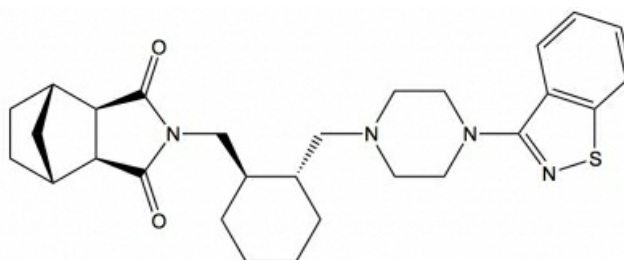


*A low-temperature phase transition in crystals of the API Lurasidone*Anthony Linden¹, Marina Ratkaj²¹Department of Chemistry, University of Zurich, Zurich, Switzerland, ²Pliva Croatia Ltd, Zagreb, Croatia
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Lurasidone is an API approved in 2013 for the treatment of schizophrenia and depressive episodes associated with bipolar I disorder. It is administered as its HCl salt. During work to confirm the absolute configuration of the Lurasidone molecule, it was discovered that a single crystal of the neutral base undergoes a reversible phase transition between room temperature and 160 K. The phase transition was induced several times in the one crystal without detriment to the crystal. Data collections at intervals of 5 K descending from 260 K with approximately four hours between steps suggest that the transition is sluggish. The transition begins near 250 K and is still not quite complete by 160 K. A crystal at room temperature fully transforms immediately if shock-cooled to 160 K. The structure determination at 260 K for the high-temperature phase (I) is completely routine: orthorhombic $P2_12_12_1$ with $Z' = 1$, $R = 0.028$ and no evidence of disorder or twinning. For the shock-cooled crystal at 160 K, the low-temperature phase (II) is monoclinic, $P2_1$ with $Z' = 2$ and twinned through a two-fold rotation about $[100]$. The unit dimensions are almost identical to those of phase (I) at 260 K, allowing for slight thermal shrinkage, and the β angle is almost exactly 90° , so automated diffractometer procedures assign the unit cell as orthorhombic and trouble for the unwary can start there. A surprisingly low R_{int} and feasible solution is obtained in $P2_12_12_1$, which might further convince one that the phase (II) crystal system is orthorhombic, but R remains above 0.16 and the systematic absences are clearly inconsistent with this space group, suggesting $P2_12_2$. No solution is found in this latter space group. Therefore, the logical next step is to try the lower symmetry space group $P2_1$. In $P2_1$, the phase (II) structure refines well with $Z' = 2$, but R is still 0.15. Introducing the twin law reduced R to 0.027, with an absolute structure parameter of 0.005(3). In the presentation, the packing of the structures of the two phases will be compared and the results of further evaluations of the phase transition behaviour will be presented.



Keywords: [phase transition](#), [active pharmaceutical ingredient](#), [Lurasidone](#)