Solid state studies of drugs and chemicals by dielectric and calorimetric analysis

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Anthracene has a highly conjugated polar fused aromatic ring system and some noteworthy properties in its solid state, during its pre-melt temperatures. It has been observed to form excimers, excited molecules as dimers, in the solid state and to continue this formation into the amorphous liquid phase. Examination of drugs and other crystalline solids, like amino acids, (Arginine & Histidine) Carbohydrates (Dextrose), Proteins (Cytochrom C), drugs and organic chemicals (Naphthalene), by Dielectric Analysis (DEA) also discovered a linear electrical conductivity in the pre-melt temperatures through to the melt as determined by DSC. The DEA activation energy (Ea) can be calculated from the slope of plots of log conductivity vs. the reciprocal temperature in Kelvin, which had a typical correlation coefficient of 0.96-0.99. The DSC and TMA defined the temperature range for melting of the solids. We further observed linear DEA electrical conductivity from below the melt temperature of a number of pure drugs well into their liquid amorphous phase. The Ea for the pre-melt charge complex for Sulfapyridine was 950 J/mole, for Acetophenetidin 1300 J/mole and for caffeine 320 J/mole. The Ea is frequency dependent and related to the degree of amorphous content in the solids. Active Pharmacy Ingredients (APIs) with known enhanced conductivity behavior include Lidocaine, Acetanilide, Carbamazepine, Nifedipine and Tolbutamide. It is our observation that the APIs studied form charged molecules as complexes just before melting. We have measured unique electrical properties of a number of pharmaceutical solids which have thermally induced “dielectric viscoelastic properties” as charge transfer complexes in the solid state. DEA and DSC studies revealed new properties in solids which will lead to new synthesis routes for drugs, chemicals, and amino acids. DEA has been used to study the electrical conductivity profile at 10^{o}C/min in nitrogen which focuses on pre-melt physical properties and transition temperatures. This has also been used to study activation energy and the effect of AC frequency on electrical conductivity and activation energy. DSC was used to study heat of fusion and heat of recrystallization which gave us a better profile of the chemicals solid state properties. Overlaying DEA and DSC melting transitions for the materials highlights solid state DEA properties. Conductivity variations from 10^{-2} to 10^{7}pS/cm i.e. a nine fold increase in electrical conductivity was detected by Dielectric measurements.

TABLE: 1 Activation energies of various chemicals calculated from Arrhenius plot.

Chemical Type	Ea (J/m at 1.0 Hz)
Organic -Anthracene	800
Organic -Naphthalene	35
Drug-Sulfapyridine	950
Drug-Lidocaine	60
Drug-Caffeine	320
Drug-Acetophenetidin	1300
Carbohydrate-Dextrose	180
Amino Acid-Arginine	340
Amino Acid-Histidine	350

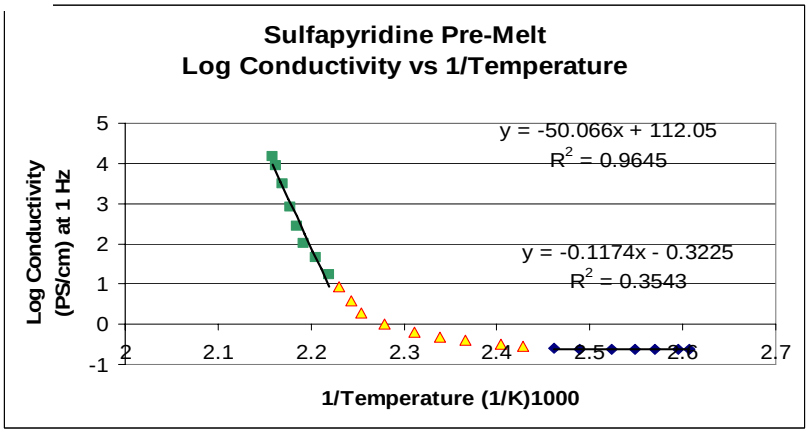

FIGURE: 1 Arrhenius plot for DEA study of Sulfapyridine at 1.0 Hz