

**B.Sc. Semester-VI
Organic Chemistry
Paper-XIV**



3. Heterocyclic Compounds

Coverage:

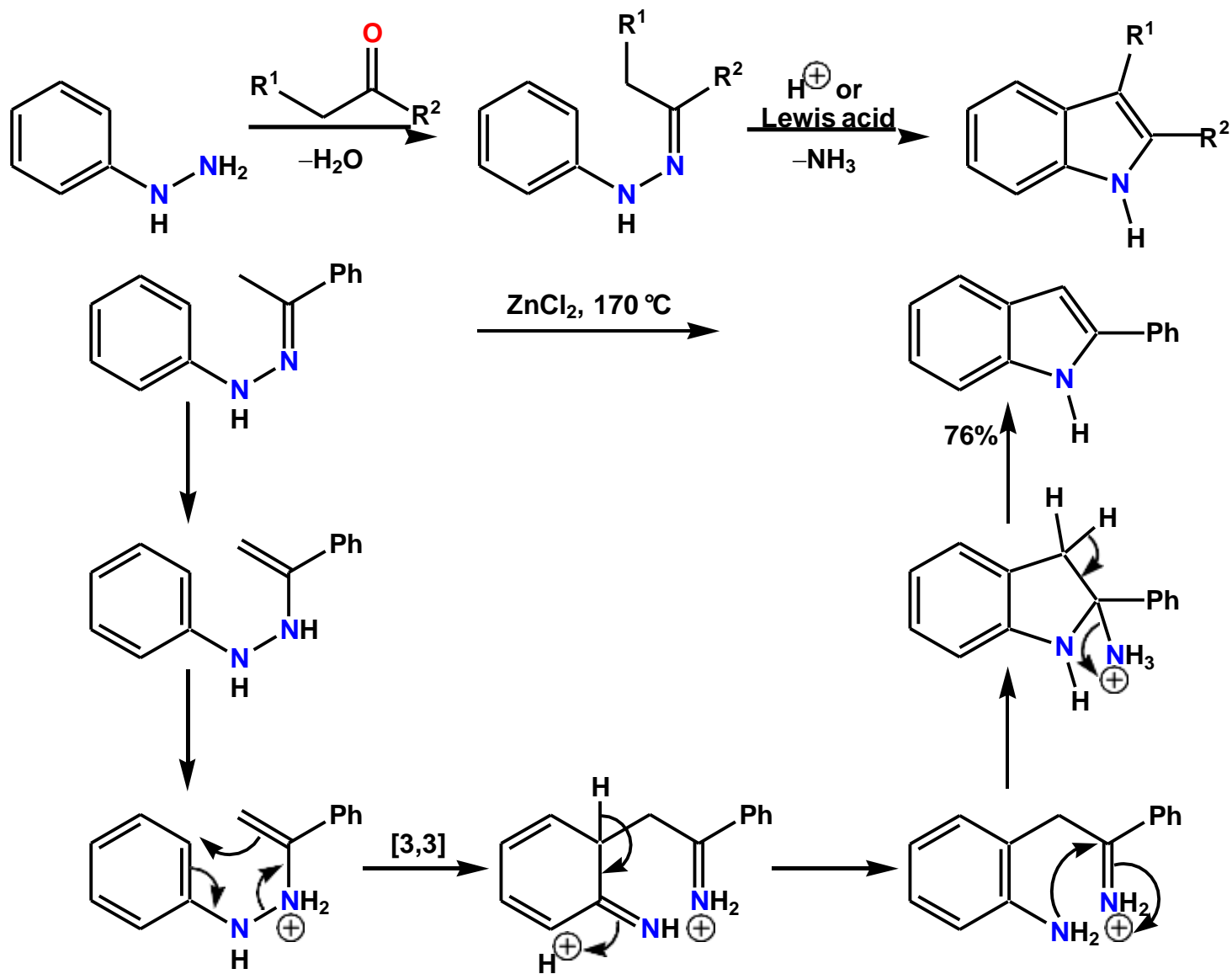
9. Indoles : Synthesis, Electrophilic Substitution Reactions



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Indoles – Synthesis

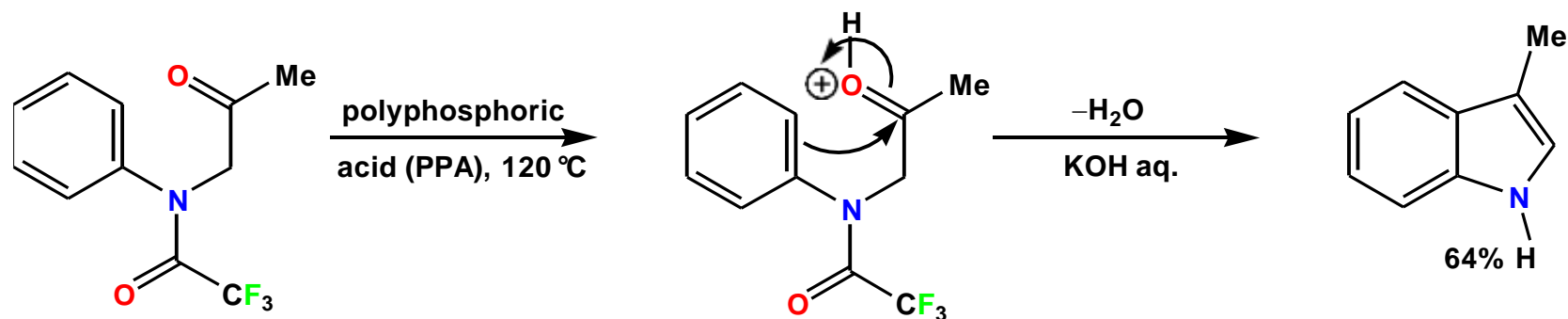
Fischer Indole Synthesis



- A protic acid or a Lewis acid can be used to promote the reaction

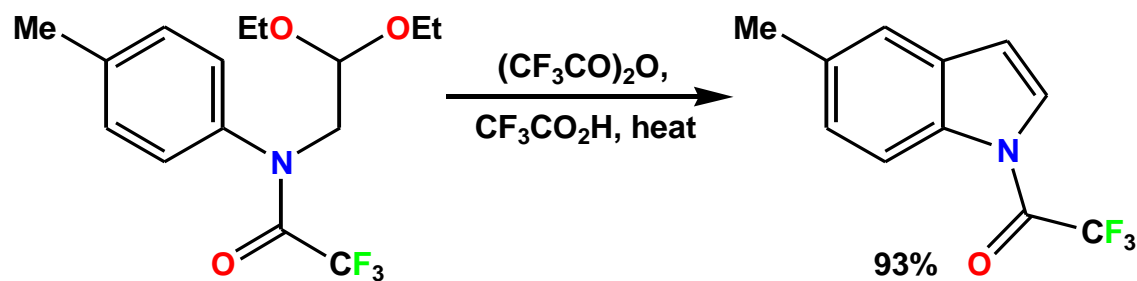
Indoles – Synthesis

Bischler Synthesis



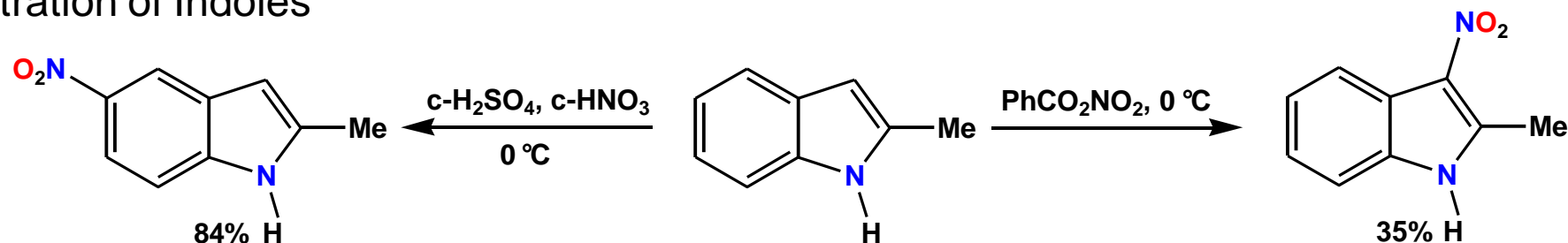
- An α -arylamino ketone is cyclised under acidic conditions

- The reaction also works with acetals of aldehydes



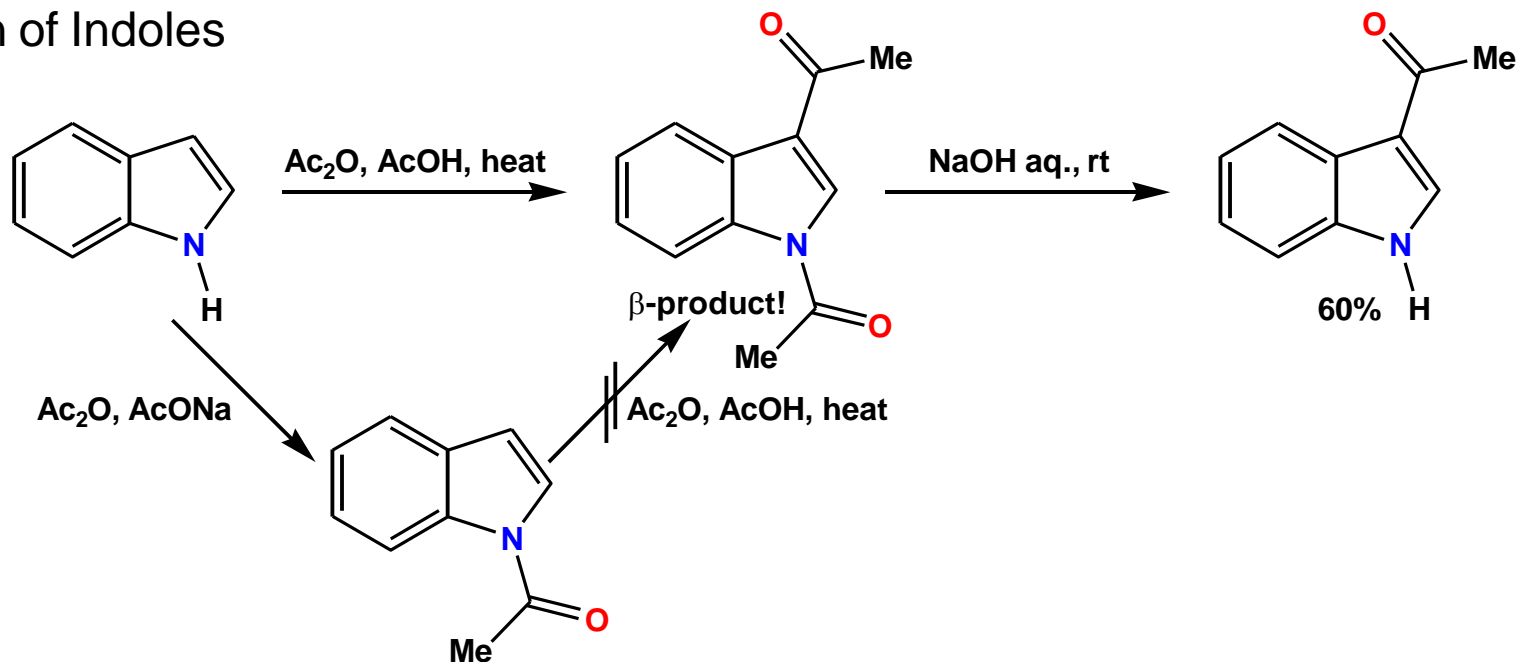
Indoles – Electrophilic Substitution Reactions

Nitration of Indoles



- Polymerisation occurs when there is no substituent at the 2-position
- Halogenation is possible, but the products tend to be unstable

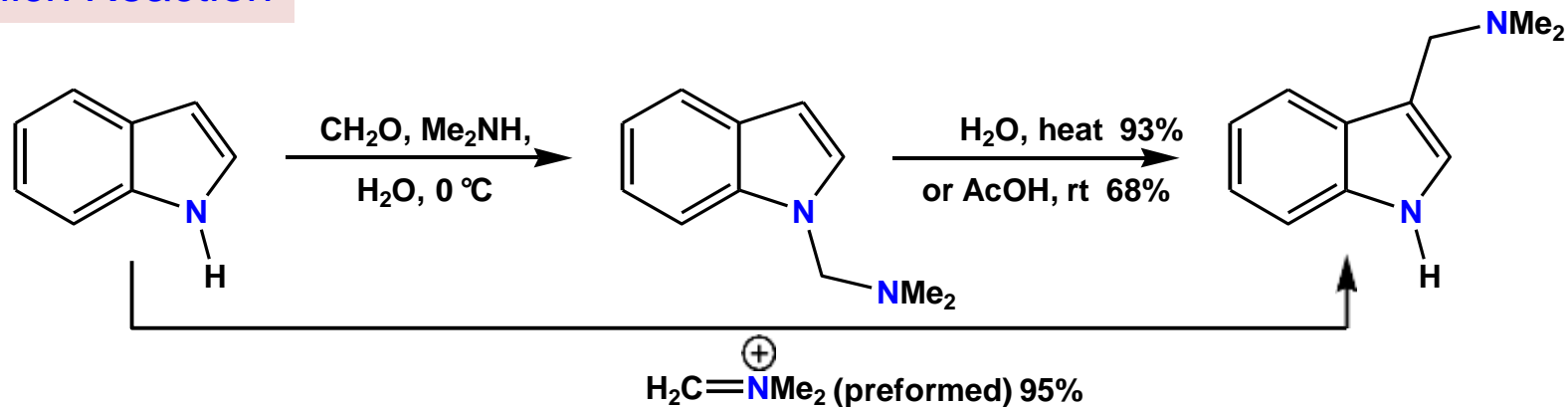
Acylation of Indoles



- Acylation occurs at C before N because the N-acylated product does not react

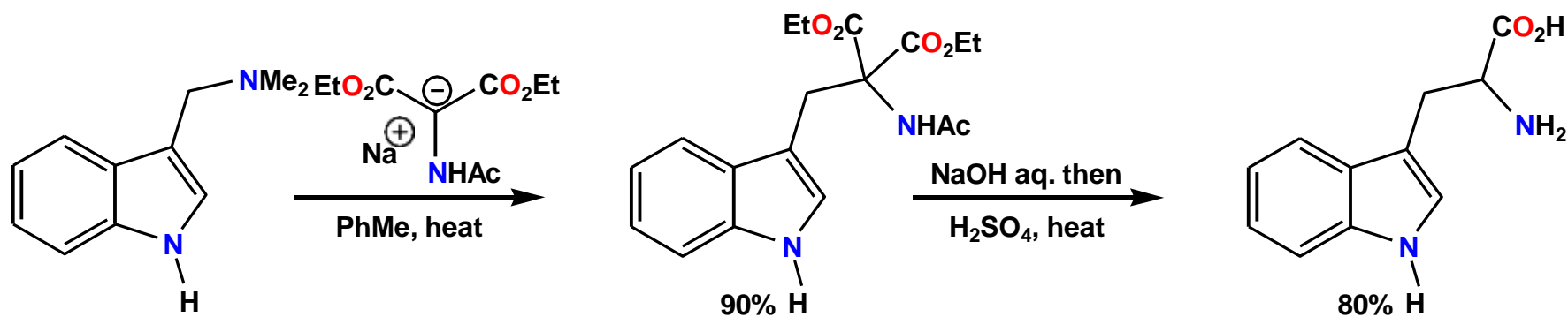
Indoles – Electrophilic Substitution Reactions

Mannich Reaction



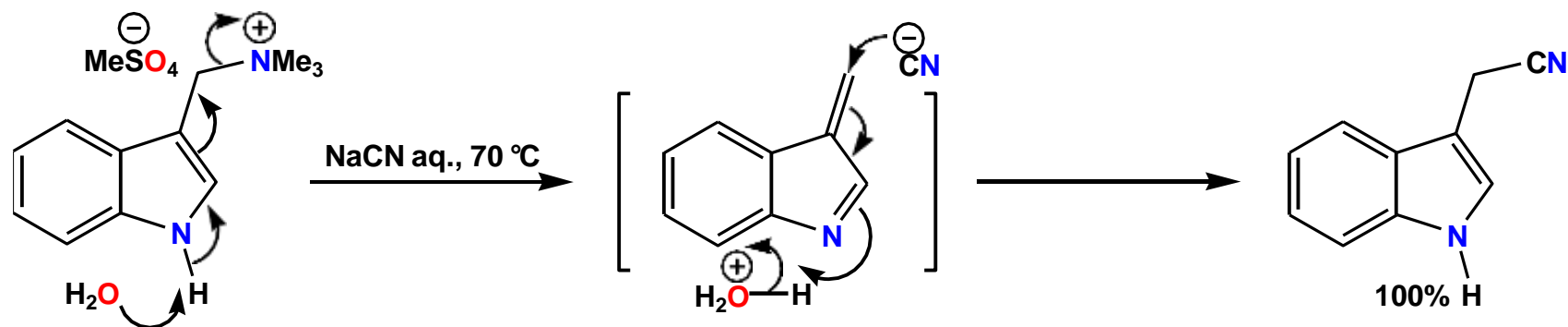
- A very useful reaction for the synthesis of 3-substituted indoles
- The product (gramine) can be used to access a variety of other 3-substituted indoles

Synthesis of Tryptophan from Gramine

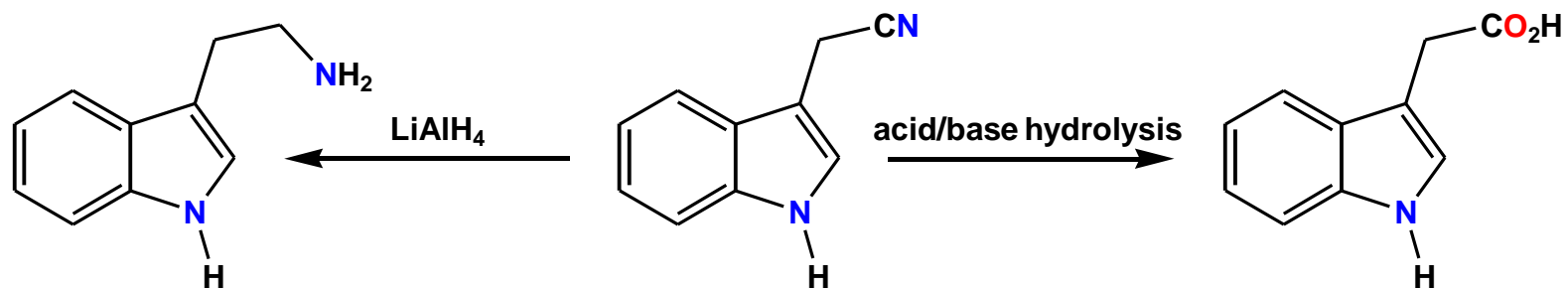


Indoles – Electrophilic Substitution Reactions

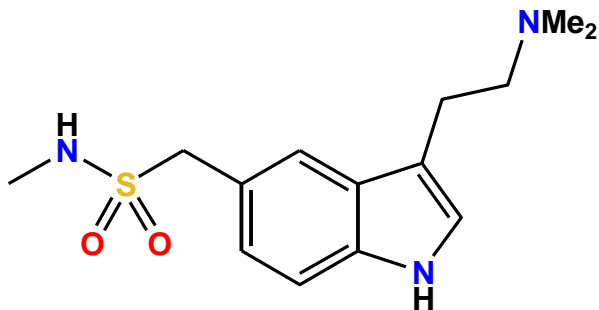
Synthesis of Other 3-Substituted Indoles from Gramine



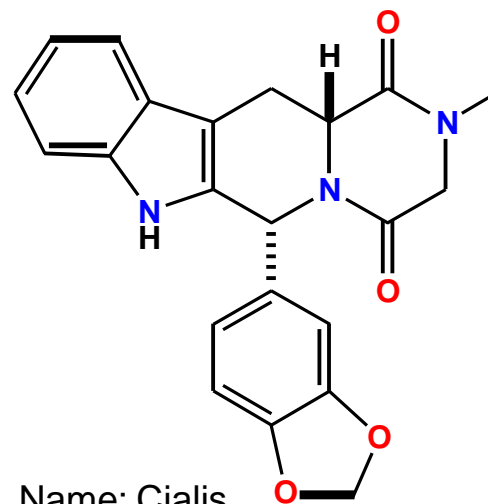
- The nitrile group can be modified to give other useful functionality



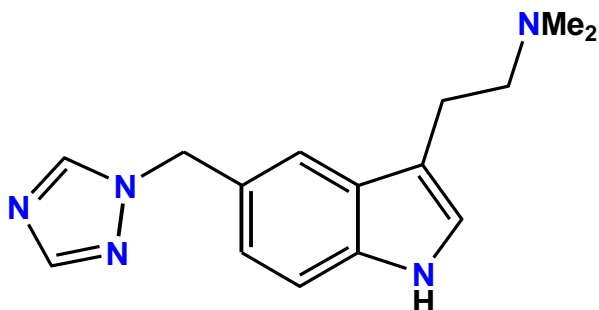
Drugs Containing an Indole



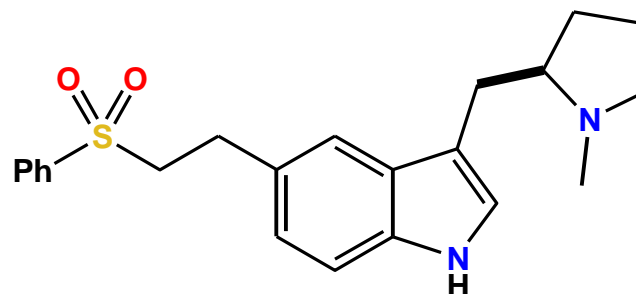
Name: Immitrex
2008 Sales: \$0.97 billion
2008 Ranking: 35 branded
Company: GlaxoSmithKline
Disease: Migraine



Name: Cialis
2008 Sales: \$0.56 billion
2008 Ranking: 66 branded
Company: Eli Lilly
Disease: Erectile dysfunction



Name: Maxalt
2008 Sales: \$0.22 billion
2008 Ranking: 148 branded
Company: Merck
Disease: Migraine



Name: Relpax
2008 Sales: \$0.21 billion
2008 Ranking: 151 branded
Company: Pfizer
Disease: Migraine