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MODULAR STRATEGY FOR DEVELOPING NON-PEPTIDE PROTEIN KINASE INHIBITORS

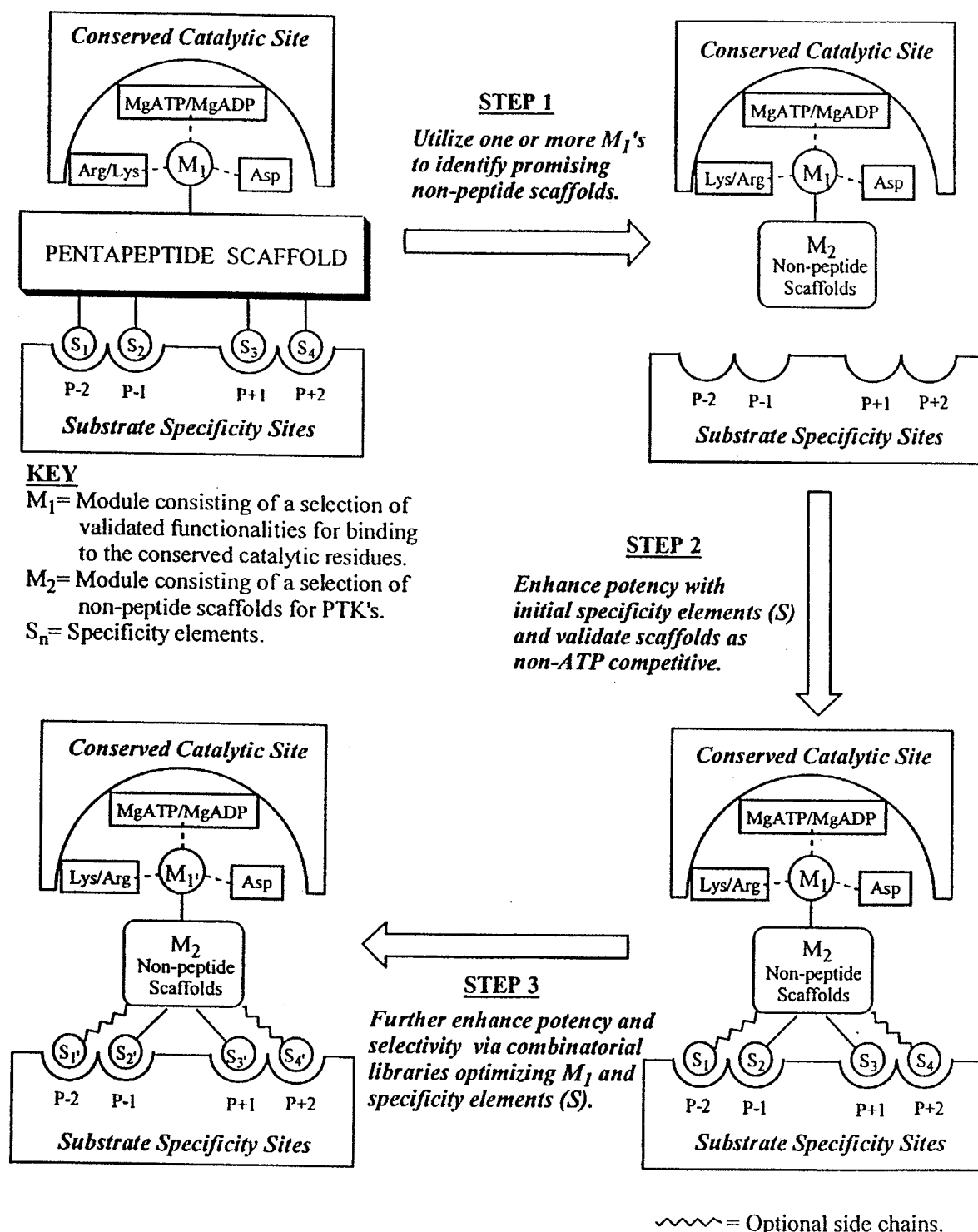
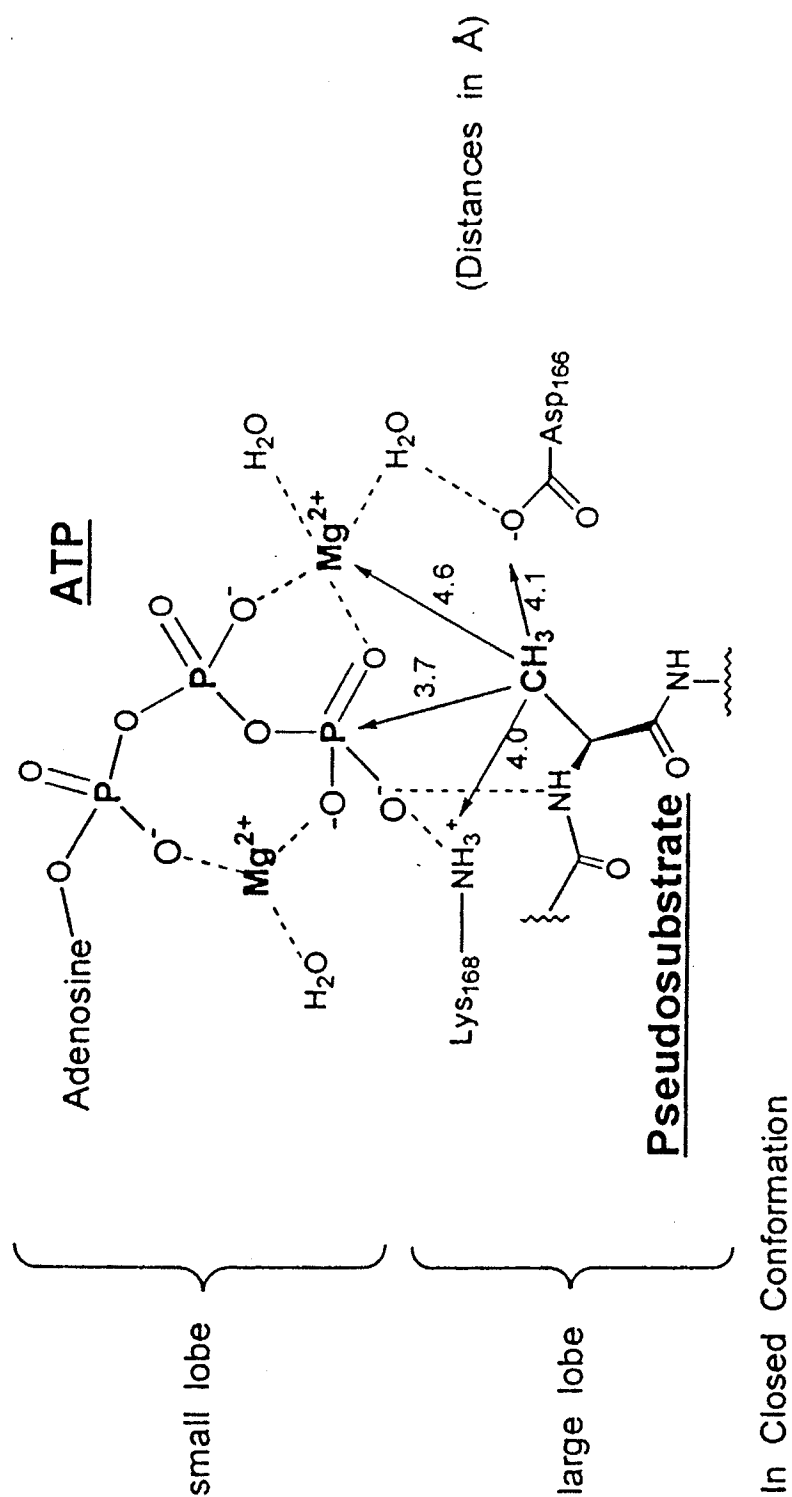


FIG. 1

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x-ray structure of (PKA):Mg₂ATP:pseudosubstrate inhibitor

**FIG. 2**

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General Module M_1 Design Features For Binding To The Conserved Protein Kinase Catalytic Region

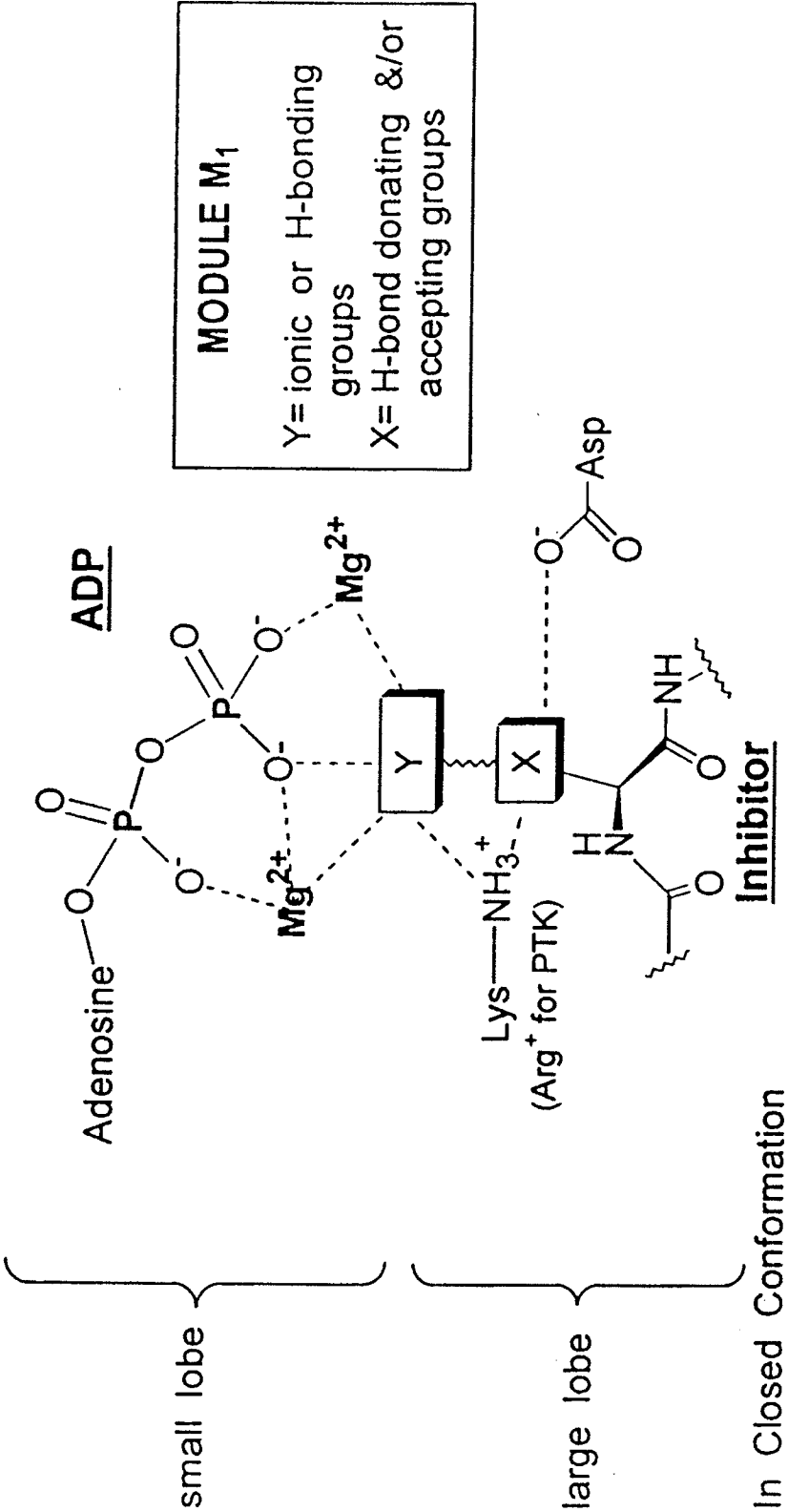


FIG. 3

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SUBSTRATE BEHAVIOR FOR BORONIC ACID PKA INHIBITORS 21 & 22

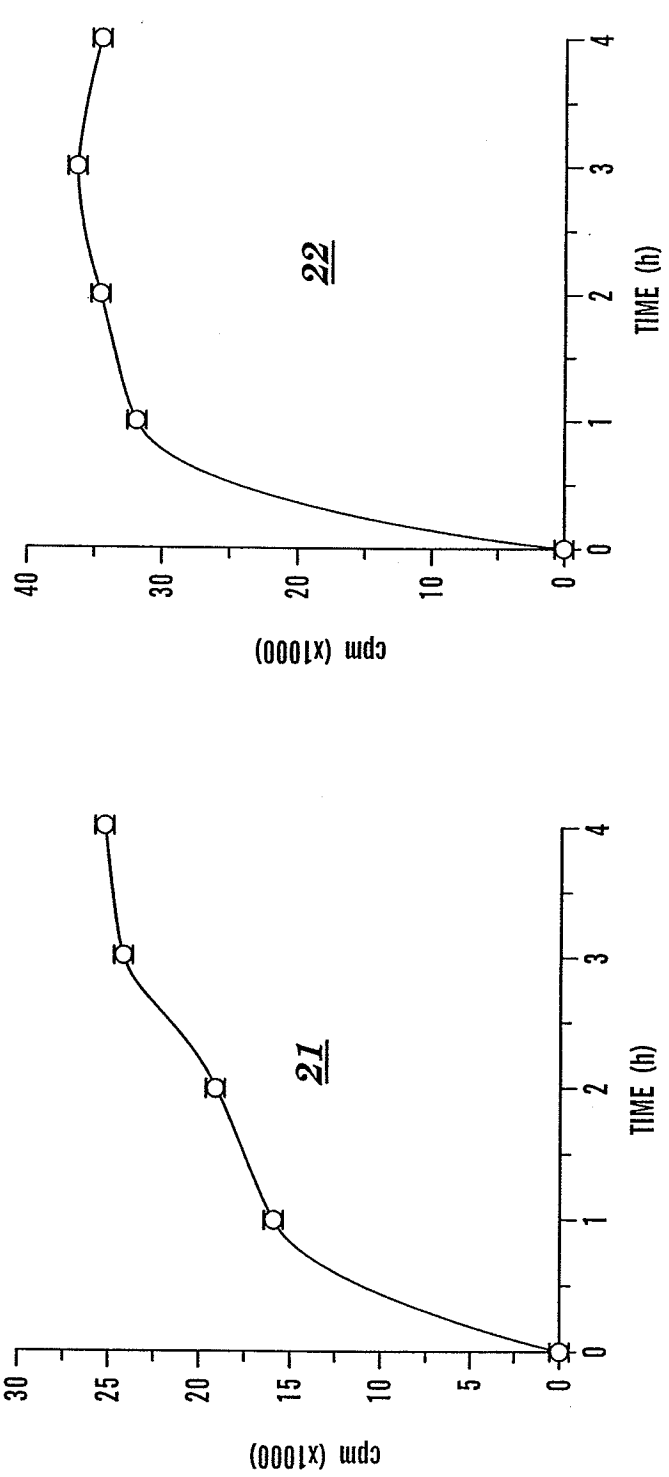


FIG. 4

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**Binding interactions of src substrate
Ac-Ile-Tyr-Gly-Phe-NH₂ in model src active site.**

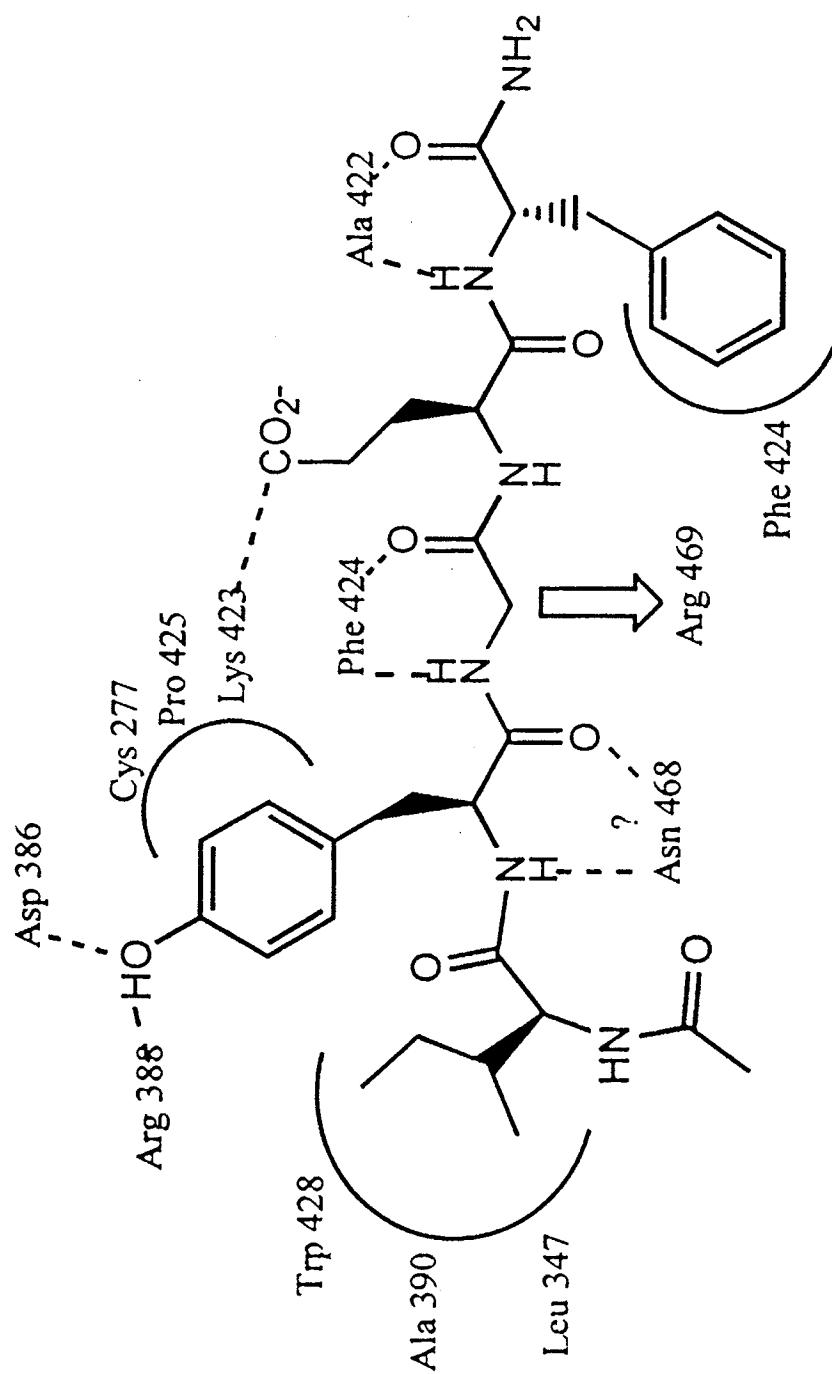


FIG. 5

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Design of naphthalene-based src inhibitor scaffold

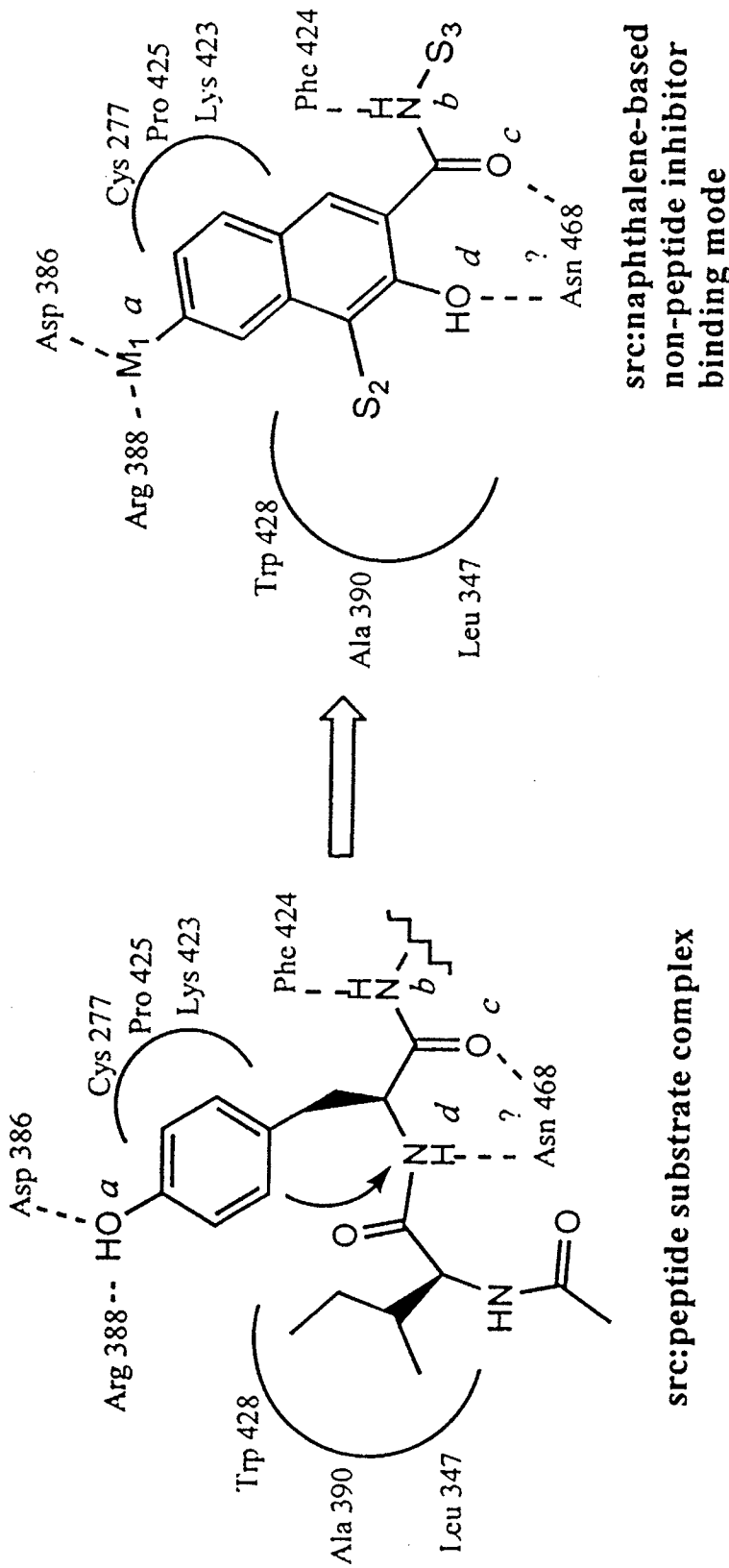
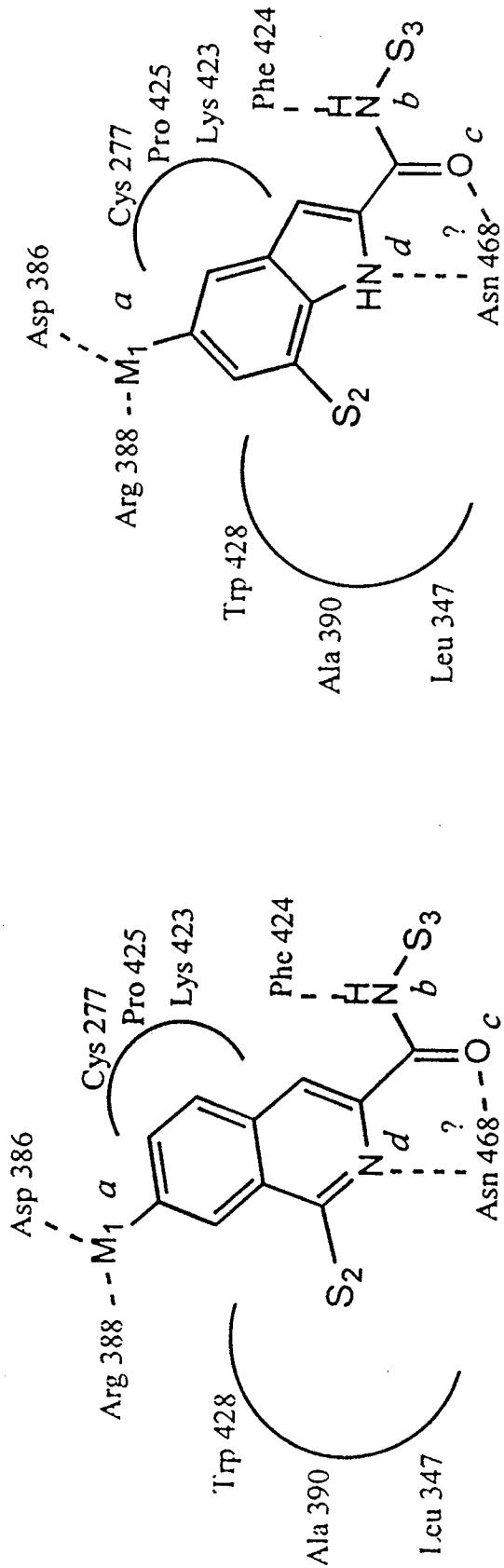


FIG. 6

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Design of isoquinoline and indole-based src inhibitor scaffolds



src:indole-based
non-peptide inhibitor
binding mode

src:isoquinoline-based
non-peptide inhibitor
binding mode

FIG. 7

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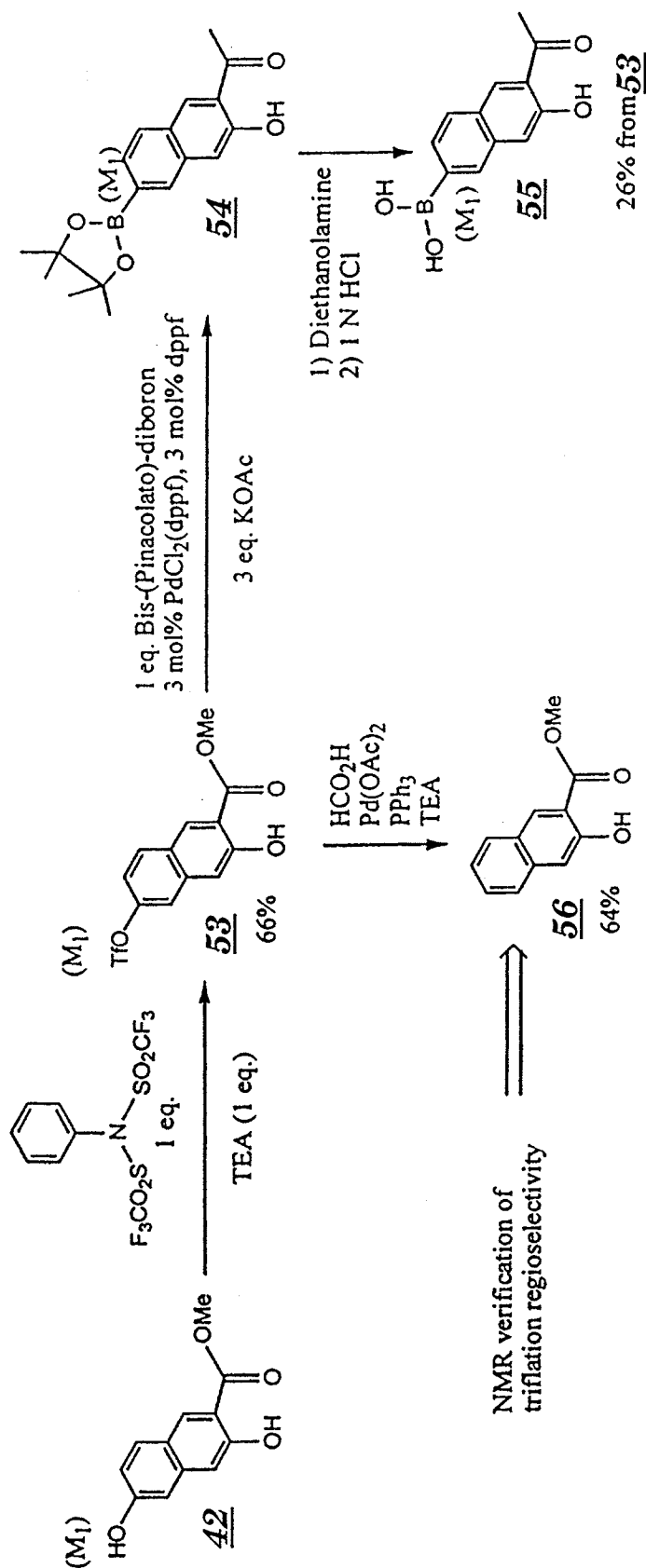
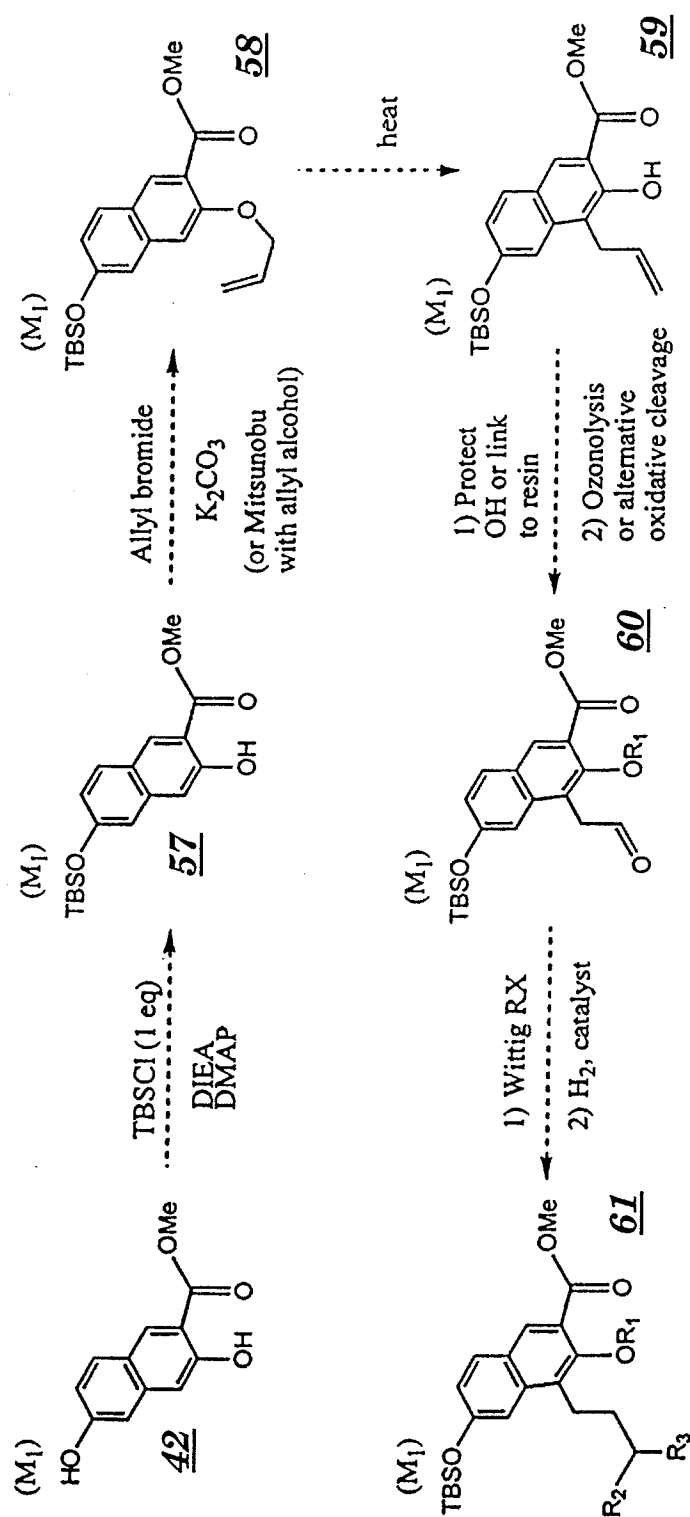


FIG. 8

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**FIG. 9**

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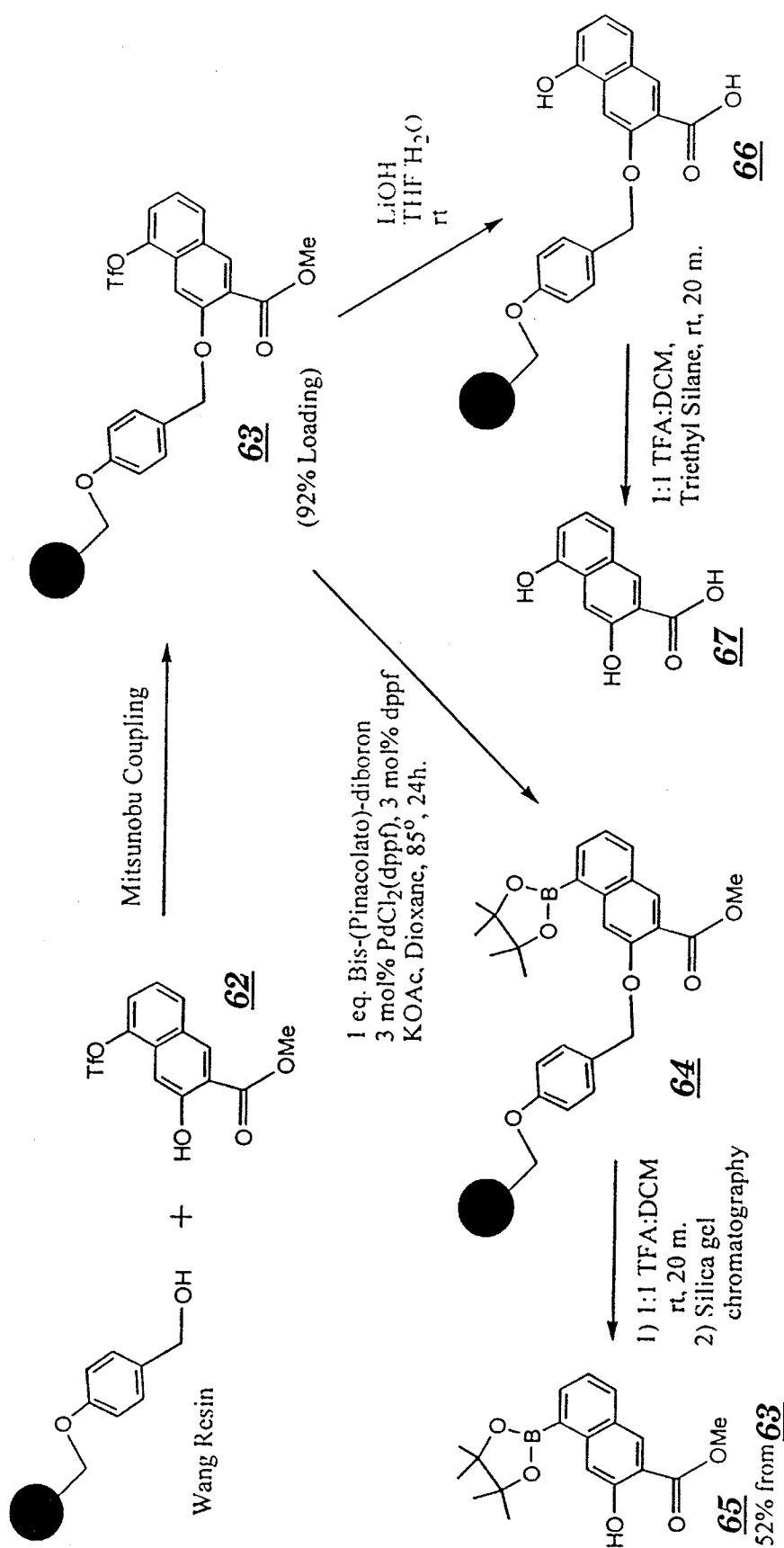


FIG. 10

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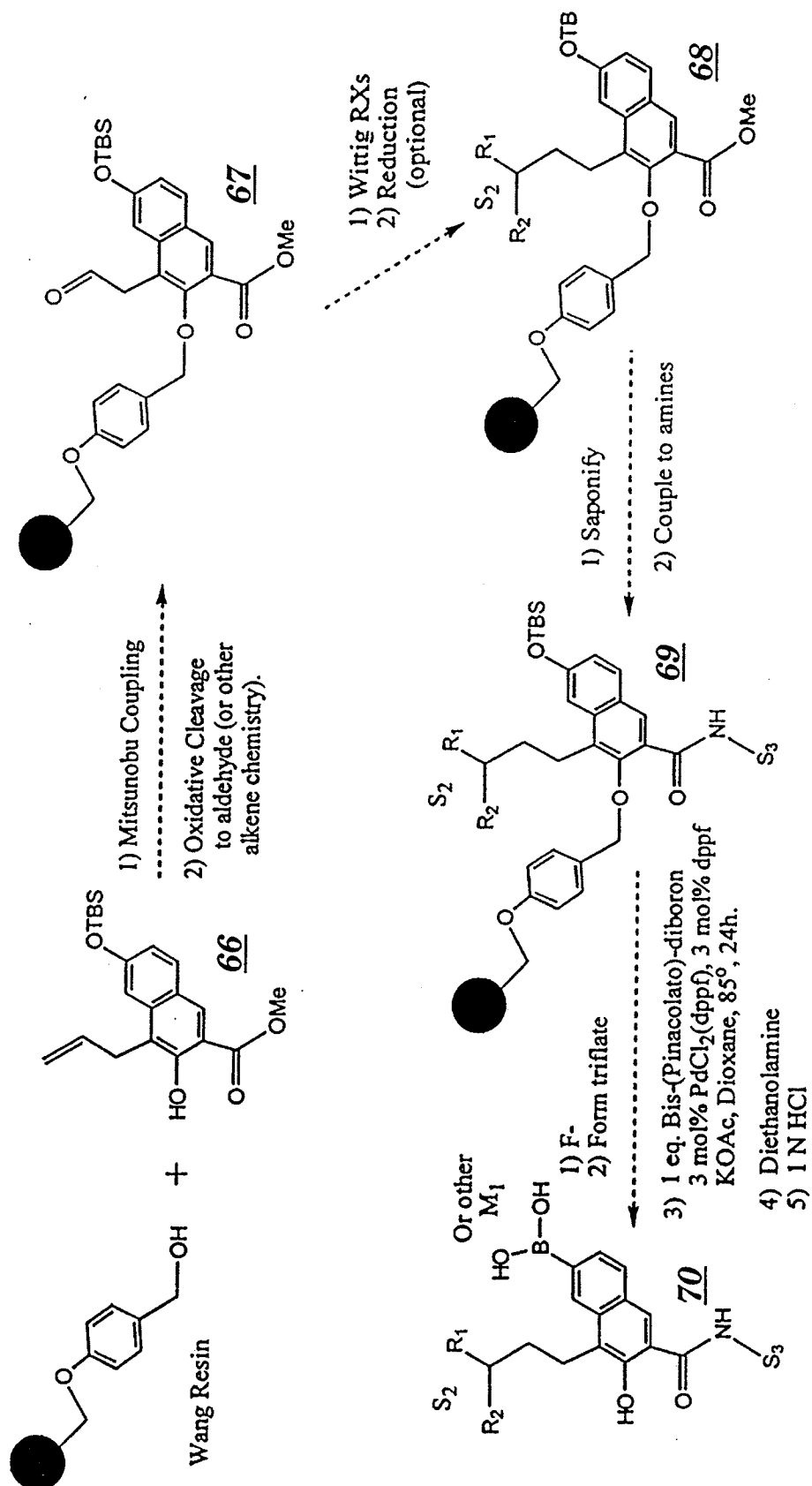


FIG. 11

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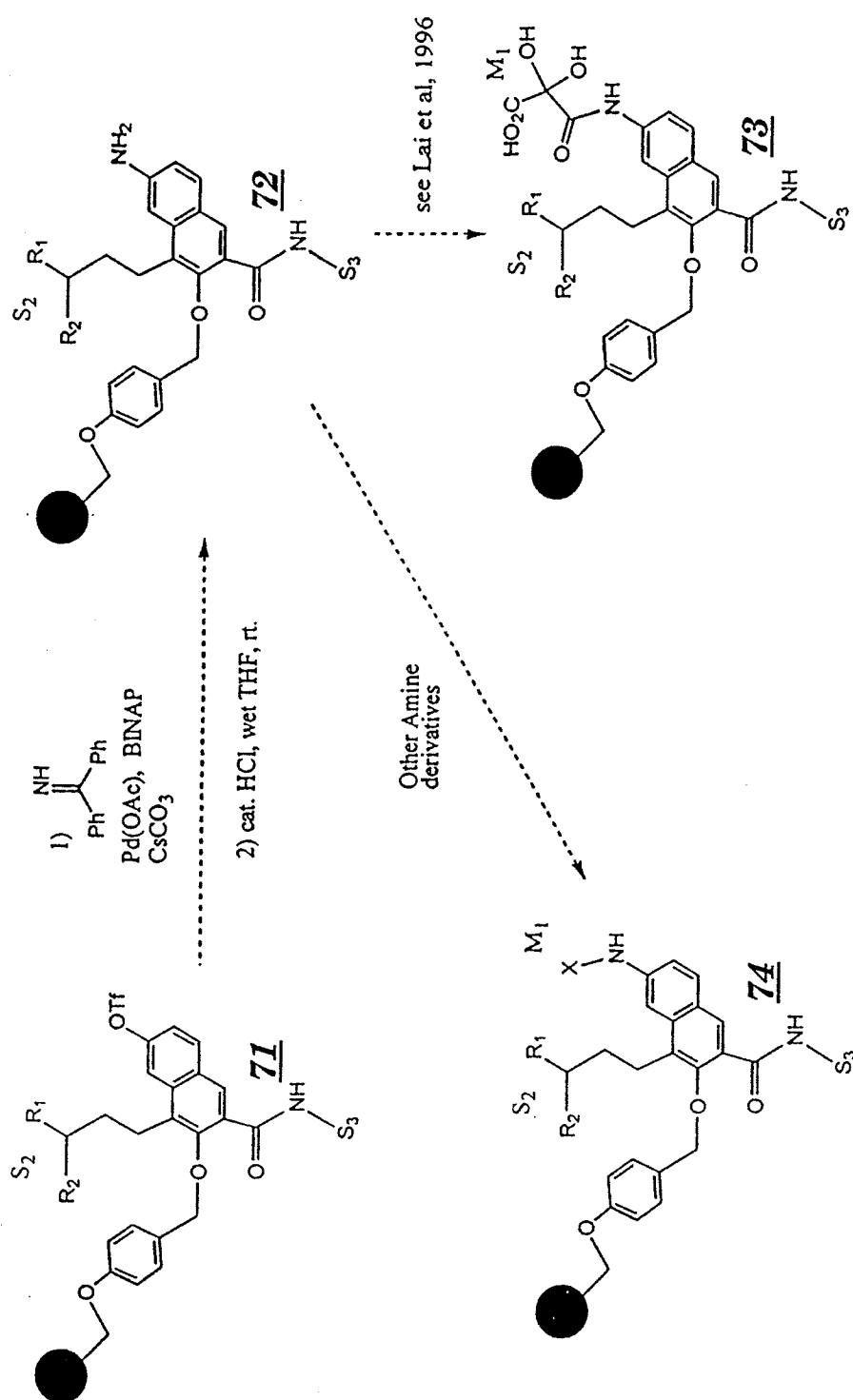
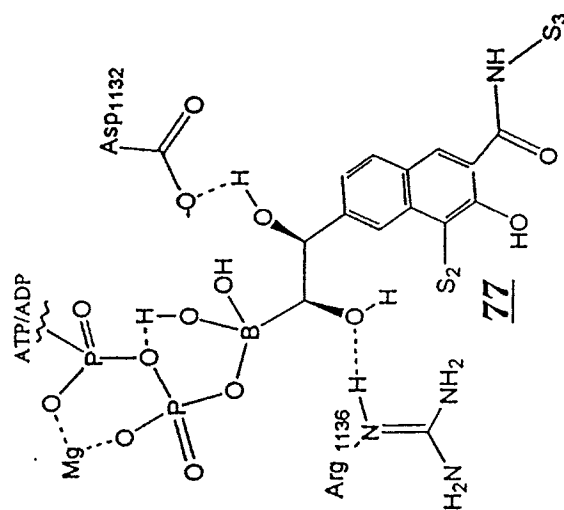
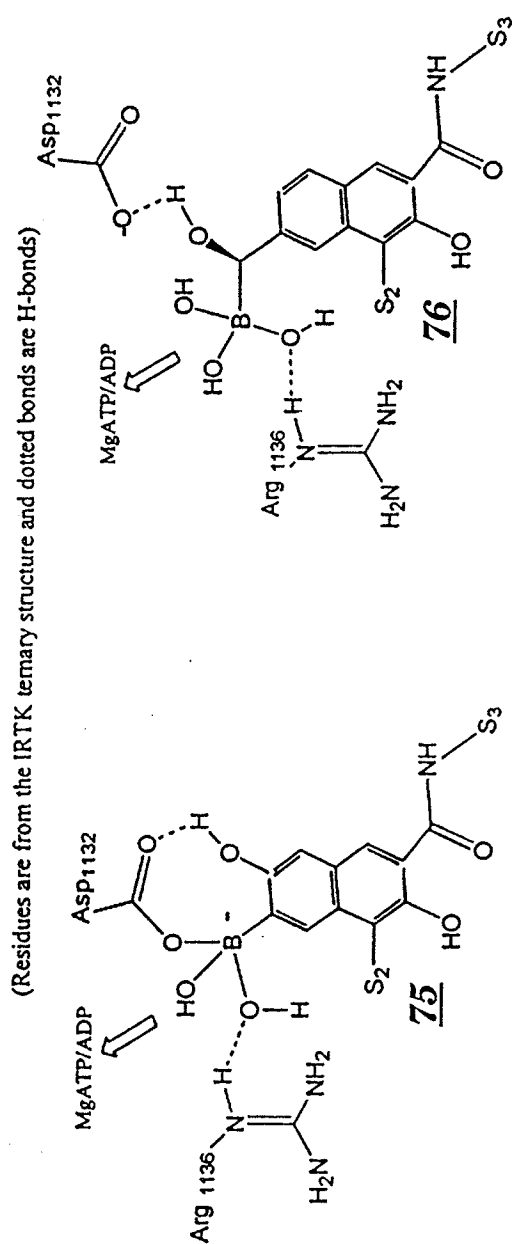


FIG. 12

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**FIG. 13**

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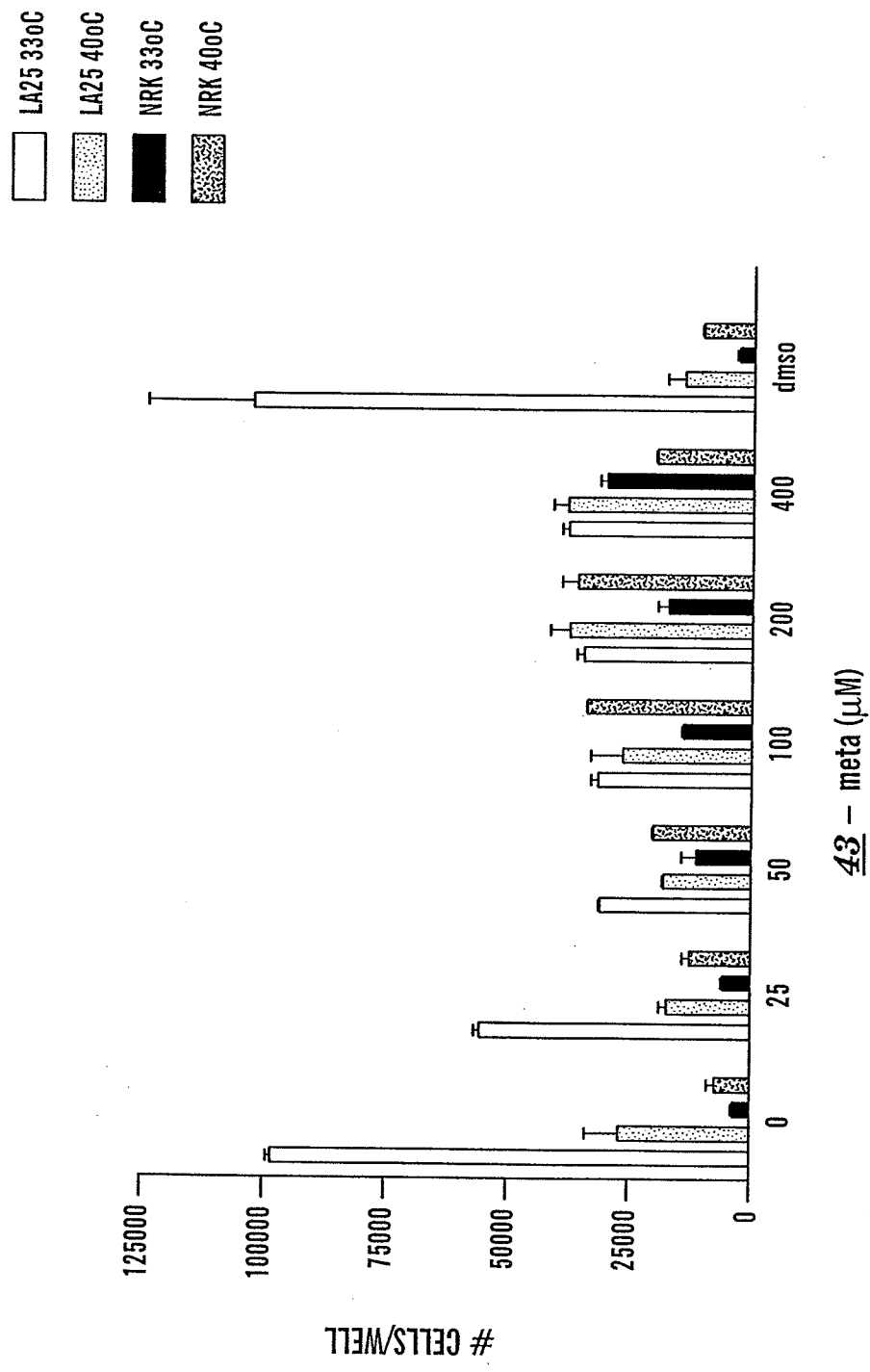
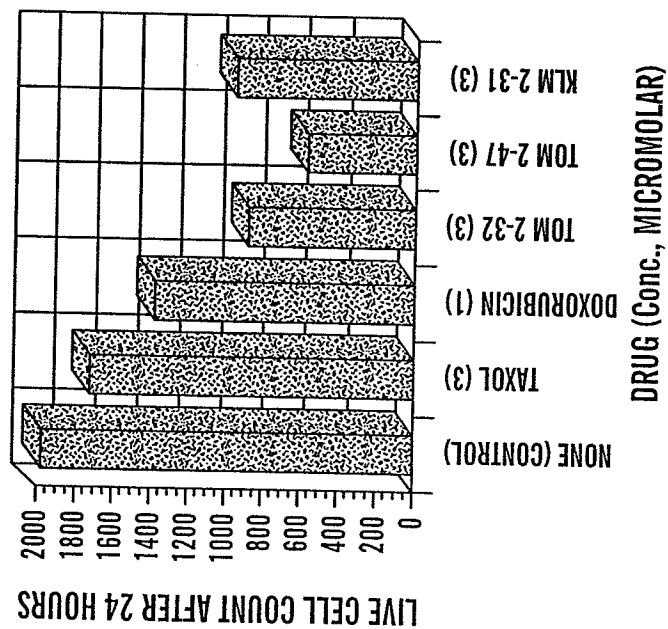


FIG. 14

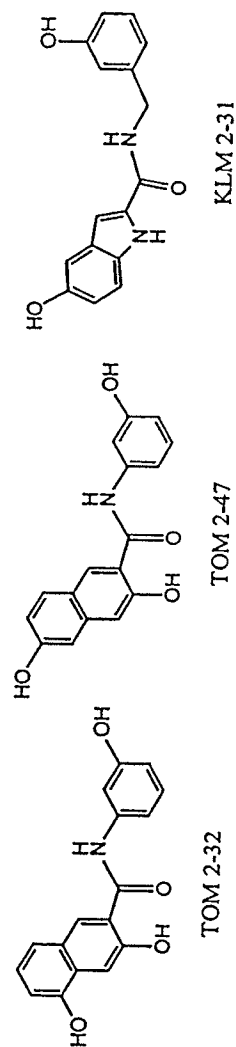
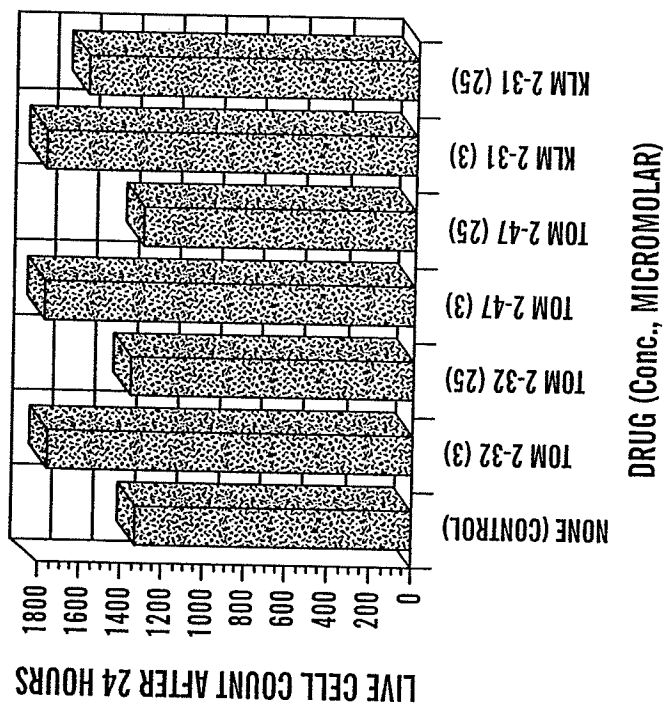
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FIG. 15A

OVARIAN TUMOR NO15 SENSITIVITY TO DRUGS:
SUSPENDED CELL CULTURE

**FIG. 15B**

NORMAL HUMAN FIBROBLASTS SENSITIVITY TO
Src INHIBITORS: SUBCONFLUENT CELL CULTURE

**FIG. 15C**