ANALYTICAL SCIENCES JUNE 2003, VOL. 19

Instrumental Achievements

Crystal Structure of 3,3-Dichloro-*N*-*p*-methoxyphenyl-4-(2-phenylstryl)-2-azetidinone

Mehmet KABAK,*† Vildan GÜNER, Yalçın ELERMAN,* and Tahsin N. DURLU*****

**Department of Engineering Physics, Faculty of Engineering, Ankara University, 06100, Tandogan, Ankara, Turkey*
***Department of Chemistry, Faculty of Sciences, University of Hacettepe, 06532, Beytepe, Ankara, Turkey*
****Department of Physics, Faculty of Art and Sciences, University of Kırıkkale, 71450, Yahşihan, Kırıkkale, Turkey*

3,3-Dichloro-*N*-*p*-methoxyphenyl-4-(2-phenylstryl)-2-azetidinone ($C_{22}H_{15}Cl_2NO_2$) was studied by X-Ray analysis, which indicated a monoclinic space group, $P2_1/c$, with a = 9.619(5), b = 13.879(4), c = 14.161(5)Å, β = 100.16(3)˚, V = 1860.8(13)Å^3, Z = 4, D_c = 1.414 g cm^{-3}, μ(Mo K$_\alpha$) = 0.366 mm^{-1} and F_{000} = 816. The structure was solved by direct methods and refined to R = 0.041 for 4026 reflections [$I > 2\sigma(I)$. The β-lactam ring (2-azetidinone) has antimicrobial affects. The substituents of the methoxyphenyl and phenyl substituents do not change the activity property of the beta-lactam ring, and the activity properties depend on the planarity of the β-lactam ring.

(Received June 24, 2002; Accepted January 6, 2003)

The β-lactam ring (2-azetidinone) has a key role in the most widely employed class of antimicrobial agents. The activity and selectivity of the β-lactam ring can be decisively influenced by the attached subtituents to the β-lactam ring,[1] and depends on some quantitave geometrical parameters of the β-lactam structures (such as the deviation of the N1 atom from the surrounding C atoms and the sum of the bond angles at the N1 atom).[2] Recently we reported some structural investigations which were made by changing the substituents around the β-lactam ring, to determine whether the substituents change the activity and selectivity of the monocyclic β-lactams. Here, we wish to report on a new crystal structure of 3,3-dichloro-*N*-*p*-methoxyphenyl-4-(2-phenylstryl)-2-azetidinone ($C_{22}H_{15}Cl_2NO_2$) (Fig. 1).

The compound was prepared as follows. A solution of dichloroacetyl chloride (0.002 mol, 1.78 ml) in dry benzene (20 ml) was added dropwise over a period of 1 h at room temperature to a mixture of β-phenylcinnamaldhyde *N*-*p*-methoxyphenylimine (0.001 mol, 0.313 g) and triethylamine (0.002 mol, 2.78 ml) in dry benzene. The mixture was stirred for 2 h at room temperature and amine salt was removed by filtration. The filtrate was washed with 5% HCl and water and dried over sodium sulfate. The title compound was crystallized from ethanol.

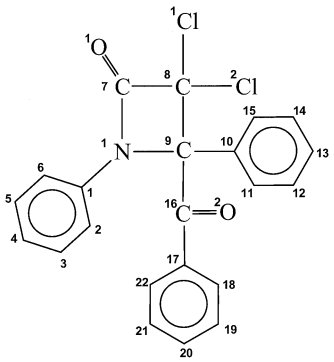

Fig. 1 Chemical diagram of the title molecule.

Table 1 Crystal and structure refinement data for the title compound

Formula: $C_{22}H_{15}Cl_2NO_2$	
Formula weight = 396.3	
Crystal system: monoclinic	
Space group: $P2_1/c$	Z = 4
a = 9.619(5)Å	α = 90.0˚
b = 13.879(4)Å	β = 100.16(3)˚
c = 14.161(5)Å	γ = 90.0˚
V = 1860.8(13)Å^3	
D_x = 1.414 g/cm^3	
F(0 0 0) = 816	
μ(Mo K$_\alpha$) = 3.66 cm^{-1}	
R; $wR^2(I > 2\sigma(I))$: 0.041; 0.112	
$2\theta_{max}$ = 65˚	
$(\Delta/\sigma)_{max}$ = 0.00	
$(\Delta\rho)_{max}$ = 0.297 eÅ^{-3}	
$(\Delta\rho)_{min}$ = –0.295 eÅ^{-3}	
No. of reflections used = 4026 ($I > 2.0\sigma(I)$)	
No. of variables = 244	
Measurement: Rigaku AFC7S	
Program system: TEXSAN	
Structure determination: direct methods (SIR92)	
Refinement: full-matrix least-squares (SHELXL-97)	

† To whom correspondence should be addressed.
E-mail: kabak@eng.ankara.edu.tr

Table 2 Atomic coordinates ($\times 10^{-4}$) and equivalent isotropic displacement parameters ($Å^2 \times 10^{-3}$) for title compound

Atom	x	y	z	U_{eq}
Cl1	1620(1)	-1475(1)	1453(1)	59(1)
Cl2	4176(1)	-1414(1)	638(1)	56(1)
O1	1492(1)	-156(1)	-554(1)	62(1)
O2	5614(1)	954(1)	1647(1)	61(1)
N1	2833(1)	742(1)	709(1)	42(1)
C1	2760(1)	1727(1)	445(1)	40(1)
C2	2272(2)	1961(1)	-509(1)	56(1)
C3	2201(2)	2922(1)	-791(1)	67(1)
C4	2593(2)	3640(1)	-133(1)	62(1)
C5	3071(2)	3406(1)	814(1)	55(1)
C6	3167(2)	2451(1)	1110(1)	49(1)
C7	2211(1)	-40(1)	220(1)	46(1)
C8	2831(1)	-725(1)	1028(1)	42(1)
C9	3385(1)	221(1)	1625(1)	37(1)
C10	2636(1)	529(1)	2440(1)	38(1)
C11	3383(2)	715(1)	3354(1)	46(1)
C12	2686(2)	1003(1)	4086(1)	59(1)
C13	1250(2)	1122(1)	3912(1)	63(1)
C14	506(2)	973(1)	3005(1)	63(1)
C15	1182(1)	674(1)	2263(1)	51(1)
C16	5005(1)	275(1)	1915(1)	41(1)
C17	5776(1)	-509(1)	2519(1)	44(1)
C18	5102(2)	-1221(1)	2962(1)	53(1)
C19	5890(2)	-1960(1)	3460(1)	70(1)
C20	7333(2)	-1982(2)	3511(1)	86(1)
C21	7995(2)	-1274(2)	3091(1)	87(1)
C22	7234(2)	-528(1)	2591(1)	63(1)

U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Table 3 Bond lengths (Å) and angles (°) for the title compound

Cl1-C8	1.746(1)	Cl2-C8	1.773(1)		
O1-C7	1.199(2)	O2-C16	1.205(2)		
N1-C7	1.368(2)	N1-C1	1.416(2)		
N1-C9	1.497(2)	C1-C6	1.385(2)		
C1-C2	1.388(2)	C2-C3	1.390(2)		
C3-C4	1.372(2)	C4-C5	1.378(2)		
C5-C6	1.387(2)	C7-C8	1.526(2)		
C8-C9	1.601(2)	C9-C10	1.526(2)		
C9-C16	1.542(2)	C10-C11	1.390(2)		
C10-C15	1.391(2)	C11-C12	1.388(2)		
C12-C13	1.370(3)	C13-C14	1.371(3)		
C14-C15	1.393(2)	C16-C17	1.498(2)		
C17-C22	1.389(2)	C17-C18	1.390(2)		
C18-C19	1.391(2)	C19-C20	1.377(3)		
C20-C21	1.364(3)	C21-C22	1.387(3)		
C13-C12-C11	120.3(2)	C7-C8-Cl1	115.7(1)	N1-C7-C8	92.1(1)
C13-C14-C15	121.1(2)	C7-C8-Cl2	108.2(1)	C20-C21-C22	121.0(2)
O2-C16-C17	121.9(1)	Cl1-C8-Cl2	110.7(1)	O1-C7-N1	134.4(1)
C17-C16-C9	119.4(1)	N1-C9-C16	113.2(1)	C20-C19-C18	119.9(2)
C22-C17-C16	116.6(1)	N1-C9-C8	84.5(1)	C4-C3-C2	120.6(1)
C17-C18-C19	119.8(2)	C16-C9-C8	114.0(1)	C4-C5-C6	120.8(1)
C21-C20-C19	120.3(2)	C11-C10-C9	121.4(1)	C22-C17-C18	119.9(1)
C21-C22-C17	119.1(2)	C12-C11-C10	120.7(1)	C18-C17-C16	123.5(1)
C7-N1-C9	96.5(1)	C12-C13-C14	119.5(2)	C2-C1-N1	118.4(1)
C6-C1-C2	119.9(1)	C10-C15-C14	119.7(1)	O2-C16-C9	118.6(1)
C7-N1-C1	129.5(1)	O1-C7-C8	133.5(1)	C10-C9-C8	118.1(1)
C1-N1-C9	133.5(1)	C7-C8-C9	86.2(1)	C11-C10-C15	118.6(1)
C6-C1-N1	121.7(1)	C9-C8-Cl1	119.1(1)	C15-C10-C9	119.9(1)
C1-C2-C3	119.6(1)	C9-C8-Cl2	114.4(1)	C10-C9-C16	112.0(1)
C3-C4-C5	119.6(1)	N1-C9-C10	112.2(1)	C1-C6-C5	119.5(1)

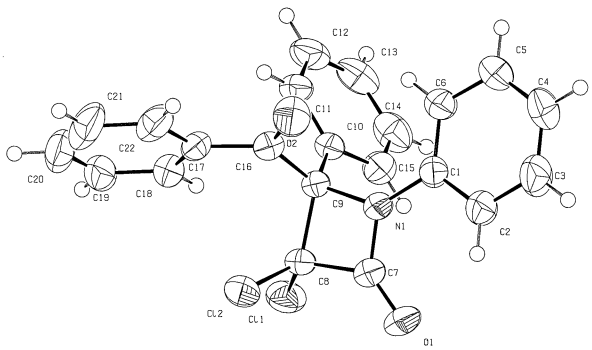

Fig. 2 Molecular structure of the title compound with the atom labeling. Thermal ellipsoids are drawn at the 50% probability level.

X-ray data were collected by a graphite-monochromated Mo K_α radiation (λ = 0.71069 Å). The crystal structure was solved by direct methods.[3] All of the non-hydrogen atoms were refined anisotropically (hydrogen atoms were included, but not refined).[4] All of the hydrogen atoms were placed geometrically at the corresponding C atoms. The crystal and experimental data are listed in Table 1. The final fractional atomic coordinates and equivalent isotropic thermal parameters for non-hydrogen atoms are given in Table 2 and selected bond distances and bond angles are listed in Table 3. The molecular structure of the title molecule is shown in Fig. 2 with the atom-labeling schemes.

Brufani and Cella[2] concluded that, when the N1 atom is deviated by 0.4 – 0.5 Å from the plane, the surrounding C atoms at the β-lactam molecules could be biologically active. The sum of the bond angles at the N1 atom is 359.5° and the torsion angles of C7–N1–C1–C6 [164.2(1)°] and C7–N1–C1–C2 [163.8(2)°] support that there is no significant deviation of the N1 atom from the surrounding C atoms. A small deviation of the N1 atom from the C1, C7, and C9 plane is 0.062(1)Å. All of these results indicate that our molecule is inactive. However, introducing these methoxyphenyl and phenyl substituents does not change the activity property of the β-lactam ring. There is no intermolecular or intramolecular proximity between the molecules and atoms.

References

1. S. D. Sharma and U. Mehra, *S. Scient. Ind. Res*., **1988**, *47*, 451.
2. M. Brufani and L. Cella, "*β-Lactam Antibiotics and Anamycins: X-ray Crystallography and Drug Action*", ed. A. S. Horn and C. J. de Ranter, **1984**, Clarendon Press, Oxford, 390 – 393.
3. A. Altomare, M. Cascarano, C. Giacovazzo, and A. Guagliardi, *J. Appl. Cryst*., **1993**, *26*, 343.
4. G. M. Sheldrick, SHELXL-97 a computer program for crystal structure determination, University of Gottingen, **1997**.