carboxylate motif alternating with the ammonium motif. Additional strings and other concerted hydrogen bond motifs are also present. *Crystal data*: $2(C_4H_{10}NO_2^+):(C_2O_4^{2-})$, M_w = 296.28 Daltons; monoclinic, $P2_1/c$; a = 7.4153(9), b = 10.2052(13), c = 9.7584(12) A, β = 108.396(3)°, V = 700.72(15) A^3; Z = 2; T = 298 K; θ_{max} = 26.4°; R_1 = 0.0482 for 939 reflns, $I_o > 2\sigma(I_o)$, ρ_{max} = 0.18 e A^{-3}.

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Keywords: cocrystals, organic phamaceutical, GABA

MS53.P20

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A new polymorph of halothane: An *in-situ* cryo-crystallographic study

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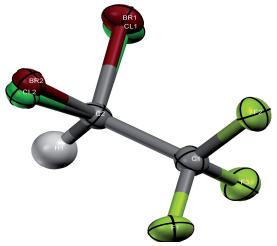
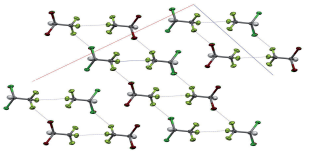
In-situ cryo-crystallographic techniques have been successfully applied to the determination of the crystal structures of compounds which are liquids at room temperature. It has become possible, using this approach to analyze intermolecular interactions of molecular species without the involvement of solvent either as a promoter for crystal growth or as incorporated solvatomorph [1]. 2-bromo-2-chloro-1,1,1-trifluoroethane (Halothane) is a clinically used anesthetic, which has been studied earlier by in situ pressure frozen method using a diamond anvil setup. The crystals were found to belong to triclinic (space group *P*-1) system [2]. The crystals generated in our experiment belong to a monoclinic system (space group *C*2/*c*) with *a* = 18.6626(1) Å, *b* = 4.5759(1) Å, *c* = 12.4030(2) Å, *β* =91.85°, and *V*=1058.59(12) Å^3, thus generates a new polymorphic form. In this structure the bromine and chlorine atoms are substitutionally disordered similar to that found in the in situ pressure frozen polymorph and the occupancies of bromine and chlorine at each site refine to 52:48 ratio. The packing is through several F….F and Cl/Br….F contacts resulting in tetrameric units as shown below.



Halothane structure
(50% Thermal ellipsoid)



Packing shows the tetramer formation in Halothane

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Keywords: cryo-crystallography, polymorphism, disorder

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Supramolecular chemistry of Anti-HIV nucleoside drugs: Toward smart crystal phases and self-assembled DNA-mimicries

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Multicomponent molecular crystals have been widely screened for several classes of APIs, including the anti-HIV drugs. Lamivudine (β-L-2',3'-dideoxy-3'-thiacytidine, 3TC) and didanosine (2',3'-dideoxyinosine, ddI) are two of the most used NTRIs in anti-HIV therapy. Here, we used a rational strategy to design a $P2_12_12_1$ orthorhombic structure of lamivudine with maleic acid on the basis of lamivudine saccharinate [1]. Likewise, based on the capability of pairing between neutral and protonated lamivudine in the cocrystal of the drug with 3,5-dinitrosalicylate [2], a helical structure in which lamivudine is self-assembled into a DNA-like duplex without phosphodiester linkages was prepared. Crystals of ddI were also prepared using solvothermal techniques and the solid state structure of this drug was solved for the first time.

Chemical aspects of salt formers and crystal assembly features were taken into account for selection of maleic acid in order to assemble into a predicted $P2_12_12_1$ orthorhombic structure with lamivudine. Acid-ionization constant, arrangement of hydrogen bonding functionalities and conformational features were considered for selection of the salt former. A rationally designed crystal preparation and the establishment of structure-property relationships were some advantages of this strategy.

The assembly of the lamivudine double helix structure consists of an interesting example of spontaneous molecular self-organization. Stacking and hydrogen bonding interactions between the cytosine bases of lamivudine were the decisive forces responsible for this structural organization in which alternating neutral and protonated lamivudine conformers are placed into each helical strand. Other contacts such as hydrogen bonds involving duplex-duplex, duplex-anions (chloride and maleate) and duplex-water interactions were also important for the molecular assembly.

Concerning ddI, the pharmaceutical solid state form of the drug has a structure equal to that of the solvothermally prepared ddI crystals described here, while they do not exhibit an identical chemical composition due to different water fraction occupying hydrophobic channels assembled within the crystals. The two crystallographic ddI conformers were in agreement with previous structural elucidation based on solid state NMR techniques [7].

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Keywords: polymorphism, lamivudine, didanosine

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Probing gels as a media for the growth of co-crystals

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