ESRF	**Experiment title:** Structure determination of compounds of pharmaceutical interest by powder diffraction	**Experiment number:** CH-334
Beamline: BM16	**Date of experiment:** from: Oct '97 to:	**Date of report:** 25/2/98
Shifts: 9	**Local contact(s):** Andy Fitch	*Received at ESRF:* 04 MAR. 1998

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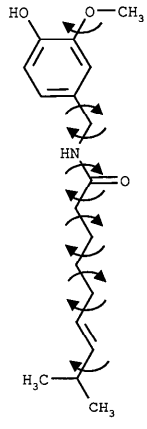
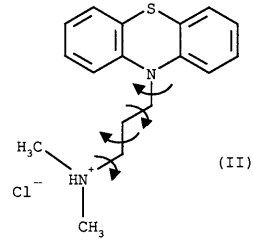
Report:

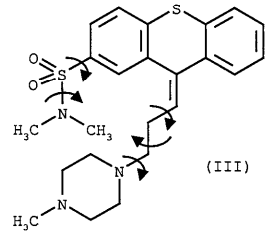
X-ray diffraction data were collected for the following conformationally flexible compounds and their previously unknown crystal structures solved as outlined below.



(I)



(II)

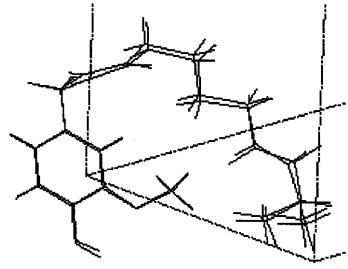


(III)

The position, orientation and conformation of an entire molecule in the refined unit cell were postulated and the level of agreement between the trial structure and the experimental diffraction data quantified by:

$$\chi^2 = \sum_h \sum_k [(I_h - c|F_h|^2)(V^{-1})_{hk}(I_k - c|F_k|^2)]$$

where I_h and I_k are Lorentz-polarisation corrected, extracted integrated intensities from a Pawley refinement of the diffraction pattern, V_{hk} is the covariance matrix from the Pawley refinement, c is a scale factor, and $|F_h|$ and $|F_k|$ are the structure factor magnitudes calculated from the trial structure. The trial structure was subjected to a global optimisation in which torsion angles were the only internal degrees of freedom and bounds on the external degrees of freedom (three fractional coordinates for position and four quaternions for orientation) were derived from the Euclidean normalisers of the relevant space groups. Finally the structure solutions were verified by Rietveld refinement of the fractional coordinates obtained at the end of the simulated annealing runs. Structure solutions were obtained with ease for all three compounds. In particular, the structure solution of capsaicin, which posseses 10 internal degrees of freedom, is outstanding. It is shown below superimposed upon a single crystal structure solution determined subsequently in order to verify the powder solution. This shows clearly that the simulated annealing algorithm has the ability to solve highly flexible structures to a high degree of accuracy. Equally impressive is the fact that the solution was obtained in only -30 hours of computing time on a Digital Alphastation.



The structure solutions of these three compounds have been submitted to ***Chem Comm.***