[*J. Biol. Chem.*, **276**, 2686-2692 (2001)] [Lab. of Pharm. Chemistry]

Blockade of the Extracellular Signal-regulated Kinase Pathway Induces Marked G_1 Cell Cycle Arrest and Apoptosis in Tumor Cells in Which the Pathway Is Constitutively Activated.

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Constitutive activation of the ERK pathway is associated with the neoplastic phenotype of a relatively large number of human tumor cells. Blockade of the ERK pathway by treatment with PD98059, a specific inhibitor of mitogen-activatied protein (MAP) kinase/ERK kinase (MEK), completely suppressed the growth of tumor cells in which the pathway is constitutively activated (RPMI-SE and HT1080 cells). Consistent with its prominent anti-proliferative effect, PD98059 induced a remarkable G_1 cell cycle arrest, followed by a modest apoptotic response, in these tumor cells. Selective up-regulation of $p27^{Kip1}$ was observed after PD98059 treatment of RPMI-SE and HT1080 cells.

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Synthesis and Reactivity of β-Sulfonylvinylselenonium Salts: a Simple Stereoselective Synthesis of β-Functionalized (*Z*)-Vinyl Sulfones.

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The treatment of alkynylselenonium salt with benzenesulfinic acid in *i*-PrOH gives (*Z*)-β-sulfonylvinylselenonium salts in good yields. The alkenylselenonium salts thus prepared react with nucleophiles such as alkoxides, halides, and acetylides to produce β-functionalized (*Z*)-vinyl sulfones in high yields. Furthermore, we succeeded in the simple stereoselective one-step synthesis of various chiral (*Z*)-β-alkoxyvinyl sulfones by the use of chiral alcohols. These reactions proceed with retention of configuration via the selenurane intermediates or through a pathway of addition-elimination.

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Synthesis and Structure of 1-Methyl-2,6-bis(electron-withdrawing group)-Substituted Selenabenzenes.

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Selenabenzenes with two electron-withdrawing groups (EWGs) at the 2- and 6-positions were synthesized from α,ω-dihalides via seven steps and isolated as stable compounds at room temperature. According to X-ray structural analysis of the dibenzoyl derivative, the six-membered ring containing a selenium atom is almost planar and the structure of the selenium atom is tetrahedral with four sp^3 hybridized orbitals. Structures of isomers of selenanes and *Se*-methylseleninium salts were discussed based on their ^{1}H- and ^{13}C-NMR spectral data.

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Dimethyl Sulfide-Boron Trihalide-Mediated Reactions of α,β-Unsaturated Ketones with Aldehydes: One-pot Synthesis of Baylis-Hillman Adducts and α-Halomethyl Enones

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The reactions of aldehydes with 3-buten-2-one were conducted in the presence of $BBr_3 \cdot Me_2S$ or $BCl_3 \cdot Me_2S$ and then worked up with aqueous $NaHCO_3$, affording the α-methylene aldol **1**, α-halomethyl aldol **2** or **4**, and α-halomethyl enones **3** or **5**, respectively. In contrast, reactions quenched with water gave the α-halomethyl enones **3** or **5** in high yields, while the work-up with an aqueous 10% trimethylamine gave the α-methylene aldol **1**. The benzylphenol **6** and half-acetal **7** were obtained from the reaction of *p*-nitrobenzaldehyde with cyclohexenone after work-up of the reaction mixture with water.