Synthesis, crystal structure and theoretical studies of N^1-substituted 5-X-uracil (X = F, H) ligands.

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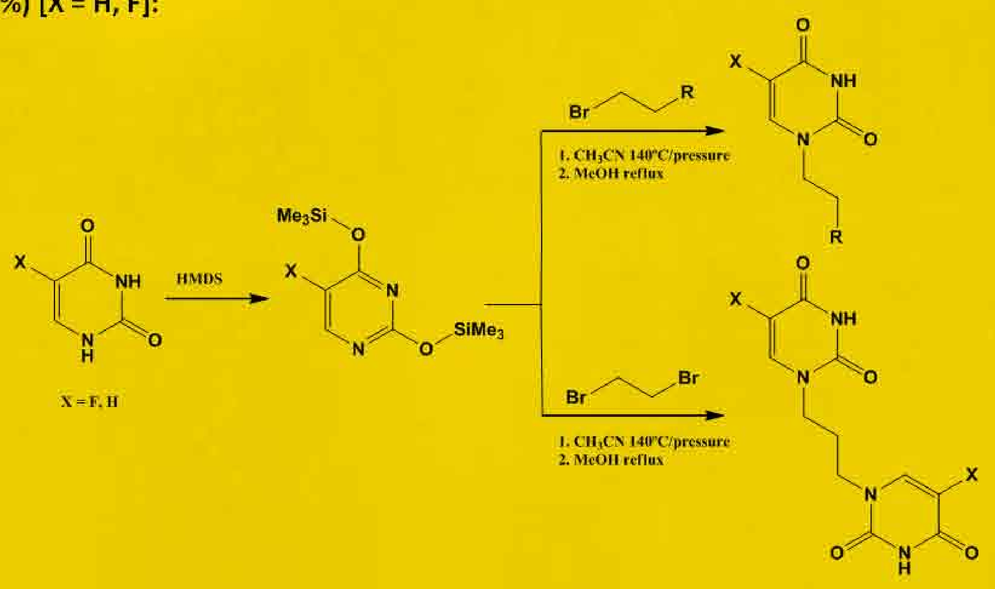
Introduction

To improve the currents models used in coordination chemistry studies of pyrimidine nucleobases, we have synthesized N^1-substituted derivatives of uracil and 5-fluorouracil. By reaction between bis-trimethylsilyloxy-pyrimidine and n-bromoalcane (or α,ω-dibromoalcane) under pressure and temperature, we have obtained, in good yields, ω-functionalized N^1-alkyl-5-X-uracils (*ca.* 60%) and also N^1,$N^{1'}$-polymethylen-bis-(5-X-uracils) (*ca.* 30%) [X = H, F]:

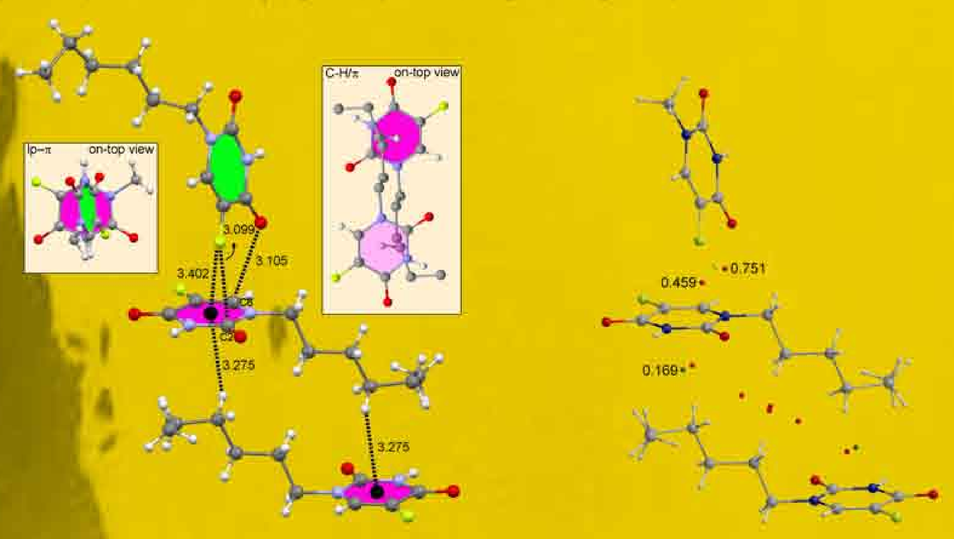


These products also permit us to study the kind of recognition patterns presents in their structures and to compare the different modes of interaction which direct the formation of adducts in the presence or absence of a fluorine atom.

Theoretical studies

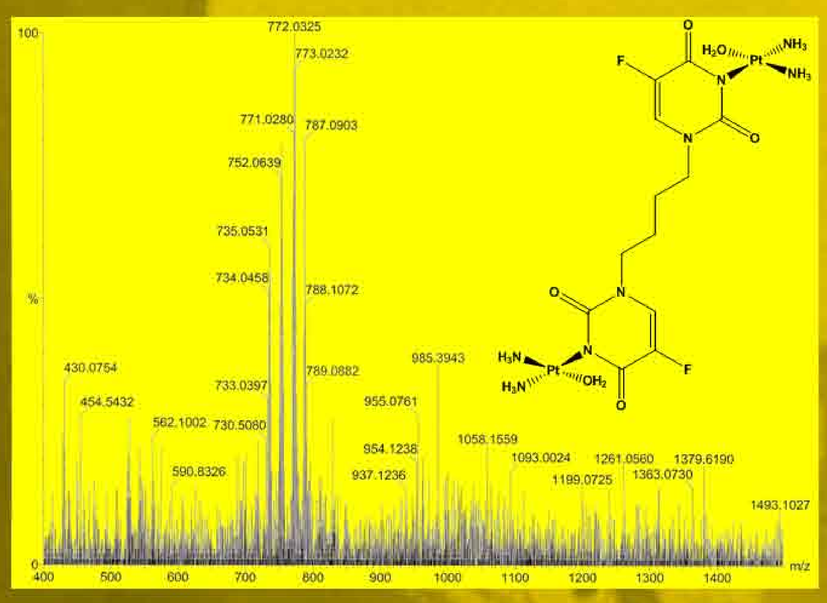
We have studied the noncovalent interactions which are present in the crystal structures and we have used MP2 calculation and the Bader's theory of "atoms in molecules" to estimate the interaction energies of several crystallographic fragments and to evaluate the cooperativity effects between them.

The left side picture (below) represents a partial view of the crystal structure of N^1-hexyl-5-fluorouracil with the lone pair (lp)-π and π-π interactions marked on it. The right side one (below), corresponds to a schematic view of the calculated critical points (bon CPs, red; ring CPs, yellow; cage CPs, green).



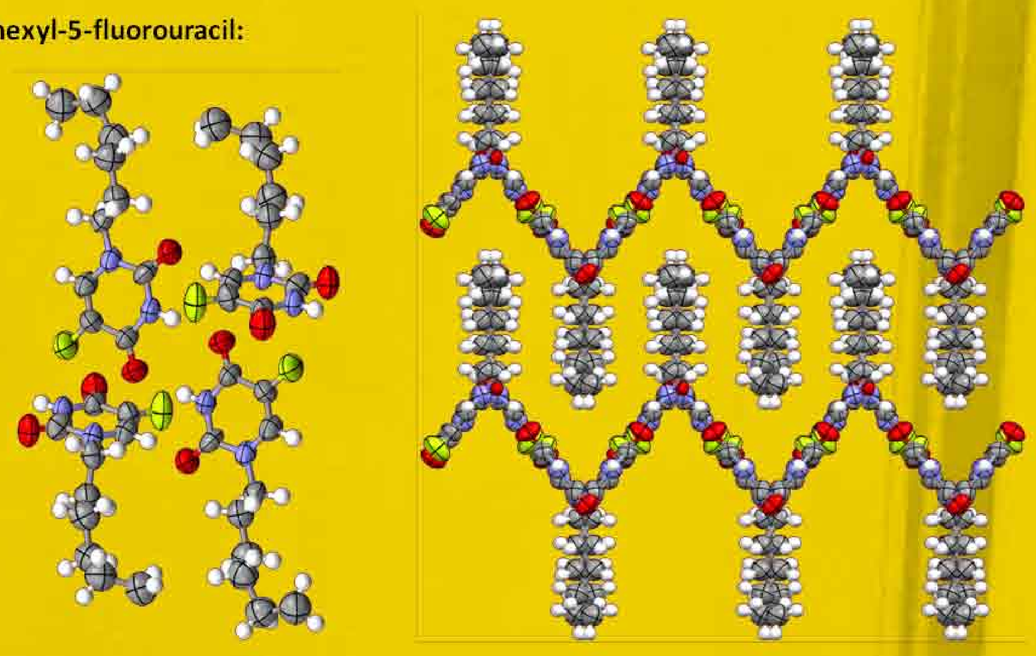
Coordination capabilities

Preliminary studies related to the coordination capabilities of these compounds, show the complexation between one molecule of N^1,$N^{1'}$-tetramethylen-bis-(5-fluorouracil) and two cisplatin moieties [M]. ESI-HRMS: [M-H_3O^+] (calc. m/Z, 787.1055); [M-H_3O^+-NH_3] (calc. m/Z, 770.0789); [M-H_3O^+-NH_3-H_2O] (calc. m/Z, 752.4686); and [M-H_3O^+-$2NH_3$-H_2O] (calc. m/Z, 735.0418).

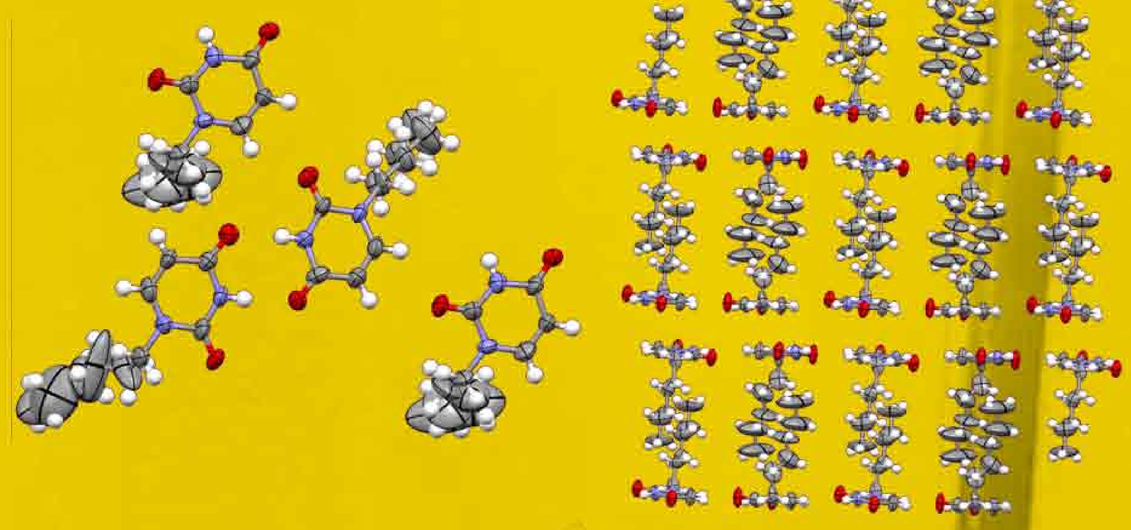


X-ray structures

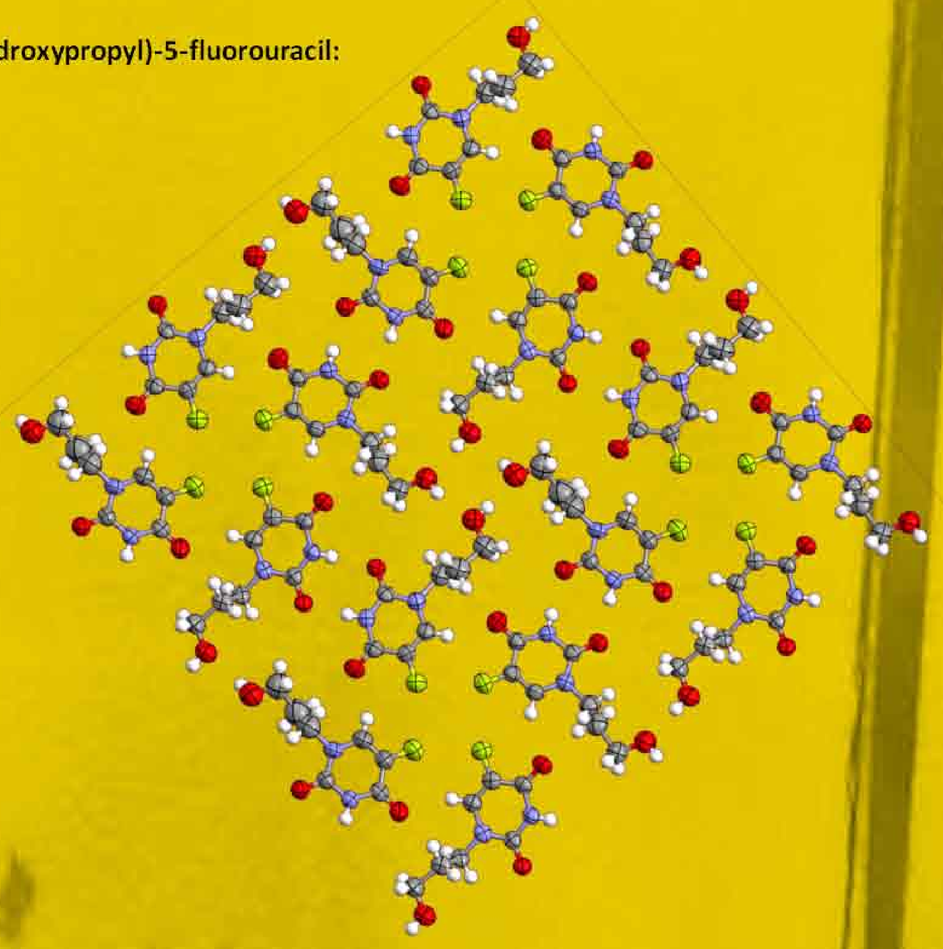
N^1-hexyl-5-fluorouracil:



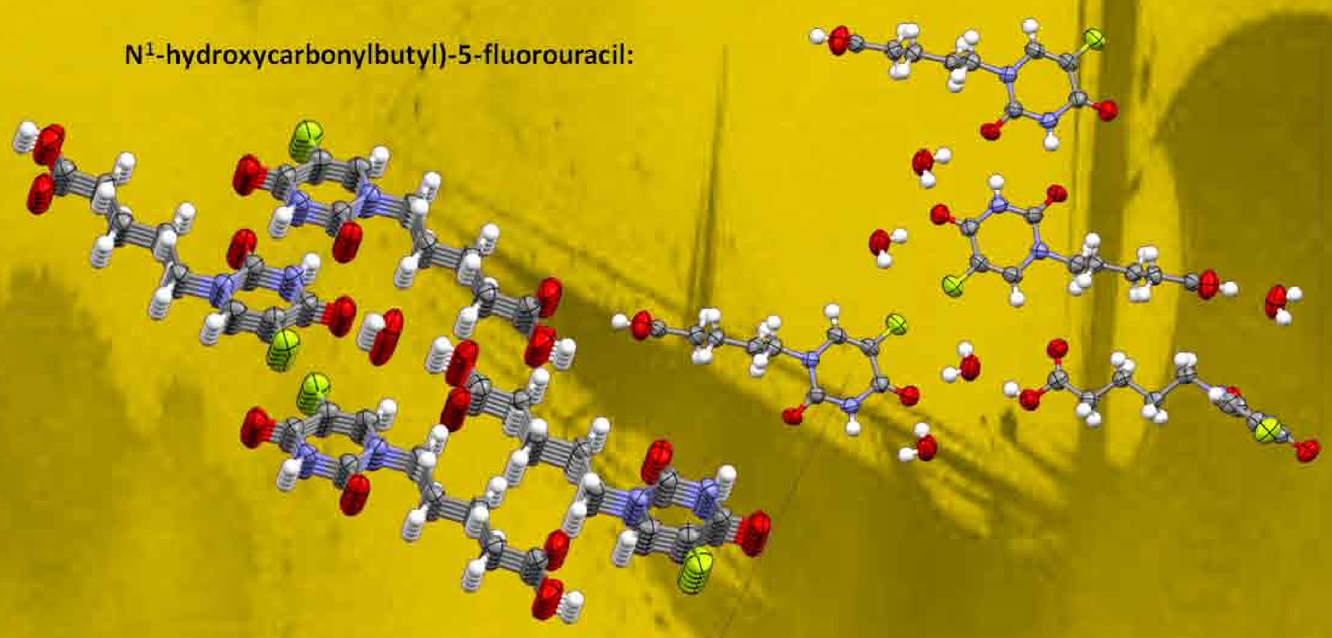
N^1-hexyluracil:



N^1-(3-hydroxypropyl)-5-fluorouracil:



N^1-hydroxycarbonylbutyl)-5-fluorouracil:



Acknowledgments

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