

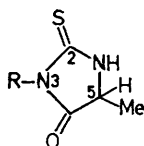
Conformational Preferences in Some Aryl Substituted Heterocyclic Compounds Exhibiting Restricted Internal Rotation About C-N Bonds

By PETER H. BIRD, LAWRENCE D. COLEBROOK,* ALAN R. FRASER, and H. GWYNNE GILES
(Department of Chemistry, Sir George Williams University, Montreal 107, Quebec)

Summary X-Ray studies of the thermodynamically less stable (in solution) diastereoisomeric rotational isomer of 3-(2-bromophenyl)-5-methyl-2-thiohydantoin (II) show that the bromine atom is *transoid* to the 5-methyl group.

Analysis of the equilibration rates yielded the following activation parameters: $\Delta H_{298}^{\ddagger}$ 17.6 ± 1.7 kcal mol⁻¹, $\Delta S_{298}^{\ddagger}$ -25.5 ± 5.2 cal K⁻¹ mol⁻¹, $\Delta G_{298}^{\ddagger}$ 25.2 ± 0.1 kcal mol⁻¹ (90% confidence limits).

We have previously reported¹ that the equilibrium ratio of the diastereoisomeric rotational isomers of the 3-aryl substituted 2-thiohydantoin (I), which exhibits restricted rotation about the aryl C-N bond, is non-unity. This observation has been repeated for a number of other examples of hydantoin and 2-thiohydantoin asymmetrically substituted at C-5.^{2,3}



(I) R = α -naphthyl

(II) R = 2-bromophenyl

We now report an X-ray crystallographic study of one of the diastereoisomeric rotational isomers of 3-(2-bromophenyl)-5-methyl-2-thiohydantoin (II). The barrier to internal rotation in this compound is such that the rotational isomers have high conformational stability at room temperature.

Slow recrystallization from methanol of the isomeric mixture of (II) obtained on synthesis yielded the thermodynamically less stable rotational isomer in > 99% isomeric purity (n.m.r.). The equilibration in pyridine of this isomer was followed over the temperature range 23.5–88.5 °C by repetitively recording the spectrum of the 5-methyl doublets (δ 1.431, J 7.1 Hz for the less stable isomer, δ 1.502, J 7.1 Hz for the more stable isomer) while the sample was maintained at a constant temperature in a 100 MHz n.m.r. spectrometer. At equilibrium, the concentration ratio of the diastereoisomeric rotamers was 1.9 ± 0.1 (90% confidence limits).

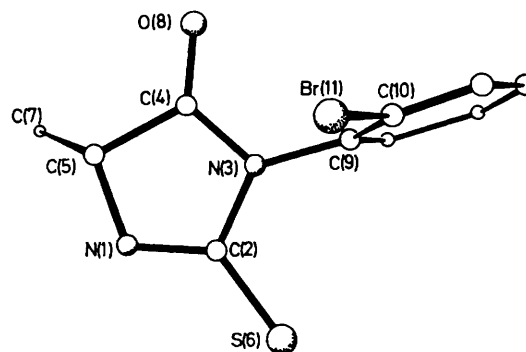


FIGURE. Molecular structure of the thermodynamically less stable rotational isomer of 3-(2-bromophenyl)-5-methyl-2-thiohydantoin.

The thermodynamically less stable (less soluble) rotational diastereomer of (II) crystallizes in orthorhombic space group *Pbca* (No. 61); $a = 10.347(6)$, $b = 19.713(11)$, $c = 11.175(4)$, $Z = 8$. The data, 783 reflections, were phased by the bromine position as determined from a Patterson synthesis. Anisotropic least-squares refinement yielded a discrepancy index of 6.9%. The Figure depicts the molecule as viewed from a direction normal to the plane of the heterocyclic ring. This ring was found to be planar,⁴ to within 0.034 Å, by computation of the least squares plane. The dihedral angle between the heterocyclic and aryl rings is 82°.

Of the factors which have been considered as possible sources of the preference for one rotational diastereomer in solution,¹ two, *viz.*, a puckered heterocyclic ring, and a long-range repulsive interaction between the 5-methyl group and

the bromine atom, do not appear to be significant. In the solid state, the heterocyclic ring is planar, and it is to be expected that in solution this situation will not change significantly. Since the bromine atom lies *transoid* to the methyl group in the less favoured conformation, long range bromine-methyl interactions cannot be important.

The evidence suggests that, in solution, the steric effect of the 5-methyl group is transmitted to the bromine atom *via* an unsymmetrical solvent shell around the carbonyl and the thiocarbonyl groups. Solvation should be favoured on

the less hindered side of the hetero-ring, *i.e.* *transoid* to the 5-methyl group. In the preferred rotational isomer, which should be the more highly solvated, the bromine atom would be *transoid* to the solvent shell and hence *cisoid* to the 5-methyl group.

This work was supported by the National Research Council of Canada. A.R.F. acknowledges receipt of a 1967 Science Scholarship.

(Received, 15th October 1973; Com. 1409.)

¹ W. E. Bentz, L. D. Colebrook, and J. R. Fehlner, *Chem. Comm.*, 1970, 974.

² L. D. Colebrook, H. G. Giles, and A. Rosowsky, *Tetrahedron Letters*, 1972, 5239.

³ L. D. Colebrook, H. G. Giles, A. Granata, S. Icli, and J. R. Fehlner, *Canad. J. Chem.*, 1973, **51**, 3635.

⁴ Planar heterocyclic rings have also been found in 2-thiohydantoin and 5,5-diphenylhydantoin: L. A. Walker, K. Folting, and L. L. Merritt, *Acta Cryst.*, 1969, **B25**, 88, and A. Camerman and N. Camerman, *ibid.*, 1971, **B27**, 2205.