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Synthesis and Molecular Structure Analysis of 4-(bis(2-chloroethyl)amino)-3-nitro-2H-chromen-2-one by Single crystal XRD Method

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ABSTRACT

A novel 3-nitro and 4-N-mustard functionalized coumarine has been synthesized using 4-chloro, 3-nitro coumarine and Diethanol amine using Isopropyl alcohol as solvent, resultant intermediate undergoes chlorination with Thionyl chloride and DMF as solvent is described. The synthesized compound characterized by spectroscopic techniques and finally confirmed by X-ray diffraction studies. The molecule crystallizes in the monoclinic crystal class in the space group P21/c with cell parameters a = 7.473(1)A^{o}b = 8.169 (1)A^{o},c = 13.957(2)A^{o},α = 87.942(5)A^{o},β = 86.073(5)A^{o},γ = 65.040(5)A^{o} and Z = 4. The Coumarine ring adopts flattened conformation.

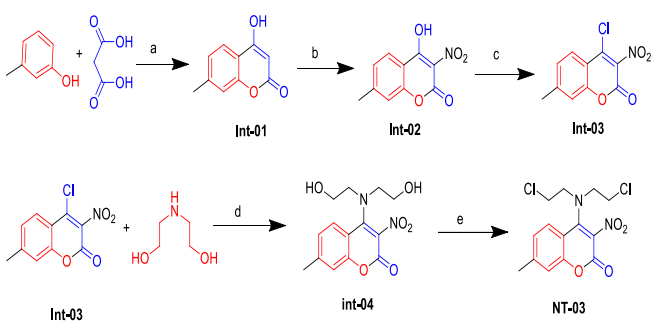
Keywords: 3-Nitro-4-Chloro Coumarine, Hydrogen Bonds

I. INTRODUCTION

Nowadays, there is considerable interest in the synthesis of Coumarine and mustard and their derivatives due to their important pharmacological and therapeutic properties such as antihypertensive, antitumor, anti-inflammatory, and behaving as calcium channel blockers [1–3]. The Coumarin Over the past few years, this class of compounds have received considerable attention after their hypotensive and spasmolytic properties were demonstrated [4, 5]. However, usualCoumarin contain an ester group in the heterocyclic scaffold [6, 7]. They can also allow other functional groups without loss of basic biological activity. The substitution of nitro group in the position 3 in the coumarin may alter their biological action. Some 4-nitrogen mustard-3-nitro-coumarine exhibit an appreciable biological activity, specifically as calcium channel modulators [8]. Moreover, nitro functionalized coumarine were synthesized and found as pyrimidine nucleoside analogues [9]. Numerous lead derivatives of coumarin compounds have been revealed to be superior in potency and duration of antihypertension activity as compared to usual DHP drugs. Recently Shkurko et al. have found, that several 3,4 substituted coumarine derivatives show a high antiarrhythmic activity. Overall, coumarine mustard compounds were found to have

pharmacological profile similar to that of classical DNA alkylating drugs[6, 7].

Among various approaches known for the synthesis of multifunctionalized coumarin and related heterocyclic compounds [7], three component biginelli reaction [12], is the most common. However, in Biginelli's reaction 1,3 diketone is used as a synthone. The ability of nitro group to enhance biological and therapeutic activities of certain organic compounds has led to widespread interest in the selective introduction of nitro groups into organic compounds [13]. For example, Coumarine are important heterocycles in both natural and synthetic compounds. The synthesis of 3-nitro and 4-nitrogrn mustard substituted Coumarine have been reported using metal salts as a catalyst [14]. Reports reveal that nitro group containing coumarine which might have potential biological activities were less studied [15]. These findings make it highly necessary to develop efficient methods for the synthesis of this class of coumarine. As a part of our ongoing research work, the development of useful synthetic methodologies by employing heterogeneous catalysts [16–18], we herein report the synthesis, crystal and molecular structure analysis of 4-(bis(2-chloroethyl)amino)-3-nitro-2H-chromen-2-one using 4-hydroxy coumarine with excellent yield.



Procedure for the development of single crystals.

In the present study, the pure, single spot (on TLC) compound was taken in Dichloromethane and heated with stirring till it dissolved. A small quantity of charcoal was added for decolorizing. The solution was then heated to boiling and immediately filtered while hot in corkable 50 ml conical flask using Whatmann filter paper. The flask was corked and kept for several days. The crystals thus grown by thin film evaporation technique were isolated and washed with chilled methanol. The constitution of 4-(bis(2-chloroethyl)amino)-3-nitro-2H-chromen-2-one was supported by IR, 1H & 13C NMR and Mass spectral studies.

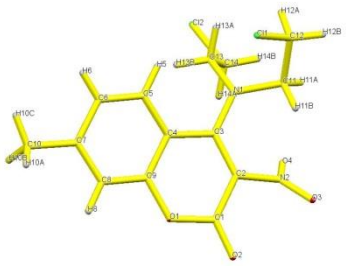
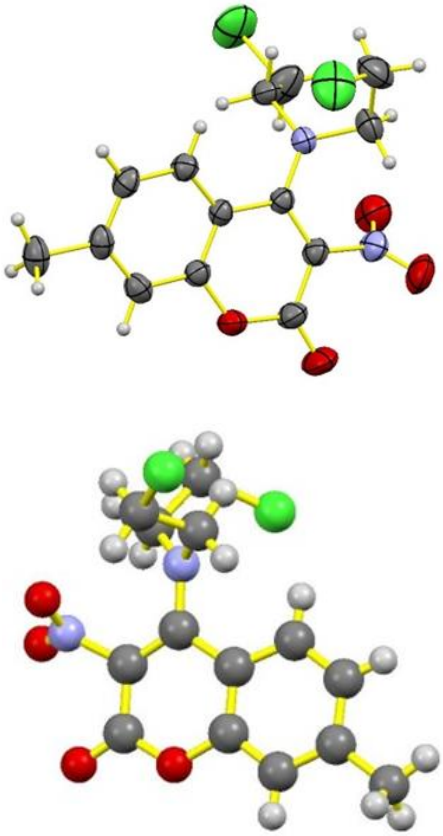


Figure 2: ORTEP of the molecule

Spectral Data of 4-(bis(2-chloroethyl)amino)-3-nitro-2H-chromen-2-one

4-(bis(2-chloroethyl)amino)-7-methyl-3-nitro-2H-chromen-2-one (NT-2c) Yellowish solid; R_f 0.41 (8:2 EA-hexane); mp 202-204°C; IR (KBr,cm^{-1}): 3302, 1681, 1603, 1513, 1451, 1315, 1204, 1104, 1061, 867, 788, 723, 643 cm^{-1}; ^{1}H NMR: δ $_{PPM}$ 8.28(s, 1H, Ar-H), 7.55(d, J=7.0 Hz, 1H, Ar-H), 7.32(d, J=7.01 Hz, 1H, Ar-H), 3.74(s, 8H, (-CH_2CH_2-)$_2$), 2.40(s, 3H, -CH_3). ^{13}C NMR (400 MHz, DMSO): 20.50, 41.05, 52.10, 111.60, 114.05, 124. 12, 125.01, 126.76, 133.99, 134.82, 145.14, 145.35,149.39, 155.50. MS (*m/z*): 344 (M^+); Anal. Calcd for: $C_{14}H_{14}Cl_2N_2O_4$: C, 55.40; H, 4.34; Cl, 21.80; N, 8.6; Found: C, 55.14; H, 4.21; N, 9.40.

II. RESULT AND DISCUSSION



Experimental Details

A. Crystal Data

Empirical Formula	$C_{14}H_{14}Cl_2N_2O_4$
Formula Weight	345.18
Crystal Color, Habit	yellow, chip
Crystal Dimensions	0.400 X 0.360 X 0.300 mm
Crystal System	triclinic
Lattice Type	Primitive
Lattice Parameters	a = 7.473(1) Å
	b = 8.169(1) Å
	c = 13.957(2) Å
	□ = 87.942(5) o
	□ = 86.073(5) o
	□ = 65.040(5) o
	V = 770.6(2) Å3
Space Group	P-1 (#2)
Z value	2
Dcalc	1.488 g/cm3
F000	356.00
μ(MoKα)	4.393 cm-1

B. Intensity Measurements

Diffractometer	SCX mini
Radiation	MoKα (λ = 0.71075 Å)
graphite monochromated	
Voltage, Current	50kV, 30mA
Temperature	20.0°C
Detector Aperture	75 mm (diameter)
Data Images	540 exposures
ω oscillation Range	-120.0 - 60.0°
Exposure Rate	10.0 sec./°
Detector Swing Angle	-30.80o
ω oscillation Range	-120.0 - 60.0o
Exposure Rate	10.0 sec./o
Detector Swing Angle	-30.80o
□ oscillation Range	-120.0 - 60.0o
Exposure Rate	10.0 sec./o
Detector Swing Angle	-30.80o
Detector Position	52.00 mm
Pixel Size	0.146 mm
2□max	55.0o
No. of Reflections Measured	Total: 7891
Unique: 3509 (Rint = 0.0171)	
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.706 - 0.877)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares on F2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$

Least Squares Weights w = 1/ [□2(Fo2) + (0.0776 . P)2 + 0.5661 . P]

where P = (Max(Fo2,0) + 2Fc2)/3

$2\theta_{max}$ cutoff 55.0o

Anomalous Dispersion All non-hydrogen atoms

No. Observations (All reflections)	3509
No. Variables	199
Reflection/Parameter Ratio	17.63
Residuals: R1 (I>2.00□(I))	0.0581
Residuals: R (All reflections)	0.0693
Residuals: wR2 (All reflections)	0.1674
Goodness of Fit Indicator	1.043
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.67 e /Å3
Minimum peak in Final Diff. Map	-0.67 e /Å3

III. CONCLUSION

We have demonstrated the crystal and molecular structure of newly synthesized compounds 4-(bis(2-chloroethyl)amino)-3-nitro-2H-chromen-2-one by the singly crystal x-ray diffraction technique. In compound 4-(bis(2-chloroethyl)amino)-7-methyl-3-nitro-2H-chromen-2-one, the coumarine ring adopts a flattened boat conformation. The nitro group is almost coplanar with the Coumarine ring. The structure exhibits intermolecular hydrogen bonds of the type N-H…O and O-H…O, which bind the molecules into one-dimensional polymeric chains. The compound 4-(bis(2chloroethyl)amino)-3-nitro-2H-chromen-2-one shows planar conformation and molecule exhibits inter molecular hydrogen bonds of the type C-H...O.

IV. REFERENCE

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