

**AB INITIO CRYSTAL STRUCTURE DETERMINATION OF TWO
POLYMORPHIC MODIFICATIONS OF AN ANESTHETIC AGENT,
TETRACAINE HYDROCHLORIDE, USING A COMBINATION OF
MOLECULAR MODELING AND SYNCHROTRON X-RAY POWDER
DIFFRACTION TECHNIQUES**

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ABSTRACT

The crystal structure determination of leocaine, a polymorphic modification of tetracaine hydrochloride (TCHC) obtained from the latter by freeze-drying and US-patented in 1995, is reported for the first time. Both leocaine and TCHC are potent ophthalmic anesthetic drugs.

Key to this crystallographic structural determination is the joint use of molecular modeling, state-of-the-art X-ray powder diffraction software [EXPO2009 / N-TREOR09 for indexing, FOX for structure solution] and synchrotron radiation. Whereas TCHC crystallizes in a triclinic spacegroup [P-1, Z=2] (Nowell et al, NJC, 2002), leocaine is found to be compatible with a monoclinic unit cell [P2₁/c, Z=4].

Two different forms (A,B) of leocaine are in fact observed, associated with distinct powder patterns and unit cells. Similarly to TCHC, both intra- and inter- molecular H-bonds are found to be present in either polymorphic modification A or B