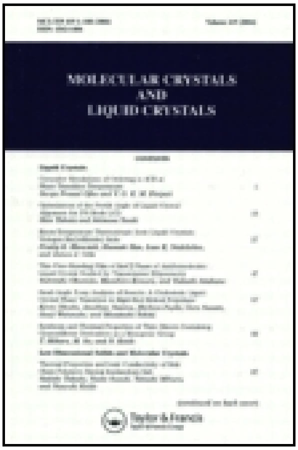

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CRYSTAL STRUCTURE AND CONFORMATION OF TWO SIMILAR PIPERIDONES

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CRYSTAL STRUCTURE AND CONFORMATION OF TWO SIMILAR PIPERIDONES[†]

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N-Chloroacetyl-3,5-dimethyl-2,6-diphenylpiperidin-4-one(CADMPO), $C_{21}H_{22}ClNO_2$, *F.W* $= 355.85$, *monoclinic,* $P2_1$, $a = 8.2082(10)$ Å, $b = 10.4889(10)$ Å, $c = 10.6175(10)$ Å, $\beta = 91.833(10)^\circ$, $V = 913.73(17)$ Å^3, $Z = 2$, $D_{calc} = 1.293\,Mg/m^3$, $\mu = 1.953\,mm^{-1}$, $F_{000} = 376$, $CuK\alpha = 1.5418$ Å, *final R1 and wR2 are 0.0399 and 0.0911, respectively N-Chloroacetyl-3-ethyl-2,6-diphenylpiperidin-4-one (CAEPO),* $C_{21}H_{22}ClNO_2$, *F.W* $= 355.85$, *monoclinic,* $P2_1/n$, $a = 10.3626(6)$ Å, $b = 8.5702(5)$ Å, $c = 21.6930(10)$ Å, $\beta = 92.25(1)^\circ$, $V = 1925.06(18)$ Å^3, $Z = 8$, $D_{calc} = 1.228\,Mg/m^3$, $\mu = 0.211\,mm^{-1}$, $F_{000} = 752$, $MoK\alpha = 0.71073$ Å, *final R1 and wR2 are 0.0623 and 0.1397, respectively. Crystal structure studies of these two 4-piperidones show that the piperidones adopt twist-boat conformation. The C-H...O type of intermolecular interactions play a role in stabilizing the molecules in the unit cell in addition to van der Waals forces.*

Keywords: crystal structure; conformation; hydrogen bonding; CADMPO; CAEPO

INTRODUCTION

Piperidine, a basic component of the piper alkaloid piper nigrum (black pepper) is a monocyclic cyclohexane with a hetero atom affixed in the first position. The skeletal ring of piperidine is contained in the molecule of many

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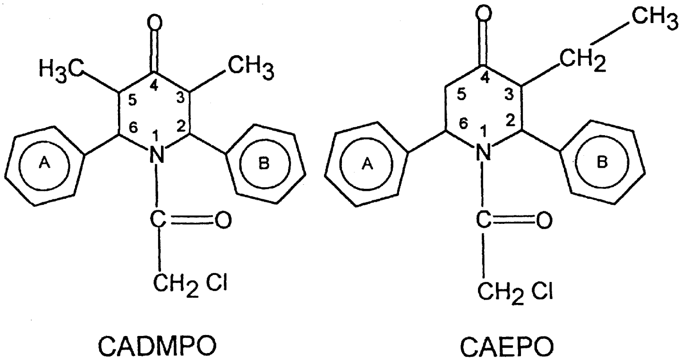

FIGURE 1 Chemical diagrams of CADMPO and CAEPO.

synthetic and natural medicaments [1]. On the contrary, its N-nitroso derivatives turn out to be effective carcinogens. The versatile characteristics of different piperidine derivatives induced the interest to carry out the crystal structure studies of N-Chloroacetyl–4-piperidones. The chemical diagrams of CADMPO and CAEPO are shown in Figure 1.

X-RAY DATA COLLECTION, STRUCTURE SOLUTION, AND REFINEMENT

Data Collection

CADMPO

Colorless transparent crystal of dimension 0.20 × 0.35 × 0.30 mm was used for intensity data collection on an Enraf Nonius CAD4 diffractometer with graphite monochromated CuKα radiation [2]. Accurate unit cell parameters were obtained from 25 reflections in the range of $15 \leq \theta \leq 25°$ from least-squares refinement. The intensities were measured to a maximum θ equal to 72.89° by $\omega/2\theta$ scan mode. Out of 2027($R_{\text{int}} = 0.0379$) independent reflections collected, 1223 reflections with $I \geq 2\sigma(I)$ were used for structure solution and analysis. The intensities were corrected for Lorentz and polarization effects.

CAEPO

A crystal of dimension 0.42 × 0.28 × 0.14 mm was chosen and used for intensity data collection in a Siemens SMART CCD area detector [3]. The data collection was covered over a hemisphere of reciprocal space

TABLE 1 Crystal Data for CADMPO and CAEPO

Parameters	CADMPO	CAEPO
Empirical formula	$C_{21}H_{22}Cl\ N\ O_2$	$C_{21}H_{22}Cl\ N\ O_2$
Formula weight	355.85	355.85
Temperature (K)	293(2)	293(2)
Wavelength (Å)	1.54184	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1$	$P2_1/n$
Unit cell dimensions		
a (Å)	8.2082(1)	10.3626(6)
b (Å)	10.4899(1)	8.5702(5)
c (Å)	10.6175(1)	21.6930(1)
β (°)	91.833(1)	92.250(1)
Volume($Å^3$)	913.73(2)	1925.06(2)
Z	2	4
Calculated density (Mg/m^3)	1.293	1.228
Absorption coefficient (mm^{-1})	1.953	0.211
F (000)	376	752
Crystal size (mm)	$0.20 \times 0.35 \times 0.30$	$0.42 \times 0.28 \times 0.14$
Theta range (°)	4.17 to 72.89	1.88 to 27.50
Index ranges	$-10 \leq h \leq 9$ $0 \leq k \leq 13$ $0 \leq l \leq 13$	$-13 \leq h \leq 10$ $-10 \leq k \leq 11$ $-28 \leq l \leq 19$
Reflections collected/unique	2027/1887 [R(int) = 0.0379]	10053/4388 [R(int) = 0.0757]
Completeness	98.0%	99.3%
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	1887/1/226	4388/0/237
Goodness-of-fit on F^2	0.997	0.869
Observed reflections [$I > 2\sigma(I)$]	1223	2050
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0399, wR2 = 0.0911	R1 = 0.0623, wR2 = 0.1397
R indices (all data)	R1 = 0.0881, wR2 = 0.1095	R1 = 0.1312, wR2 = 0.1670
Largest diff.peak and hole ($eÅ^{-3}$)	0.165 and −0.202	0.314 and −0.313

by a combination of three sets of exposures, and each set had a different ϕ angle (0, 88, and 180°) for the crystal and each exposure of 30 s covered at intervals of 0.3° in ω. The crystal-to-detector distance was 4 cm and the detector swing angle was −35°.

Structure Solution and Refinement

The structures CADMPO and CAEPO were solved by direct methods using the program SHELXS97 [4] and were refined by full-matrix

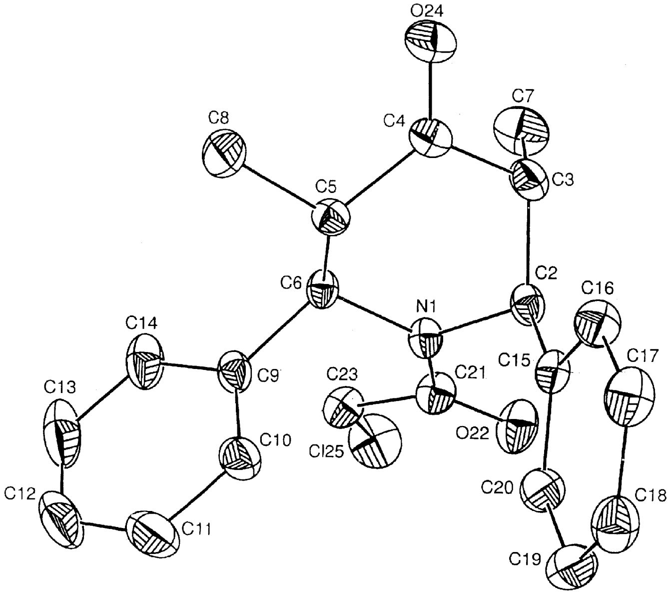

FIGURE 2 ORPTEPIII diagram of CADMPO showing the thermal ellipsoids at 30% probability level.

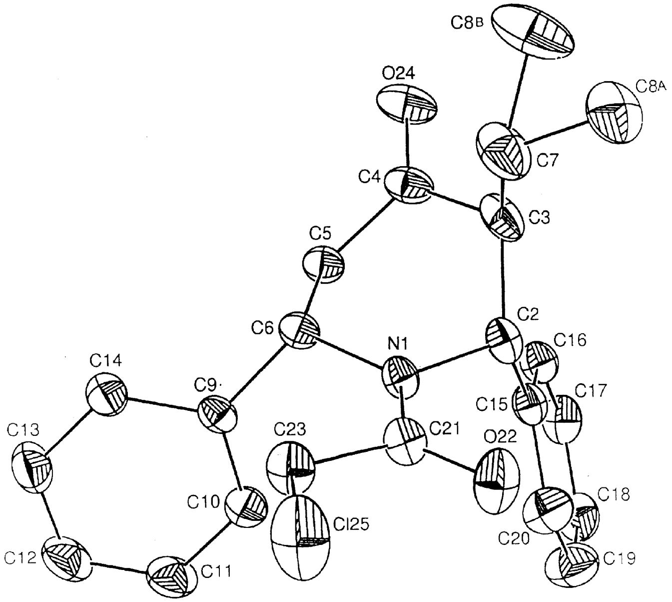

FIGURE 3 ORTEPIII diagram of CAEPO showing the thermal ellipsoids at 30% probability level.

least-squares using the program SHELXL97 [5]. All the hydrogen atoms were placed in estimated positions and constrained to ride on the parent atoms for both the structures. The final cycle of refinement converged to R1 = 0.0399 and 0.0623, wR2 = 0.0911 and 0.1397 for CADMPO and CAEPO, respectively. For the geometric calculations and the vibration ellipsoids, the programs PARST [6] and ORTEP [7] were used, respectively. The crystal data and refinement details are given in Table 1.

Results and Discussion

The perspective view of the molecules CADMPO and CAEPO are shown in Figures 2 and 3, respectively [7]. The atomic coordinates for the two molecules are presented in Table 2.

TABLE 2A Positional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters (Å^2 × 10^3) for the Nonhydrogen Atoms of CADMPO

Atom	*x*	*y*	*z*	$^{\$}$U(eq)
N1	7307(4)	1038(3)	8196(3)	36(1)
C2	6149(5)	65(4)	8622(4)	37(1)
C3	6923(5)	−682(4)	9721(4)	44(1)
C4	8464(5)	−1326(4)	9333(4)	42(1)
C5	9286(5)	−777(4)	8189(4)	34(1)
C6	9046(5)	674(4)	8061(4)	34(1)
C7	7330(7)	197(5)	10855(4)	68(2)
C8	11068(5)	−168(5)	8162(5)	61(1)
C9	9741(5)	1077(4)	6803(4)	41(1)
C10	11151(6)	1825(4)	6791(5)	60(1)
C11	11804(8)	2150(6)	5662(8)	89(2)
C12	11135(9)	1736(7)	4545(7)	92(3)
C13	9753(8)	999(7)	4550(5)	81(2)
C14	9050(6)	670(5)	5671(4)	56(1)
C15	5471(5)	−739(4)	7530(4)	37(1)
C16	5292(5)	−2056(4)	7580(4)	46(1)
C17	4597(6)	−2722(5)	6587(5)	54(1)
C18	4047(5)	−2103(5)	5522(5)	53(1)
C19	4174(6)	−804(5)	5457(5)	54(1)
C20	4879(5)	−128(5)	6452(4)	48(1)
C21	6783(6)	2280(4)	8179(4)	46(1)
C22	5368(4)	2553(3)	8335(3)	65(1)
C23	8057(6)	3300(4)	7966(5)	48(1)
O24	9017(4)	−2237(3)	9912(3)	64(1)
C125	7352(2)	4824(1)	8392(2)	81(1)

$^{\$}U(eq) = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^{*} a_j^{*}\, \mathbf{a_i}.\mathbf{a_j}$.

TABLE 2B Positional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{Å}^2 \times 10^3$) for the Nonhydrogen Atoms of CAEPO

Atom	*x*	*y*	*z*	$^{\$}$U(eq)
N1	2483(2)	7168(2)	3465(1)	39(1)
C2	3513(2)	8153(3)	3762(1)	45(1)
C3	4792(2)	7256(3)	3777(1)	54(1)
C4	4688(3)	5717(4)	4116(1)	51(1)
C5	3334(2)	5130(3)	4187(1)	44(1)
C6	2401(2)	5496(3)	3638(1)	38(1)
C7	5257(3)	6984(4)	3115(2)	77(1)
C8a[†]	6166(2)	8100(20)	2938(6)	77(6)
C8b[†]	6580(4)	6556(11)	3042(2)	104(3)
C9	1060(2)	4973(3)	3801(1)	38(1)
C10	245(3)	5888(3)	4142(1)	50(1)
C11	−958(3)	5366(4)	4287(2)	64(1)
C12	−1374(3)	3928(4)	4100(2)	69(1)
C13	−579(3)	2986(4)	3768(2)	66(1)
C14	630(3)	3509(3)	3611(1)	51(1)
C15	3104(2)	8870(3)	4369(1)	43(1)
C16	3735(3)	8618(3)	4934(1)	50(1)
C17	3323(3)	9339(3)	5462(1)	59(1)
C18	2288(3)	10334(4)	5433(1)	64(1)
C19	1658(3)	10606(4)	4874(2)	75(1)
C20	2063(3)	9884(4)	4348(1)	63(1)
C21	1815(2)	7771(3)	2969(1)	45(1)
O22	1916(2)	9136(2)	2805(1)	66(1)
C23	908(3)	6664(3)	2620(1)	53(1)
O24	5622(2)	5018(3)	4320(1)	74(1)
Cl25	333(1)	7409(1)	1908(1)	90(1)

$^{\$}U(eq) = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a_i}.\mathbf{a_j}$.

[†] Disordered.

A study on the difference map in the structure CAEPO reveals that the atom C8 of the ethyl group is disordered. The refinement of the positions shows the equal occupancy on the two sites.

The twist-boat conformation of the heterocyclic rings of the two piperidones show the relaxed state of the moieties from ideal chair conformations, a common feature observed in most piperidine analogues. The mean plane calculated using the PARST program [6] clearly points out that the atoms N1, C3, C4, and C5 constitute the best plane in both the molecules. The atoms C2 and C6 deviate from the mean plane by 0.750(4) Å and −0.532(4) Å for CADMPO and −0.753(3) Å and 0.515(2) Å for CAEPO.

In both the piperidine structures, the hetero nitrogen atom is blocked by chloroacetyl groups, which act as a barrier to the pyramidal inversion of nitrogen. The acetyl groups in the two molecules are intermediate to the planar and perpendicular orientation [11] of the nitrogen atom in relation to the best plane of the piperidone. The synclinical orientation of the acetyl carbonyl group in both the structures is seen from the dihedral angles 40.36(17)°(CADMPO) and 44.36(7)°(CAEPO), with respect to the best plane of the piperidine moiety.

The phenyl rings positioned at 2 and 6 of the piperidine ring in both the structures orient axially and equatorially. The torsion angles [C4-C3-C2-C15=]67.7(5)° (CADMPO), 71.6(3)° (CAEPO) and [C4-C5-C6-C9=]−173.2(3)° (CADMPO), −174.7(2)° (CAEPO) delineate these orientations.

Involvement of C-H...O type of intermolecular interactions in their packing is the common structural feature of the two compounds. The C-H...O interactions formed by C3-H3...O22, C6-H6...O24 and C23-H23B...O24 (Table 3) enhance the stability of structure CADMPO. The same set of acceptor atoms O22 and O24 lead to different intermolecular interactions such as C6-H6...O22, C23-H23B...O22 and C12-H12...O24 (Table 3) in the case of CAEPO.

TABLE 3 Possible Nonbonded Interactions (Hydrogen bonds) for CADMPO and CAEPO

d(D-H)Å	d(H...A)Å	d(D...A)Å	< (DHA)°
CADMPO*			
C6-H6	H6...O24	C6...O24	C6-H6...O24(i)
0.980(4)	2.484(3)	3.427(5)	161.44(2)
C23-H23B	H23B...O24	C23...O24	C23-H23B...O24(i)
0.970(5)	2.341(3)	3.288(6)	165.19(3)
C3-H3	H3...O22	C3...O22	C3-H3...O22(ii)
0.980(5)	2.498(3)	3.387(6)	150.74(3)
CAEPO**			
C6-H6	H6...O22	C6...O22	C6-H6...O24(i)
0.981(2)	2.503(2)	3.440(3)	159.90(2)
C23-H23B	H23B...O22	C23...O22	C23-H23B...O22(i)
0.970(3)	2.384(2)	3.285(3)	154.44(2)
C12-H12	H12...O24	C12...O24	C12-H12...O24(ii)
0.930(3)	2.600(2)	3.303(4)	132.76(2)

*Equivalent positions: (i)−x+2,+y+1/2,−z+2; (ii)−x+1,+y−1/2,−z+2.

**Equivalent positions: (i)−x+1/2,+y−1/2,−z+1/2; (ii)x−1,+y,+z.

Preparation of CADMPO and CAEPO

The two compounds CADMPO and CAEPO result from reactions of their corresponding archetype piperidones (N-free piperidones), with chloro-acetyl, in excess of triethylamine. The technique of slow evaporation was used to crystallize the two piperidine derivatives. The solvent of crystallization is ethanol for both of the compounds.

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