Conformation of 1-(2-Bromophenyl)azetidin-2-one and 1-(2-Bromophenyl)pyrrolidin-2-one

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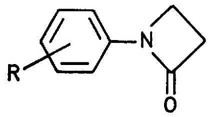
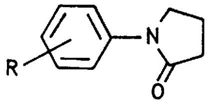
U.v. data suggest that 1-(2-bromophenyl)pyrrolidin-2-one (2a) is substantially non-planar in solution while the related 1-(2-bromophenyl)azetidin-2-one (1a) is planar. Crystal structure studies of these two compounds show this effect exists in the solid also and that there is a 72° dihedral angle between normals to the phenyl and five-membered rings in the γ-lactam (2a), while the rings in the β-lactam (1a) are coplanar. Compound (1a) crystallizes in space group *C*2/*c* with cell dimensions *a* = 15.91(1), *b* = 7.70(1), *c* = 14.48(1) Å, β = 103.84(1)° while compound (2a) crystallizes in space group $P2_1/c$ with *a* = 10.55(1), *b* = 6.83(1), *c* = 15.41(1) Å, β = 112.02°(2). Both structures were solved by heavy atom methods.

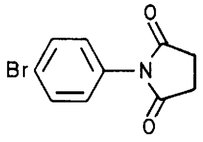
U.v. and n.m.r. spectra of β- and γ-*N*-phenyl-lactams in solution suggest that the intensity of the absorption band at *ca.* 250 nm can be used as an indication of the coplanarity of the *N*-phenyl substituent and the heterocyclic four- or five-membered ring. β-Lactams are of particular interest because they are part of the ring system in penicillin and cephalosporin antibiotics. Table 1 shows u.v. data for lactams (1) and (2).[1] Manhas *et al.* interpreted these spectra as indicating that there is a substantial dihedral angle between the *N*-phenyl substituent and the γ-lactam ring in (2a) (*i.e.* the angle between normals to the two rings) while in the β-lactam (1a) the corresponding dihedral angle was very small. This would interfere with resonance interaction in the γ-lactam resulting in a wavelength shift from 247 nm to weak multiple bands at 267, 273, and 293 nm with a substantial diminution of the extinction coefficient. There is some effect on the extinction coefficient in the



(1)



(2)



(3)

a; R = *o* - Br
b; R = *p* - Br

Table 1

U.v. spectra of β- and γ- (*o*- and *p*-bromophenyl)-lactams

Compound	$\lambda_{\text{max.}}$/nm	ε
(1a)	247	8 650
(1b)	254	21 000
(2a)	293sh	190
	273sh	350
	267sh	425
(2b)	254	18 100

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[1] M. S. Manhas, S. Jeng, and A. K. Bose, *Tetrahedron*, 1968, **24**, 1237.

β-lactam (1a) but no comparable change in the absorption wave length.

In order to test these hypotheses we have solved the crystal structures of 1-(2-bromophenyl)azetidin-2-one (1a) and 1-(2-bromophenyl)pyrrolidin-2-one (2a). The reported crystal structures of *N*-phenyl-substituted β-lactams contain halogen in the *para*-position [2,3] and do not show the striking u.v. effects seen in the *ortho*-substituted phenyl compounds (1a) and (2a). There are no reports of γ-*N*-aryl-lactams although the related structure *N*-4-bromophenylsuccinimide (3) [4] shows a 65° dihedral angle between the plane of the phenyl group and five-membered ring. This angle has been ascribed to steric interaction between the *ortho*-hydrogens and the carbonyl oxygen atoms.

EXPERIMENTAL

Compound (1a) was prepared by established methods from *o*-bromoaniline and β-bromopropionic acid.[5] Recrystallization from hexane yielded needle-like crystals elongated along the *b* axis. The space group and cell dimensions were determined from precession and equi-inclination Weissenberg photographs.

TABLE 2

Fractional co-ordinates (× 10^4) and thermal parameters (× 10^3) for the β-lactam (1a). The numbers in parentheses are the estimated standard deviations of the positional and thermal parameters

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Br(2)	−915(1)	1 211(2)	1 300(1)	61(1)	96(1)	52(1)	7(1)	27(1)	17(1)
C(1)	−1 052(6)	1 688(15)	−21(6)	37(4)	44(7)	39(4)	3(6)	15(3)	−5(4)
C(2)	1 855(6)	1 297(19)	−605(9)	33(4)	73(10)	65(6)	0(6)	19(4)	−11(6)
C(3)	−2 009(7)	1 513(19)	−1 566(9)	39(5)	68(10)	61(6)	3(7)	3(4)	−24(6)
C(4)	−1 369(7)	2 210(21)	−1 963(7)	51(5)	84(10)	39(5)	9(8)	8(4)	−12(6)
C(5)	−573(6)	2 607(16)	−1 385(7)	40(4)	42(6)	42(4)	10(6)	8(4)	−3(4)
C(6)	−400(5)	2 392(16)	−399(6)	30(4)	43(7)	39(4)	2(6)	8(3)	−3(4)
N(1)	430(5)	2 819(14)	150(5)	36(3)	59(7)	31(3)	−5(5)	9(3)	−1(4)
C(7)	886(7)	2 702(19)	1 181(7)	47(5)	68(9)	39(5)	−2(8)	2(4)	10(6)
C(8)	1 697(8)	3 476(21)	881(9)	41(5)	73(10)	62(6)	5(8)	1(5)	−9(7)
C(9)	1 141(6)	3 485(16)	−229(8)	34(4)	57(9)	55(5)	2(6)	14(4)	1(6)
O(1)	1 258(6)	3 922(15)	−884(6)	64(5)	116(10)	57(5)	−24(6)	30(4)	1(5)
H(1)	−2 227	853	−310	57					
H(2)	−2 257	1 129	−1 981	69					
H(3)	−1 492	2 466	−2 668	65					
H(4)	−101	3 068	−1 676	71					
H(5)	641	3 665	1 633	56					
H(6)	911	1 580	1 443	56					
H(7)	1 743	4 602	1 147	68					
H(8)	2 297	3 056	1 008	68					

Thermal parameters are expressed in the form $T = \exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c)]$.

Crystal data.—Compound (1a) C_9H_8BrNO, $M = 226.07$. Monoclinic, $a = 15.91(1)$, $b = 7.70(1)$, $c = 14.48(1)$ Å, $\beta = 103.84(1)°$, $U = 1\,772$ Å^3, $D_m = 1.71$, $D_c = 1.73$ g cm^{-3}, $Z = 8$. Space group $C2/c$ (hkl: $h + k = 2n + 1$ absent; $h0l$: $l = 2n + 1$ absent; $0k0$: $= 2n + 1$ absent). Ni-filtered Cu-K_α radiation, $\lambda = 1.541\,8$ Å; μ(Cu-K_α) = 67.5 cm^{-1}.

Intensity data was collected along the *a* and *b* axes from two different crystals measuring 0.3 × 0.4 × 0.3 and 0.2 × 0.4 × 0.3 mm respectively. It was necessary to mount the crystals in a thin-walled glass capillary as significant sublimation occurred over the period used for data collection. Multiple film Weissenberg techniques were used to collect the data with intensities estimated by visual comparison with a calibration strip. The data was then merged with the computer program of Hamilton *et al.*[6] Of 1 240 reflections collected within the Cu-K_α sphere, 993 were considered observed. All calculations were performed on the PDP-10 computer using Stewart's *X*-ray-72 computer programs.[7]

The data was placed on an absolute scale by Wilson's method,[8] and the bromine located in a Patterson map. All non-hydrogen atoms were evident on the first Fourier map phased on bromine alone. After block diagonal isotropic refinement the agreement factor *R* was 0.17. Three cycles of anisotropic full matrix refinement with Hughes [9] weighting scheme reduced the weighted *R* to 0.097. Inclusion of calculated hydrogen positions at a C–H distance of 1.0 Å and two full matrix least square cycles (isotropic hydrogen and anisotropic C, N, O, Br) gave a final weighted *R* of 0.088. The largest shift : error ratio by this time was 0.5. The final positional parameters are listed in Table 2. Table 3 listing calculated *versus* observed structure factors is available in Supplementary Publication No. SUP 21920 (5 pp.).* Table 4 lists bond distances and angles using the numbering scheme shown in Figure 1.

Compound (2a) was supplied by Dr. M. S. Manhas. Recrystallization from methylene chloride yielded hexagonal shaped crystals which were used for data collection. A small crystal, *ca.* 0.4 mm × 0.5 mm × 0.4 mm, was mounted on a glass fibre along the *b* axis perpendicular to the main face. Space group and cell dimensions were

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* For details of Supplementary Publications see Notice to Authors No. 7, in *J.C.S. Perkin II*, 1975, Index issue. Items less than 10 pp. are supplied as full-size copies.

[2] R. Parthasaratky, *Acta Cryst.*, 1970, **B26**, 1283; J. L. Luche, H. B. Kagan, R. Parthasaratky, G. Tsoucaris, C. DeRango, and C. Zelwer, *Tetrahedron*, 1968, **24**, 1275.

[3] G. Kartha and G. Ambady, *J.C.S. Perkin II*, 1973, 2043.

[4] J. Barassin, G. Tsoucaris, and H. Lumbroso, *Compt. rend.*, 1961, **253**, 2546.

[5] M. S. Manhas and S. J. Jeng, *J. Org. Chem.*, 1967, **35**, 1246.

[6] W. C. Hamilton, J. S. Rollett, and R. A. Sparks, *Acta Cryst.*, 1965, **18**, 129.

[7] J. M. Stewart, G. J. Kruger, H. L. Ammon, C. Dickinson, and S. R. Hall, Technical Report TR-192, 'The *X*-ray System,' Computer Science Center, University of Maryland.

[8] A. J. C. Wilson, *Nature*, 1942, **150**, 151.

[9] E. W. Hughes, *J. Amer. Chem. Soc.*, 1941, **63**, 1737.

determined from Weissenberg and precession photographs.

Crystal Data.—$C_{10}H_{10}NOBr$, $M = 240.01$. Monoclinic, $a = 10.55(1)$, $b = 6.83(1)$, $c = 15.41(1)$ Å, $\beta = 112.02(2)$, $U = 1\,029$ Å^3, $D_m = 1.505$, $D_c = 1.548$ g cm^{-3}, $Z = 4$. Space group $P2_1/c$ ($h0l$: $l = 2n + 1$ absent; $0k0$: $k = 2n + 1$ absent). Ni-filtered Cu-K_α radiation, $\lambda = 1.541\,8$ Å, $\mu = 57.1$ cm^{-1}. Multiple film Weissenberg data was collected along the b axis with intensities estimated by comparison with a calibration strip. Data was merged for each layer [6] and then put on an approximate scale for each of four layers by means of a Wilson plot. The initial layer scale factors were refined separately once the structure had been solved. Of 1 084 measured reflections 886 were considered observed. The bromine atom was located in a Patterson map and the rest of the structure was apparent in the first Fourier map phased on bromine. Anisotropic full matrix refinement of the non-hydrogen atom positions reduced R to 0.108 using a Hughes weighting scheme. Positonal and thermal parameters are shown in Table 5 while the structure factor Table 6 is available in SUP 21920. Bond distances and angles as shown in Table 7 using the numbering system shown in Figure 2.

TABLE 4

β-Lactam (1a) bond distances and bond angles. Estimated standard deviations are given in parentheses (× 10^2 for distances)

Bond distances (Å)			
Br(1)–C(1)	1.91(1)	C(6)–N(1)	1.41(2)
C(1)–C(2)	1.39(3)	N(1)–C(7)	1.50(2)
C(2)–C(3)	1.36(2)	C(7)–C(8)	1.57(2)
C(3)–C(4)	1.39(2)	C(8)–C(9)	1.51(2)
C(4)–C(5)	1.38(3)	N(1)–C(9)	1.38(3)
C(5)–C(6)	1.40(2)	C(9)–O(1)	1.21(2)
C(6)–C(1)	1.39(2)		
Bond angles (°)			
Br(1)–C(1)–C(2)	115.9(0.8)	C(1)–C(6)–N(1)	123.7(0.8)
Br(1)–C(1)–C(6)	123.5(0.6)	C(6)–N(1)–C(7)	135.5(0.9)
C(2)–C(1)–C(6)	120.6(0.9)	C(6)–N(1)–C(9)	130.5(0.8)
C(1)–C(2)–C(3)	120.6(1.1)	C(7)–N(1)–C(9)	94.0(0.7)
C(2)–C(3)–C(4)	119.0(0.9)	N(1)–C(7)–C(8)	86.3(0.8)
C(3)–C(4)–C(5)	119.5(1.0)	C(7)–C(8)–C(9)	86.3(0.9)
C(4)–C(5)–C(6)	121.6(1.0)	N(1)–C(9)–C(8)	93.4(0.9)
C(5)–C(6)–C(1)	117.6(1.0)	N(1)–C(9)–O(1)	132.4(0.9)
C(5)–C(6)–N(1)	118.2(0.9)	C(8)–C(9)–O(1)	134.1(1.0)

TABLE 5

Fractional co-ordinates (× 10^3) and thermal parameters (× 10^3) for the γ-lactam (2a). Numbers in parentheses are the estimated standard deviations of the positional and thermal parameters

Atom	x	y	z	U_{11}	U_{22} †	U_{33}	U_{12}	U_{13}	U_{23}
Br(1)	64(2)	−309(1)	88(1)	69(1)	85	53(1)	−14(1)	14(1)	14(1)
C(1)	146(2)	−253(3)	218(1)	46(7)	0	48(6)	2(9)	−18(6)	2(9)
C(2)	106(2)	−362(4)	282(1)	70(10)	42	77(1)	46(8)	−10(13)	4(13)
C(3)	160(2)	−325(4)	376(1)	79(11)	6	61(18)	21(14)	32(8)	5(12)
C(4)	255(2)	−176(4)	408(1)	46(14)	86	64(10)	11(18)	46(10)	−32(15)
C(5)	300(2)	64(4)	347(1)	64(6)	10	49(6)	8(10)	20(6)	3(10)
C(6)	242(1)	−109(4)	249(1)	53(8)	1	48(6)	−3(1)	22(6)	1(10)
N(1)	291(1)	−2(4)	188(1)	47(7)	50	53(6)	−8(1)	19(5)	0(12)
C(7)	265(2)	21(5)	171(1)	80(11)	2	79(12)	−5(10)	32(4)	6(16)
C(8)	330(2)	258(5)	101(1)	91(14)	119	83(14)	−32(1)	36(11)	14(17)
C(9)	423(2)	84(4)	103(1)	97(14)	16	108(14)	−4(16)	65(12)	0(16)
C(10)	377(1)	−77(6)	153(1)	47(9)	12	66(9)	4(12)	24(7)	−7(15)
O(1)	417(1)	−241(4)	163(1)	70(9)	69	91(10)	−4(11)	52(8)	−17(13)

Thermal parameters are expressed in the form $T = \exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$.

† No standard deviation is reported for U_{22} as the data were only collected along the b axis.

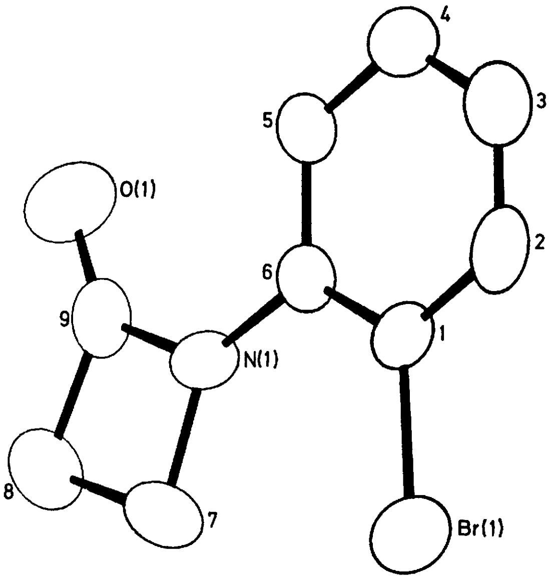

FIGURE 1 Numbering system, conformation, and thermal ellipsoids for the β-lactam (1a)

DISCUSSION

The bond lengths and angles are normal in the two molecules except for some distortion in the β-lactam ring similar to that observed in related compounds.[10] The β-lactam ring is planar ($X^2 = 0.25$) with N(1) 0.003 Å from the mean plane of its substituents. In biologically active lactam structures the amide nitrogen is *ca.* 0.4 Å from the plane of its substituents.[10] It has been proposed that this non-planarity is partly responsible for the β-lactam's physiological effect. The β-lactam ring in (1a) forms a dihedral angle of 2.2° with the attached *N*-phenyl aromatic ring with the carbonyl group pointed away from the direction of C–Br bond. In addition there is a close interaction of 2.20 Å between the hydrogens attached to C(5) and O(1). The dihedral angle in

[10] Robert M. Sweet, in 'Cephalosporines and Penicillins; Chemistry and Biology,' ed. E. H. Flynn, Academic Press, New York, 1972, pp. 281—307.

xylene solution of (1a) is 53° as determined by dipole moment measurements and quantum chemical calculations.[11] The difference between this dipole moment study in xylene solution and the previous n.m.r. study in $CDCl_3$ which suggested (1a) should be planar is not explained. The *X*-ray results are in agreement with the n.m.r. solution work. Perhaps the discrepancy lies in assumptions made in the dipole moment study. There are no intermolecular contacts less than the sum of van der Waals radii which could explain a different conformation in the solid from that in solution. There are rather close intramolecular contacts of 3.13, 3.06, 2.86, and 2.28 Å for the Br(1) • • • C(7), Br(1) • • • H(5), Br(1) • • • H(6), and O(1) • • • H(4) bonds respectively. [H(4) is attached to C(5) while H(5) and H(6) are attached to C(7)].

TABLE 7

γ-Lactam (2a) bond distances and bond angles. Estimated standard deviations are given in parentheses ($\times 10^2$ for distances)

Bond distances (Å)			
Br(1)–C(1)	1.90(1)	C(6)–N(1)	1.43(3)
C(1)–C(2)	1.42(3)	N(1)–C(7)	1.48(5)
C(2)–C(3)	1.37(2)	N(1)–C(10)	1.33(3)
C(3)–C(4)	1.39(3)	C(7)–C(8)	1.52(4)
C(4)–C(5)	1.42(3)	C(8)–C(9)	1.54(4)
C(5)–C(6)	1.44(2)	C(9)–C(10)	1.52(4)
C(1)–C(6)	1.36(3)	C(10)–O(1)	1.19(4)
Bond angles (°)			
Br(1)–C(1)–C(2)	119(1)	C(6)–N(1)–C(7)	122(2)
Br(1)–C(1)–C(6)	120(1)	C(6)–N(1)–C(10)	123(3)
C(2)–C(1)–C(6)	121(1)	C(7)–N(1)–C(10)	115(2)
C(1)–C(2)–C(3)	122(2)	N(1)–C(7)–C(8)	103(2)
C(2)–C(3)–C(4)	118(2)	C(7)–C(8)–C(9)	106(3)
C(3)–C(4)–C(5)	122(2)	C(8)–C(9)–C(10)	104(2)
C(4)–C(5)–C(6)	118(2)	C(9)–C(10)–N(1)	109(3)
C(1)–C(6)–C(5)	120(2)	C(9)–C(10)–O(1)	126(2)
C(1)–C(6)–N(1)	123(1)	N(1)–C(10)–O(1)	125(3)
C(5)–C(6)–N(1)	118(2)		

The five-membered ring β-lactam (2a) is puckered with C(8) out of the plane of the other four atoms. The aromatic ring forms a dihedral angle of 72° with the plane of lactam ring with the C–Br bond turned toward the carbonyl group. Thus the suggestion that the u.v. spectrum of *N*-(*o*-bromophenyl)-lactams in solution is due to a non-planar conformation is confirmed in the solid. Qualitatively the spectral effects in (2a) are substantially different from the simple diminution in extinction seen in (1a) (Table 1).

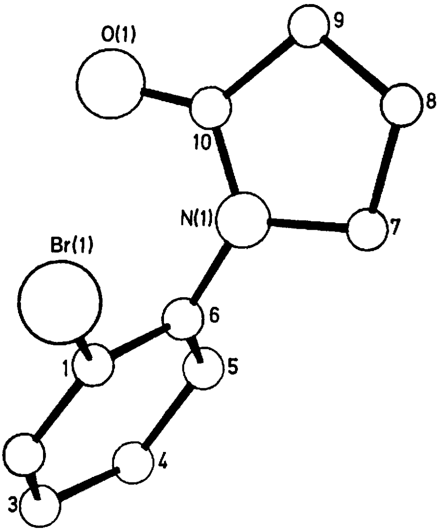

FIGURE 2 Numbering system and conformation of the γ-lactam (2a)

We thank Mr. R. Ohanian for assistance in the initial work on the β-lactam.

[6/487 *Received*, 11*th March*, 1976]

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[11] E. R. Malinowski, M. S. Manhas, M. Goldberg, and V. Fanelli, *J. Mol. Structure*, 1974, **23**, 321.