان المسافة بين ذرتين من النحاس الثنائى هو ٢,٦١٤٧انجستروم .

ABSTRACT

The crystal and molecular structure of $Dic_4(DMF)_2Cu_2$ ($C_{62}H_{54}C_{18}Cu_2N_6O_{10}$)was determined by direct method and Fourier techniques. The structure was refined by full-matrix least-squares methods to a weighted *R* factor of 0.0705. The compound is binuclear with monoclinic. The two cupper(II) atoms are bridged by four carboxylate groups, while the apical ligands DMF molecules. The Cu–Cu distance is 2.6147(5) Å.

Keywords: Cupper(II); Diclofenac; Crystal structure

1. INTRODUCTION

It has been suggested that the presence of metal ions in biological fluids, could have a significant effect on the therapeutic action of drugs. Many diverse applications of metal species are aimed at understanding the natural roles of metal ions, or at exploiting the unique properties of metal centers in the study of the biology or biochemistry of nucleic acid and nucleic-acid constituents. Diclofenac (marketed as Voltaren and under a number of other trade names, see below) is a non-steroidal anti-inflammatory drug (NSAID) taken to reduce inflammation and as an analgesic reducing pain in conditions such as arthritis or acute injury. It can also be used to reduce menstrual pain, dysmenorrhea. The name is derived from its chemical name: 2-(2,6-dichloranilino) phenylacetic acid. In the United Kingdom, India, and the United States, it may be supplied as either the sodium or potassium salt, in China most often as the sodium salt, while in some other countries only as the potassium salt. Diclofenac is available as a generic drug in a number of formulations. Over the counter (OTC) use is approved in some countries for minor aches and pains and fever associated with common infections. Diclofenac originated from Ciba-Geigy (now Novartis) in 1973. Diclofenac was first introduced in the UK in 1979 [1].

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2. Experimental

2.1. Material

2.1.1 Inorganic material, the metal salt used in this paper ($CuCl_2.2H_2O$) is Merck (GR) grade.

2.1.2. Diclofenac SodIUM

The Diclofenac sod. We use was optained from Sigma-Aldrich company.

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2.2. Elemental Analysis

Elemental analysis for C, H and N were carried out at the Inorganic Chemistry Department at the University of Karlsruhe.

2.3. Synthesis of $Dic_4(DMF)_2Cu_2$:-

Diclofenac sod. was dissolved in 25 ml DMF and then addition of $Cu(NO_3)_2$ with continuously stirring for about 3 hours, the deep green crystals was settle down after 3 weeks and filtered off, washed several times by minimum amounts of hot methanol and dried under *vacuo* over anhydrous $CaCl_2$.

2.4. Instrumentation

X-ray single crystal measurement

The most powerful method for analyzing and confirming the structure of molecules is by single crystal X-ray structural analysis. The data were collected at 150 K on a Stoe IPDS II area detector diffractometer or at 100 K on a Bruker SMART Apex CCD diffractometer using graphite-monochromated Mo-Kα radiation. The structures were solved using SHELXTL software. The following factors are important while refining the structures. First, the residual factors, R1 and R2 are defined as :

$R1 = \{\sum \| F0 | - | Fc \| \} / \{ \sum | F0 | \}$

$wR2=\{\sum[w(F02-Fc2)^2]/\sum[w(F02)2]\}^{1/2}$

where, | F0 | is the data of the diffraction intensity and background exposure time obtained from the raw data after collection, reduction and correction. | Fc | is the corresponding calculated data after structural analysis. R1 < 0.05 normally indicates good structural analysis. The value w is the weight for each diffraction point and depends on the accurasy which F02 was measured, It is defined as:

$$w = 1/\sigma^2$$

Where, wR2 is sensitive to the little differences in the structural analysis, such as the disorder of atoms and the defined H atoms. Normally wR2 should be lower than 0.15 when the data is reasonable, but 0.2 is still acceptable.

The goodness-of-fit is another important factor for the quality of the structural analysis, and is defined as:

$S = \{\sum[w(F02 - Fc2)^2] / (n - p) \}^{1/2}$

Where, n and p are the number of the unique reflections and the number of parameters involved in the refinement, respectively. When S is far from 1.0, it indicates that the weighing scheme could be wrong and should be made better if the collected data is adequate [2].

3. RESULT AND DISCUSSIONS

The complex **$Dic_4(DMF)_2Cu_2$** is a binuclear molecule. The four carboxylato groups from four ligands are in a bidentate. The square pyramid geometry with an oxygen donor from a dimethylformamide molecule occupying both apical positions was established by single crystal X-ray study [3-5]. The absence of large systematic shifts of the γ (NH) and δ (NH) bands in the spectra of the complex compared with those of the ligand indicates that there is no interaction between the NH group and the metal ions. The difference of bands of the prepared complex ν_{as}(COO) and ν_s(COO) compared to that of sodium Diclofenac characterizes the carboxylate ligation. The ν_{as}(COO) Figure 1. Structural representation of the complexes $[CuL_2(DMF)]_2$, where DMF is the axially bonded solvent molecule and νs(COO) bands of the complex are at 1620–1640 and 1450–1460 cm^{-1} respectively. The difference Δ(Δ =ν_{as}COO/ ν_sCOO) 190–170 cm^{-1} is close to the ionic value (for sodium Diclofenac the Δ value is 170 cm^{-1}), as expected for the bidentate bridging mode of carboxylato ligation. The multiple medium band at 400–360 cm^{-1} and the medium weak band at 320–320 cm^{-1} of the complex are assigned to the ν(Cu-O)COO and ν(Cu-O) DMF respectively [6,7].

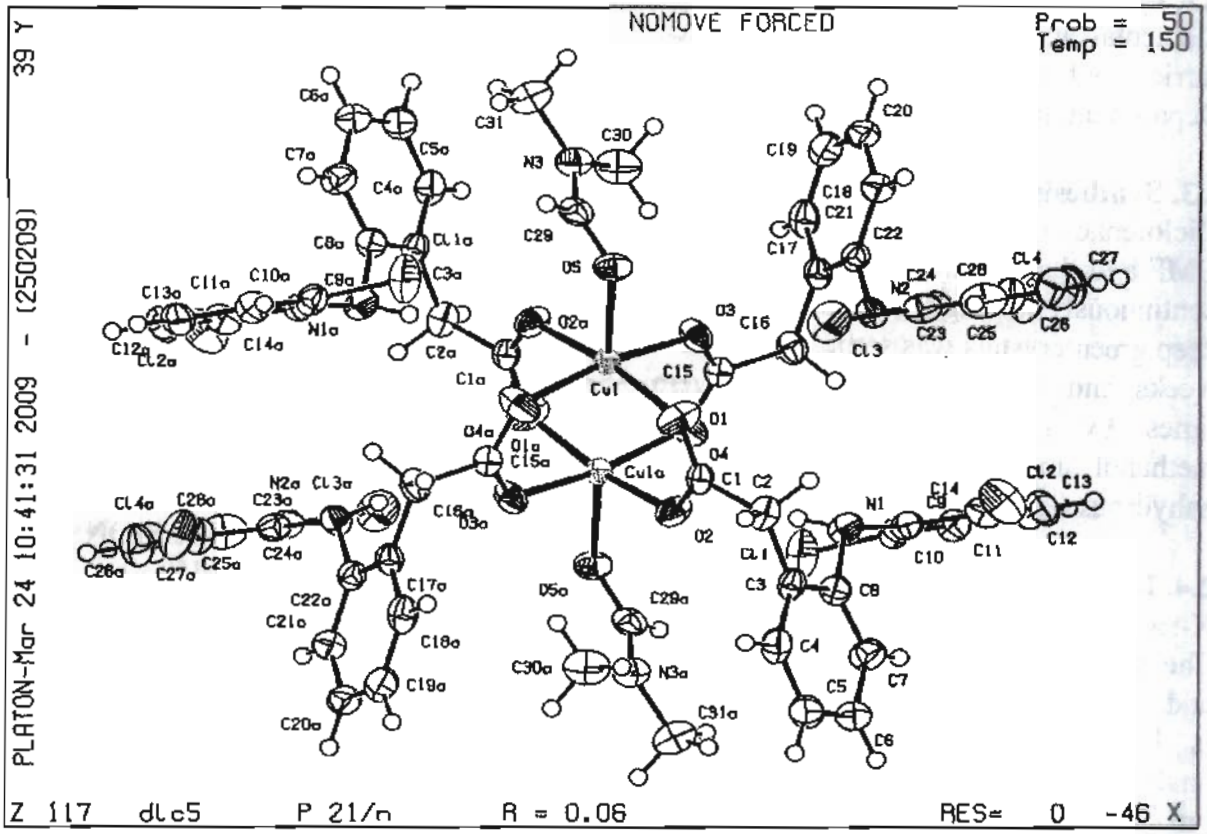

Fig. 1 The chemical structure of $Dic_4(DMF)_2Cu_2$

The two Cu(II) ions are bridged by four carboxylate groups acting as bidentate ligand [Cu-O1(carboxylate) = 1.951(3), Cu-O (carboxylate)= 1.962(2) for ligand A and [Cu-O3(carboxylate) = 1.978(2), Cu-O4(carboxylate)= 1.974(2) for ligand B A for molecules A and B, respectively]. Four carboxylate O atoms define each equatorial coordination plane. Two DMF Molecules are bonded in axial sites [Cu-O(DMF) 2.120(2) Å]. The Cu-Cu distance of 2.6147(5). In particular, the structural characteristics close to the mean values calculated for binuclear Cu(II)-acetate compounds (Hoang et al., 1993) [8], i.e. Cu-Cu 2.621 (8),Cu-O(equatorial) 1.976 (5), Cu-NbO(apical) 2.16 (2). a comparison between the structural characteristics our complex and those of a copper(II)-acetate hydrate complex [Cu-Cu 2.616 (1), Cu-O(equatorial) 1.969 (3), Cu-O (apical) 2.156 (4) and Cu·· ·equatorial plane 0.19 A; (Meester etal., 1973) [9] shows a substantial coincidence of these geometrical details in spite of Diclofenac being a stronger acid than acetic acid (pKa 3.8 versus 4.76). The C-O distances of the carboxylate groups are similar [1.251 (4) and 1.249 (4) A for A, and 1.254 (4) and 1.254 (4) A for B] and suggest complete charge delocalization. Two intermolecular hydrogen bonds are observed in each molecule; N1.....O1[10,11], as shown in tables (2 and 3). The structural of the comlex is confirmed as shown in Figures (2 and 3), and the symmetry elements of the complex was determined and listed in Figure (2) and Table (4).

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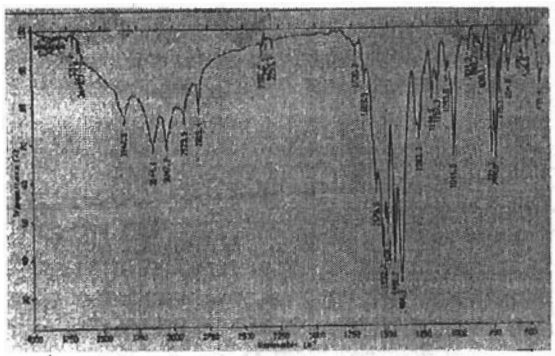

Fig. 2. IR of $Dic_4(DMF)_2Cu_2$.

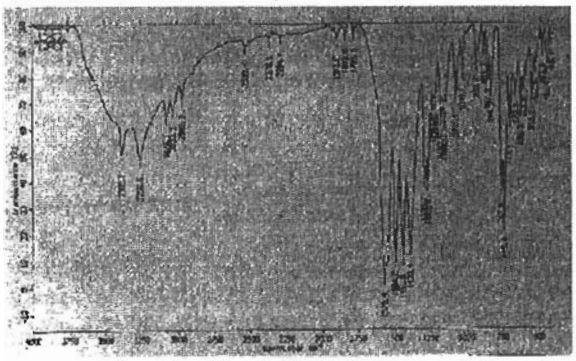

Fig. 3. IR of diclofenac sod.

Table 1 . Crystal data and structure refinement details for $Dic_4(DMF)_2Cu_2$

A Wavelength	0.71073
Cryst size[mm]	0.26 x 0.21 x0.16
Colour	Deep green
Cryst Syst	Monoclinic
Space group	P 21/n
T[K]	150 K
a [Å]	10.7518(9)
b [Å]	15.2889(14)
c [Å]	19.1655(15)
alpha [deg]	90
Beta [deg]	92.301
Gamma [deg]	90
V [Å3]	3148.0(5)
*R*int	0.06
parameters/restraints	441/6
GOF on *F* 2	1.154
R1 [*I* > 2_(I)]	0.0628
wR2 (all data)	0.1397
reflns obsd [*I* >2_(I)]	6442
Larg. residuals [e Å-3]	+1.13/-1.01

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Tabel . 2 Some selected Bond length of $Dic_4(DMF)_2Cu_2$

Atom1	Atom2	Length	Atom1	Atom2	Length
O5	C29	1.236(4)	N1	H1	0.91(5)
O4	C15	1.254(4)	Cu1	O5	2.120(2)
O4	Cu1	1.974(2)	Cu1	O3	1.978(2)
O4	C15	1.254(4)	Cu1	O1	1.951(3)
O3	C15	1.254(4)	Cu1	O5	2.120(2)
O2	Cu1	1.962(2)	Cu1	Cu1	2.6147(5)
O2	C1	1.251(4)	Cu1	O2	1.962(2)
O1	C1	1.249(4)	Cu1	O4	1.974(2)
N3	C31	1.459(5)	Cu1	O3	1.978(2)
N3	C29	1.323(5)	Cu1	O1	1.951(3)
N3	C31	1.459(5)	C28	Cl4	1.732(3)
N3	C30	1.453(5)	C28	Cl4	1.732(3)
N3	C30	1.453(5)	C24	Cl3	1.728(3)
N2	H2	0.88(4)	C24	Cl3	1.728(3)
N2	C23	1.400(4)	C22	N2	1.429(4)
N2	H2	0.88(4)	C22	N2	1.429(4)
N2	C23	1.400(4)	C15	C16	1.515(4)
N1	C9	1.409(4)	C14	Cl2	1.735(3)
N1	H1	0.91(5)	C14	Cl2	1.735(3)
C10	Cl1	1.739(3)	C13	C14	1.381(5)

Table 3. Some selected Angle list for $Dic_4(DMF)_2Cu_2$

Atom1	Atom2	Atom3	Angle	Atom1	Atom2	Atom3	Angle
O1	Cu1	O3	87.8(1)	Cu1	Cu1	O4	85.44(8)
O1	Cu1	O5	97.9(1)	Cu1	Cu1	O1	85.76(8)
O1	Cu1	Cu1	85.76(8)	Cu1	Cu1	O3	83.16(7)
O1	Cu1	O2	168.3(1)	Cu1	Cu1	O5	175.55(6)
O1	Cu1	O4	90.0(1)	O2	Cu1	O4	87.6(1)
O3	Cu1	O5	94.44(9)	O2	Cu1	O1	168.3(1)
O3	Cu1	Cu1	83.16(7)	O2	Cu1	O3	92.29(9)
O3	Cu1	O2	92.29(9)	O2	Cu1	O5	93.72(9)
O3	Cu1	O4	168.5(1)	O4	Cu1	O1	90.0(1)
O5	Cu1	Cu1	175.55(6)	O4	Cu1	O3	168.5(1)
O5	Cu1	O2	93.72(9)	O4	Cu1	O5	97.0(1)
O5	Cu1	O4	97.0(1)	O1	Cu1	O3	87.8(1)
Cu1	Cu1	O2	82.65(7)	O1	Cu1	O5	97.9(1)
Cu1	Cu1	O4	85.44(8)	O3	Cu1	O5	94.44(9)
O2	Cu1	O4	87.6(1)	Cu1	O1	C1	121.5(2)
Cu1	O1	C1	121.5(2)	Cu1	O2	C1	124.5(2)
C1	O2	Cu1	124.5(2)	O1	C1	O2	125.3(3)
O1	C1	O2	125.3(3)	Cu1	O3	C15	124.5(2)
Cu1	O3	C15	124.5(2)	Cu1	O4	C15	122.0(2)
C15	O4	Cu1	122.0(2)	O3	C15	O4	124.8(3)

Atom1	Atom2	Atom3	Angle	Atom1	Atom2	Atom3	Angle
O3	C15	O4	124.8(3)	Cu1	O5	C29	135.8(2)
Cu1	O5	C29	135.8(2)	O5	C29	N3	126.5(3)
O5	C29	N3	126.5(3)				
Cu1	Cu1	O2	82.65(7)				

Tab.4 Elemental Analysis of $Dic_4(DMF)_2Cu_2$

Element	Theoretical	Practical
C	51,22%	51,13%
N	5,78%	5,31%
H	3,74%	3,66%

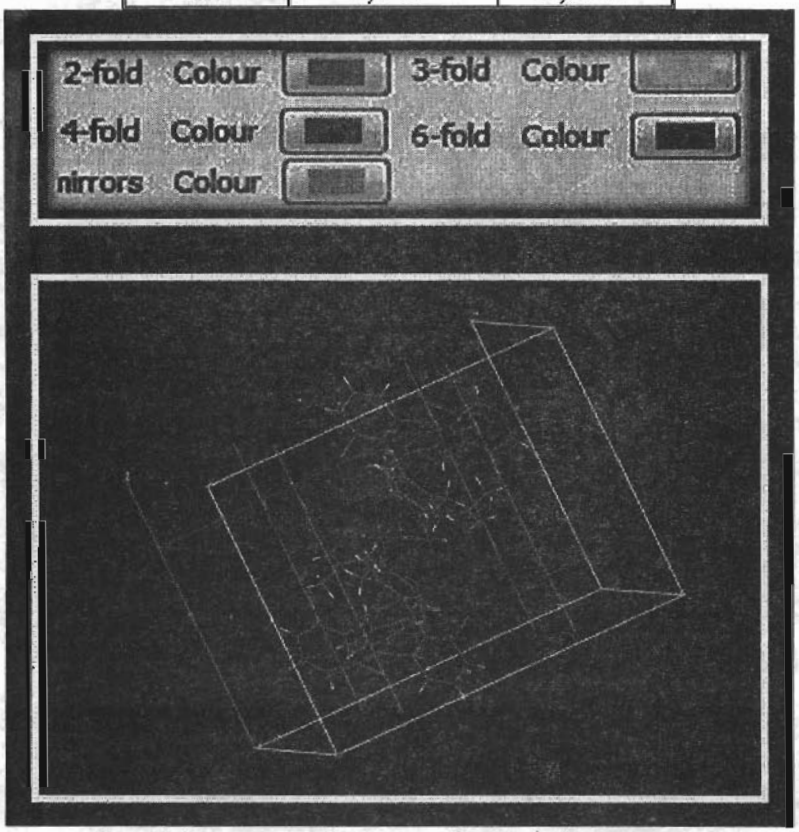


Fig. 2 Symmetry elements for $Dic_4(DMF)_2Cu_2$

Table 4. Symmetry elements

No.	Symm. Op.	Description	Detailed Description	Order	Type
1	x,y,z	Identity	Identity	1	1
2	1/2-x,1/2+y,1/2-z	Screw axis (2-fold)	2-fold screw axis with direction [0, 1, 0] at 1/4, y, 1/4 with screw component [0, 1/2, 0]	2	2
3	-x,-y,-z	Inversion centre	Inversion at [0, 0, 0]	2	-1
4	1/2+x,1/2-y,1/2+z	Glide plane	Glide plane perpendicular to [0, 1, 0] with glide component [1/2, 0, 1/2]	2	-2

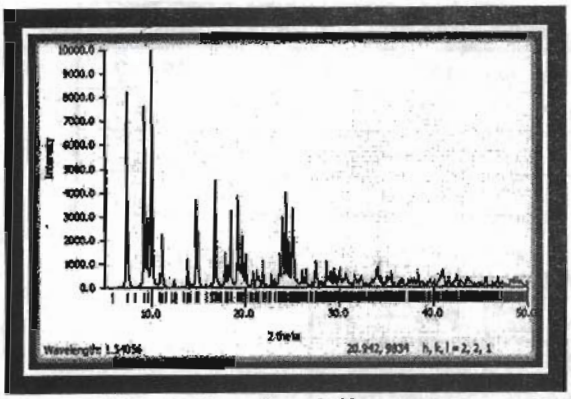
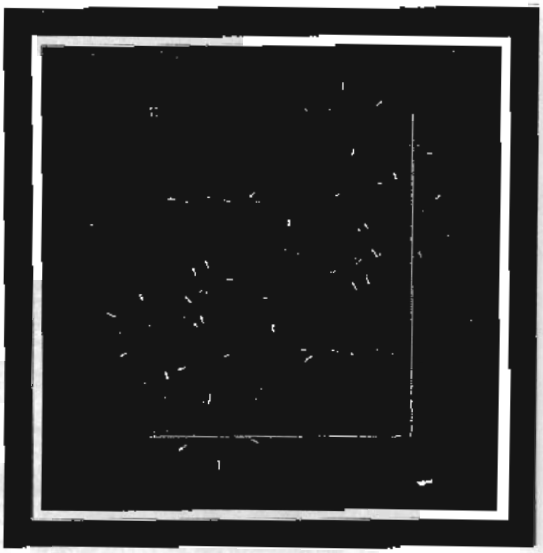
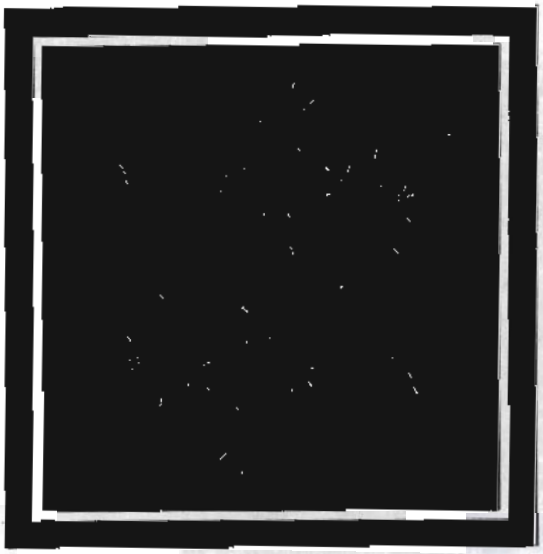
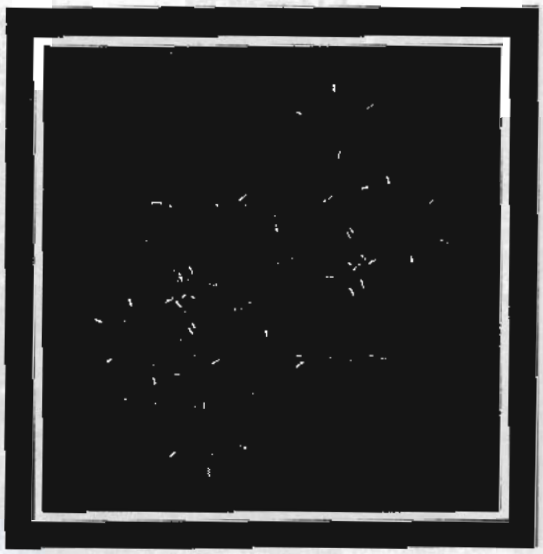
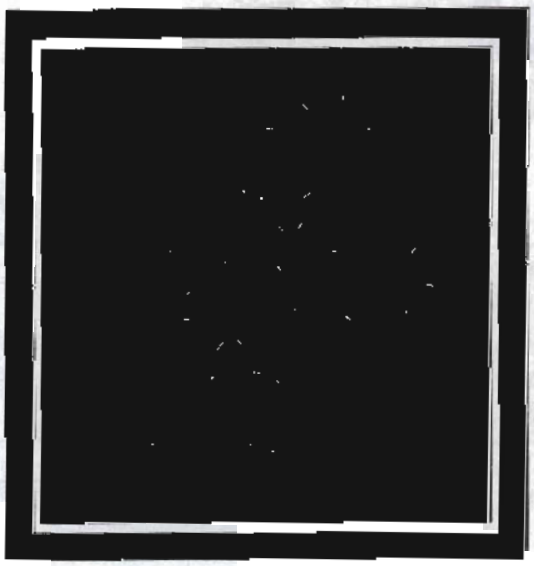


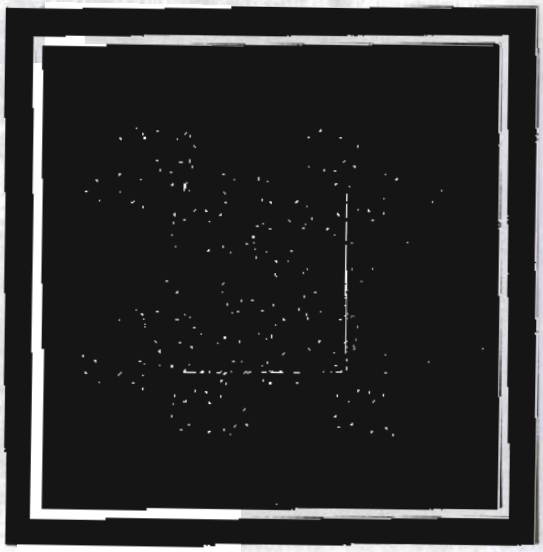
Fig. 3 Powder diffraction











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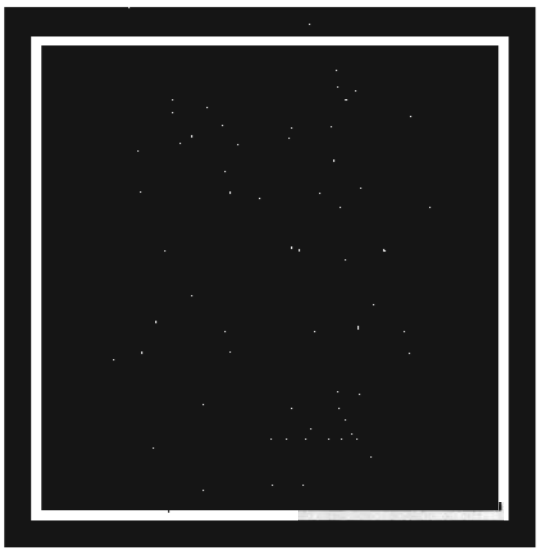

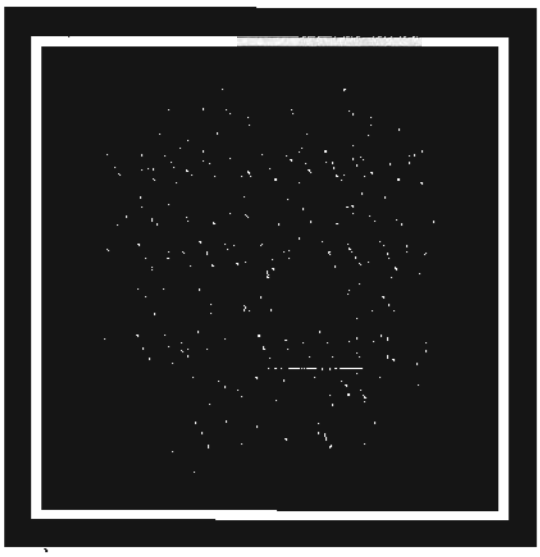

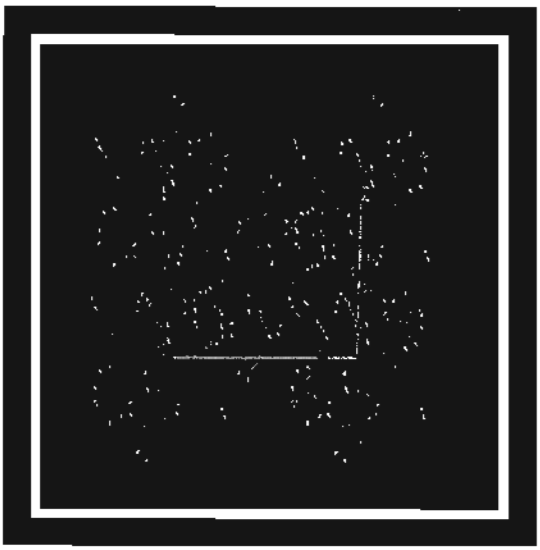

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