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NOVEL AROMATIC LACTONES FROM DIHYDROCOUMARIN THROUGH ELECTROPHILIC HETEROATOM CYCLIZATION

Dihydrocoumarin was converted to some novel medium ring aromatic lactones through iodocyclization reactions of the hydroxy allyl-ester derivatives. Products of *endo*- and *exo*-cyclizations were obtained in very good yields but with poor selectivity. The cyclization process is believed to be enhanced by two factors: a positive oxygen effect and the presence of a rigid ring system.

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UTILIZING STRUCTURE PROPERTY CORRELATIONS TO PREDICT AND ANALYZE TWO DERIVATIVES OF AN AMPICILLIN HOMOLOGOUS SERIES

Structure Property Correlation methods such as regression analysis and pattern recognition are applied to predict the molecular properties of two members of an ampicillin homologous series. The pentyl and hexyl esters of ampicillin are also evaluated for their similarity to other penicillins by use of multiple regression, contingency tables, cluster analysis, correspondence analysis, self organizing tree algorithms, factor analysis, principal component analysis, box plots, and other graphing methods. Other members of the homologous series include methyl, ethyl, propyl, and butyl esters of ampicillin which have been previously synthesized and tested in tissue culture against *Escherichia coli*. All of the tested esters of ampicillin significantly inhibited penicillin susceptible and ampicillin resistant bacteria, as well as streptomycin resistant bacteria. Drug homologous series has been observed with other antibiotics and medicinal compounds. Homologous series activity is a trend observed for ampicillin by graphing the reciprocal equi-effective concentrations versus the number of carbons comprising the ester group. Regression analysis and contingency tables predict the molecular properties of the hexyl and pentyl esters, while cluster analysis, factor analysis, correspondence analysis, principal component analysis, and tree algorithms correlate them to the parent ampicillin and other members of the β-lactam class of antibiotics. This work demonstrates the effectiveness of applying numerical analysis methods to drug design and development.

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CRYSTALLIZATION KINETICS OF CYCLOALKANONE THIN-FILMS ON Al_2O_3 (0001)

The crystallization kinetics of several cycloalkanones as adlayers on an Al_2O_3 surface were investigated by monitoring the phosphorescence emission. The Kolmogorov-Johnson-Mehl-Avrami (KJMA) model for nucleation and crystallization was used to simulate the observed changes in the intensity of the emission from the adlayer as the surface was heated. For cyclobutanone, the Avrami exponent for these adlayer molecules indicated pre-determined nucleation due to defect sites on the Al_2O_3, followed by two-dimensional growth in the crystal. For cyclopentanone, the dimensionality was almost unity, perhaps indicative of more needle-like growth. For cyclohexanone, the dimensionality of growth was mixed. When the surface was heated, crystallization occurred almost one-dimensionally, and when the surface was cooled, growth was more two-dimensional. The rates of crystallization were also determined from the KJMA equation. In general, two-dimensional crystal growth was less temperature dependent when compared to growth that took place with a smaller dimensionality.

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PREDICTIVE MODELING OF CHEMICAL REACTIONS

We have used readily available desktop molecular modeling software to model the outcomes of a variety of chemical reactions. Geometries of the reactant molecules are separately optimized, and the molecules are given an initial orientation that might correspond to a reactive collision. Geometry optimization is then run on the assembly. Application of this procedure with a low level *ab initio* Hamiltonian has replicated the correct products and relative reactivities for the reduction of hydroquinone by various alkylammonia borane complexes. Application of this method to larger systems involving chiral catalysis, with the use of a semi-empirical Hamiltonian, gives the correct products and also reproduces the enantioselectivity of these reactions; these results will be reported at a later time.

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A CONFORMATIONAL SEARCH AND CALCULATION OF THE CIRCULAR DICHROIC SPECTRUM OF THE FLEXIBLE PEPTIDE CYLCO(GLY-PRO-GLY)$_2$ USING THE DIPOLE INTERACTION MODEL

A backbone conformational search of cyclo(Gly-L-Pro-Gly)$_2$ began with a conformational search of linear structures using molecular mechanics. These structures were edited to be cyclic and minimized again. Minimizations employed different means of including the solvent. Boltzmann weighting factors were created based on the minimized energies. The structures that received significant weighting factors in molecular mechanics were then optimized by AM1 (semi-empirical quantum mechanics). Prediction of the UV $\pi-\pi^*$ circular dichroic spectrum was calculated with the dipole interaction model exploring the use of parameters. Agreement with experiment could be achieved for ensembles optimized in with a constant dielectric, the solvent dielectric (32.82) and a dielectric of 1, or with explicit solvent (methanol). The dipole interaction model successfully weeds out poor geometries, and demonstrates how very flexible cyclo(Gly-L-Pro-Gly)$_2$ is in solution suggesting that structures can interconvert between β- and γ-turns easily.

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SYNTHESIS OF BENZYLIDENEPHTHALIDE DERIVATIVES

A series of simple aromatic analogs of 3-benzylidenephthalide have been synthesized from phthalide and the requisite functionalized benzaldehydes. The *Z*-isomer was the predominant isomer for the majority of compounds synthesized, with two analogs providing exclusively the *Z*-isomer, and two analogs affording the *E*-isomer as the major product.

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