Studies on conformationally strained puckered ring of four membered saturated heterocycles: A case study of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine

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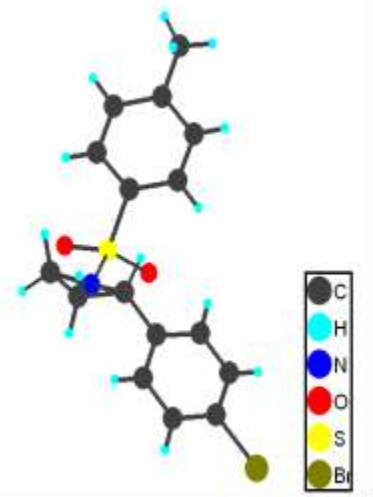
Abstract:

Studies on conformationally strained puckered ring of four membered saturated heterocycle 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine gives deep insight on the nonplanarity of central azetidine ring. Data indicates the ring is puckered and puckering angle is 5.28° from the plane. The stereochemical preferences of the substituents attached to the azetidine ring are also affected by non-planarity. The intermolecular CH…π interactions are responsible for tightly packed crystal lattice in the solid state.



Key words: Heterocycles, Azetidine, Puckered, Conformationally strained

Introduction:

The conformation of a cyclic compound is result of various interactions present in the molecule. The Bayer and Pitzer strains qualitatively determine the conformation for four to six membered cyclic systems.[1-3] The geometry of four membered ring compounds significantly affected by large amplitudes, out of plane vibrations and several ring puckering motions.[4,5]

Studies revealed that azetidine (four membered saturated nitrogen heterocycle) ring conformation is highly related to steric demand of the alkyl substituent of the nitrogen atom. The increase of bulk on the *N*-substituent in the azetidine ring leads it towards planarity.[6] In N,N-

dialkylsubstituted azetidinium compound the central ring is puckered by 14 ± 1º.[7] Some crystallographic studies supports non-planarity of the azetidine ring.[8,9] On the other hand in 1,1-dibenzyl-3,3-dimethylazetidinium bromide azetidine ring found planar ring.[10] Recently rigid and concave structure of some 2, 4-disubstituted azetidine were also reported.[11] Similarly several studies supported the nonplanarity of the azetidine ring.[12,13] Hence, the X-ray diffraction analysis of azetidines molecule can provide interesting results on the conformational aspects of these heterocycles.

Experimental:

Synthesis and crystallization:

The 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine was synthesized through reaction of 1-(4-toluenesulfonyl)aziridine with corresponding sulfur ylide under microwave irradiation.[14] Its ^{1}H NMR spectra of showed a multiplet for aromatic protons in the range of δ 7.92-6.79 and a singlet for methyl protons of -$SO_2C_6H_4CH_3$-4 tosyl group around δ 2.40. Besides this, one proton triplet with coupling constant 8.0 Hz at δ 4.78, a two protons multiplet in the range of δ 3.83-3.71 and a two protons multiplet in the range of δ 2.33-2.04 was also observed. These signals are due to C2-H, C4-H2 and C3-H2 ring protons of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine respectively. (Figure-1)

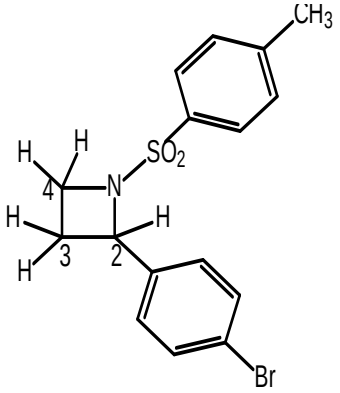


Figure-1 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine

The X-ray diffraction analysis further confirms the geometry of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine. The suitable single crystal of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine was grown by gentle evaporation of its solution (chloroform-hexane). Crystallization was without inclusion of any solvent in its crystal lattice.

Single crystal X-ray data, Refinement and Structure-Solution:

Single crystal X-ray data was collected by the use of *BRUKER AXS SMART-APEX* diffractometer. The diffractometer was furnished with Graphite monochromated Molybdenum K_α radiation (λ = 0.71073 Å) and CCD detector (area). Several frames were collected (ϕ,2θ-rotation and ω) at 10 s per frame. Anisotropic refinement of nonhydrogen atoms were carried out. Full-matrix least-squares calculation on F2 were used for the refinement of measured

intensities. The structure solution and final output-data were recorded with the SHELXTL program.[15-17] The CIF of crystal data has been deposited to Cambridge Crystallographic Data Centre (CCDC) with CCDC number - 762724. These data can be obtained from www.ccdc.cam.ac.uk/structures.

Results and Discussion:

The ORTEP representation of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine shows that azetidine ring is not planar (Figure 2).

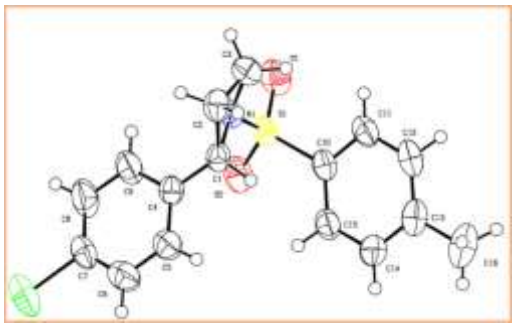


Figure 2: ORTEP diagram of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine

The N-(*p*-toluenesulfonyl) group and C2-(*p*-bromophenyl) ring are oppositely directed from the azetidine ring. This crystal related to monoclinic crystal system and space group P*c*. The bond lengths C-N and C-C in central ring is ~ 1.50 A°. The angle-summation of central four membered ring is 354.72°, which indicates its deformation from perfect square planar geometry and the ring is puckered.

The torsion angle amongst azetidine ring atoms is ≈ 17.50 ± 1.00º (<N1-C1-C2-C3 = -17.58º, <C1-C2-C3-N1 = 16.58º, <C2-C3-N1-C1 = -18.46º and <C3-N1-C1-C2 = 16.52º). The torsion angle of N-(*p*-toluenesulfonyl) group and azetidine ring is 128.12º. The torsion angle of N-(*p*-toluenesulfonyl) group and C2-(*p*-bromophenyl) ring is –83.73º. There are two azetidine molecules in its unit cell packing (Figure 3).

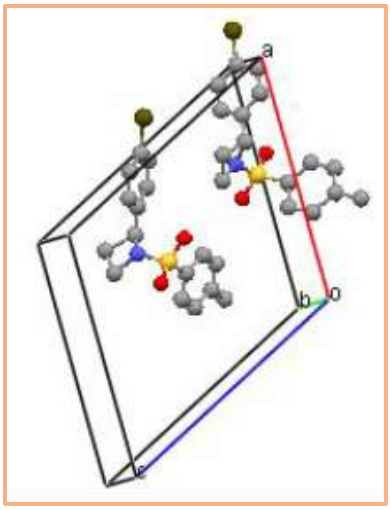


Figure 3: Unit cell packing of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine

Single crystal X-ray diffraction data of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine are shown in table-1 .

Table 1- Single crystal X-ray data of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine

Deposition no.	**CCDC 762724**
Chemical Formula	$C_{16}H_{16}BrNSO_2$
Crystal-System	Monoclinic
Space Group	Pc
a,Å	12.354(3)
b,Å	5.4778(14)
c,Å	13.225(3)
α,degree	90.00
β,degree	116.913(4)
γ,degree	90.00
V, $Å^3$	798.0 (4)
Z, d_{calc}, $g\cdot cm^{-3}$	2, 1.524
Temperature (K)	273(2)
Wavelength (Å)	0.71073
Absorption coefficient (mm^{-1})	2.709

F (000)	372
Single crystal size (mm)	0.424 × 0.167 × 0.110
Total θ range for entire data collection,degree	3.05<θ<26.70
Range of indices	-14<=h<=14
	-6<=k<=6
	-16<=l<=15
No. of collected reflection	2495
No. of unique reflection	1491
Type of absorption correction	Multi Scan
Refinement-methodology	Full-matrix least-squares on F^2
Data / parameters	2855 / 191
Restraints	2
Goodness - fit - F^2	0.963
Final R factor [I>2σ(I)]	0.0304
wR_2 (F^2)	0.0713
R indices (all data) R_1	0.0341
R indices (all data) wR_2	0.0727

Molecular Structure:

The molecular structure of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine is shown in figure-4. The structure depicts the existance of an intermolecular H bond (ArH$^{\cdots}$OSO) of 2.780 Å. It is present between the sulfonyl oxygen and *m*-hydrogen of N-(*p*-toluenesulfonyl) group. The staircase arrangement of the crystal lattice is the result of this intermolecular H bonding interplay.

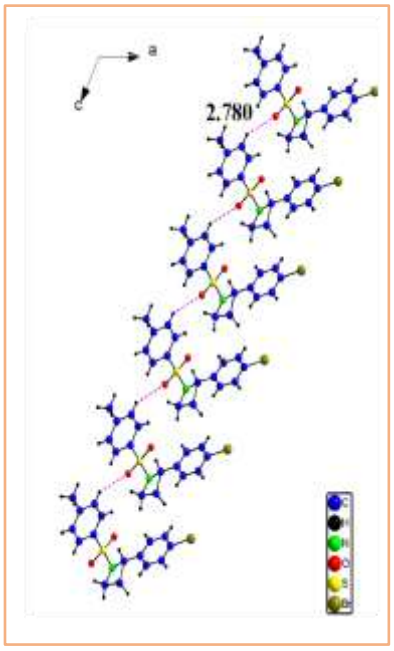


Figure 4: Intermolecular H bond (ArH···OSO) in crystal lattice of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine

In addition, each molecule is also involved in three intermolecular CH···π interactions. The π-electrons of C2-(*p*-bromophenyl) ring interact with C4-proton of azetidine ring and two methyl protons of tosyl group with distances of 3.201 Å, 3.324 Å and 3.738 Å, respectively (Figure 5). All of these interactions lead to the compact packing of crystal lattice.

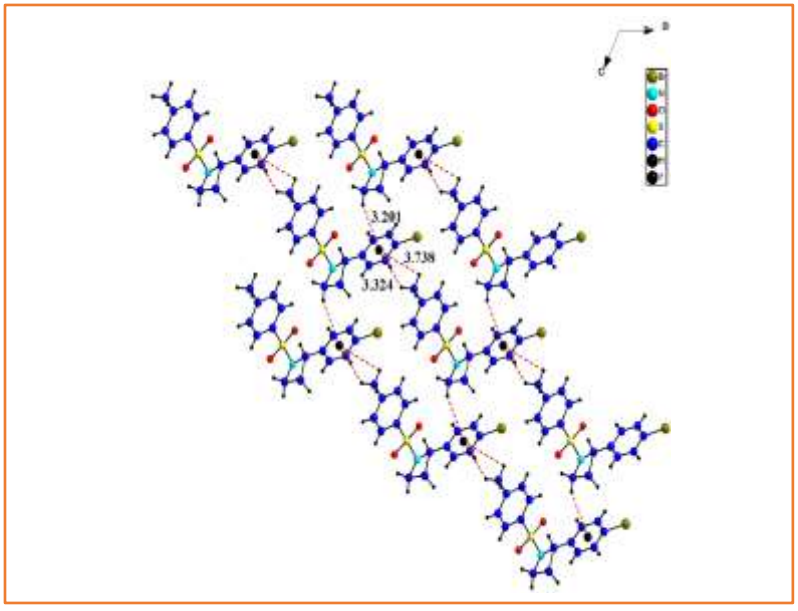


Figure 5: Intermolecular CH···π interactions in crystal lattice of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine

Conclusions:

The ^{1}H NMR and X-ray diffraction-crystallographic studies of 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine reveal that steric effect due to specific ring substituent brings about a non-planar ring conformation to the azetidine ring. Both results are complementing to each other and show similar results. The deviation from planarity for 2-(*p*-bromophenyl)-N-(*p*-toluenesulfonyl)azetidine is 5.28° and torsion angle among azetidine ring atoms are 17.50 ± 1.00°. The non-planarity of the azetidine ring also affect the stereochemical preferences of the attached substituents. The intermolecular CH…π interactions results a tightly packed crystal lattice in the solid state.

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