**PS05.01.20 IMIDAZOLE AND TETRAZOLE AS LIGANDS FOR CALCIUM AND MAGNESIUM.** Drake S. Eggleston, R. Curtis Haltiwanger, Dana Sherman, Lisa Garber, SmithKline Beecham Pharmaceuticals, 709 Swedeland Road, King of Prussia PA 19406 USA

With an eye toward the potential utility of such heterocycles as components of molecules with pharmacological action we have prepared and characterized structurally a number of Mg(II) and Ca(II) complexes with neutral imidazoles or ionized tetrazole in the primary coordination sphere. A desire to understand the roles of the group IIa metal ions Mg(II) and Ca(II) in biological processes and biomolecular structure stabilization has prompted many previous investigations into the nature and extent of their coordination environment(s). Magnesium always exhibits octahedral coordination while Ca(II) can easily expand its coordination sphere[1]. Based on observations from biological systems it is also generally accepted that oxygen containing ligands present a preferred coordination milieu for both ions, consistent with hard-soft acid-base theory. In a majority of Mg(II) binding sites one or more protein carboxylate ligand(s) are found coordinated, with oxygen(s) from backbone carbonyl or alcohol groups also heavily represented. Histidine nitrogen has been reported once as a Mg(II) ligand[2], but apparently no such examples with Ca(II) are known. Small molecule crystal structure data provides a corroborating view of preferred ligands; ie. there is only a single example of magnesium[3] or calcium[4] structures with an imidazole (a model for histidine residues in proteins) ligand. Further database examination suggests, however, sufficient general potential for imino-type ($sp^2$) nitrogen coordination to both metals with energetically favorable interactions. To examine the possibilities further, complexes containing neutral imidazole, N-methyl imidazole, 2-methyl imidazole, imidazole acetic acid or ionized tetrazole ligands for Mg(II) and Ca(II) have been isolated and studied.

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**PS05.01.21 SULFAMATE ANTICONVULSANTS: STUCTURE AND FUNCTION.** P.W. Codding, S.A. Litster, M. Kubicki, M.B. Szkaradzinska, and H.A.R. Bassyouini, Departments of Chemistry and Pharmacology and Therapeutics, University of Calgary, Calgary, Alberta T2N 1N4, Canada

Studies of novel sulfamate anticonvulsant drugs developed by E.B. Maryanoff1 show that activity correlates with a skew conformation of the central ring and an extended conformation of the sulfonamide side chain. Additionally, the crystal structures of active compounds demonstrate unique hydrogen bonding networks. Clinical trials of compound **1** (topiramate) it is effective against partial-onset seizures. We have determined the crystal structures of six related compounds; conformational, graph set and modeling analysis of these data will be presented. Compound **1**: (topiramate) 2,3:4,5-bis-O-(1-methylethylidene)-b-D-fructopyranose sulfamate, Compound **2**: 4,5-O-cyclohexylidene-2,3-O-(1-methylethylidene)-6-D- fructopyranose sulfamate, Compound **3**: 2,3-O-(1-methylethylidene)-b-D-fructopyranose sulfamate, Compound **4**: 1,2:3,4-bis-O-(1-methylethylidene)-a-D-galactopyranose sulfamate, Compound **5**: 1,2,3,4,-Tetrahydro-2-naphthalenyl methyl sulfamic acid ester, Compound **6**: 1,4 benzodioxin-2-(3H) methyl; sulfamic acid ester.

1 E.B. Maryanoff, The R.W. Johnson Pharmaceutical Research Institute.

## Peptides

**PS05.02.01 COORDINATION OF LITHIUM TO AMINO ACIDS AND DIPEPTIDES.** Gerd-Michael Maier, Gerhard Müller, Martin Lutz, Fakultät für Chemie der Universität Konstanz, Universitätsstr. 10, D-78464 Konstanz, Germany,
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The coordination of $Li^+$ to neutral (zwitterionic) and deprotonated (anionic) amino acids and dipeptides was investigated in the solid state. The results of structure determinations on 7 amino acid complexes and 13 dipeptide complexes may be summarized as follows:

Lithium is always tetrahedrally coordinated. The coordinating atoms are predominantly carboxylate and keto oxygen atoms as well as amino N atoms. In some cases additional coordination by solvent molecules is found. A chelating coordination mode of the ligands is never observed. The donor strength of the ligating atoms towards $Li^+$ in these complexes is approximately

$Li^+$ complexes of neutral amino acids and dipeptides:
$-COO^- >> H_2O > -C(O)NH- > H\text{-}O\text{-}R$

$Li^+$ complexes of anionic amino acids and dipeptides:
$-COO^- >> -NH_2 > -C(O)NH- > H_2O > H\text{-}O\text{-}R$

The carboxylate groups are coordinated to one, two or three $Li^+$ counterions, respectively. In the crystal the coordination polymers form strands, sheets, or threedimensional networks of $Li^+$ and the ligands with extensive hydrogen bonding between the latter which may include solvent molecules.

The results allow the conclusion that the $Li^+$ ligand interaction in these complexes may be compared to hydrogen bonds what regards their structural properties and probably also their energetics.

**PS05.02.02 L-VALYL-L-GLUTAMINE AND L-GLUTAMYL-L-VALINE.** Carl Henrik Gorbitz and Paul Hoff Backe, Department of Chemistry, University of Oslo, PO.Box 1033 Blindern, N-0315 Oslo, Norway.

The structure of L-Val-L-Glu [Eggleston, (1984). Acta Cryst. C40, 1250-1252] has a crystal packing arrangement and H-bond pattern rather similar to L-Val-L-Gln, but radically different from L-Glu-L-Val, which contains the same amino acid residues in reversed order. Nevertheless, the specific hydrogen bond interactions are almost identical for L-Val-L-Glu and L-Glu-L-Val, indicating very distinct hydrogen bonding preferences. This is the first demonstration of such a coincidence among dipeptide structures.

The differences between L-Val-L-Glu and L-Val-L-Gln structures stem from modifications of the molecular geometry and cell parameters due to formation of an additional hydrogen bond from the extra donor in the L-Gln side chain.

Both molecular geometries are normal, except for a unique eclipsed orientation of the main chain amino group of L-Glu-L-Val.

Crystal data and refinement Both data sets were collected on a Nicolet P3 diffractometer at 120 K.
L-Val-L-Gln: Space group $P2_12_12$, a= 16.419(3), b = 15.309(3) and c = 4.708(1)Å, final $wR(F_o^2)$ = 0.100 for 2044 independent reflections, $R(F_o)$ = 0.050 for 1475 refl. with $I > 2.0\sigma(I)$.
L-Glu-L-Val: Space group $P2_1$, a = 6.487(2), b = 5.505(2), c = 16.741(4) Å and ß= 97.22(2)°, final $wR(F_o^2)$ = 0.111 for 1920 independent reflections, $R(F_o)$ = 0.047 for 1576 refl. with $I > 2.0\sigma(I)$.