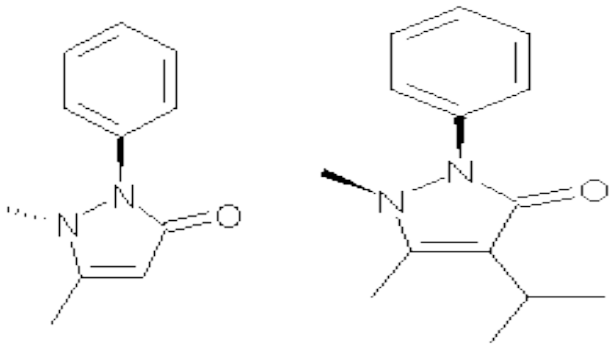
CONFORMATION OF PROPYPHENAZONE

Compounds like antipyrine **1** might be expected to have two pyramidal nitrogens with their substituents on opposite sides of the ring. Interestingly, a new polymorph of propyphenazone **2** has both *N*-methyl and *N*-phenyl groups on the same side of the ring. Just how unusual is this?



1 **2**

Roumanos and Kertesz[1] have sampled the crystallographic database and found 334 structures with the antipyrine backbone.

The vast majority of them have the nitrogen substituents on opposite sides, and a few structures have these groups essential co-planar with the ring. The new propyphenazone structure does seem to be unusual. However, they also performed a BLYP/DNP scan of the potential energy surface of **2**. When this surface is overlayed on the distribution of the x-ray structures, one sees that most structures are within 3 kcal mol^{-1} of the energy minimum (with the nitrogen groups on opposite sides). However, the structure with both groups on the same side is about 4 kcal mol^{-1} higher in energy than the minimum energy structure, and the nearly planar structures are higher in energy still. Thus, the authors conclude that while this new structure is unusual, it is *not* an outlier.

Source: http://comporgchem.com/blog/?p=1568