



CHEMISTRY 4000

Problem Set #3: Gefitinib (aka Iressa[®])

Spring 2022

Dr. Susan Findlay



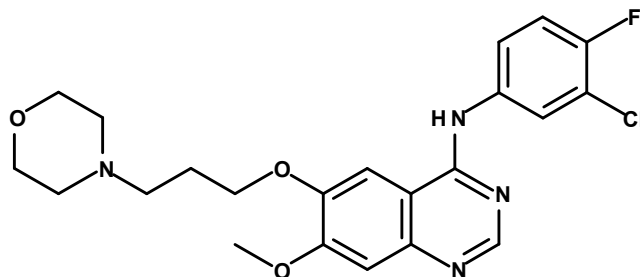
Gefitinib (aka Iressa[®])

- Gefitinib was approved in 2003 as a “third line therapy of locally advanced or metastatic non-small cell lung cancer (NSCLC)”¹.
- In 2015, the FDA approved it as a first line treatment for NSCLC. New Zealand did the same in 2012.
- Gefitinib acts by inhibiting epidermal growth factor receptor (EGFR) which is overexpressed on the surfaces of certain types of tumour cells. When EGFR is activated, it signals other proteins which initiate pathways leading to DNA synthesis, cell proliferation and migration. Thus, by inhibiting activation of EGFR, gefitinib shrinks tumours in which it was overexpressed.
- Since gefitinib functions by interfering with processes that turn healthy cells into cancerous ones, its side effects are much milder than most chemotherapeutic drugs. Its use in treating other cancers (e.g. esophageal cancer) is still being studied.

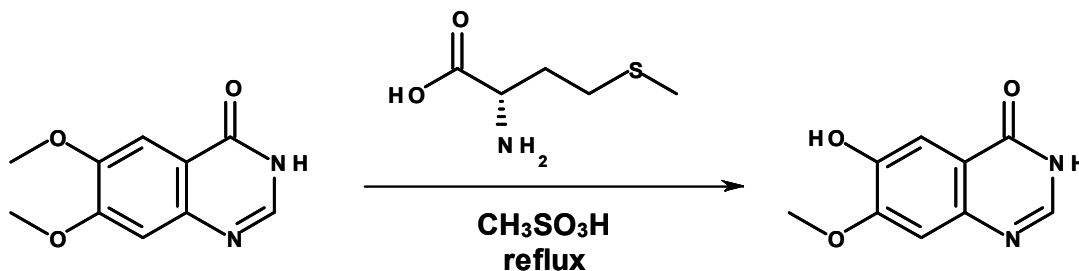
¹ http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/fs-fi/fact_iressa-eng.php

Gefitinib (aka Iressa®)

- The structure of gefitinib is:



- We will be looking at the AstraZeneca synthesis of gefitinib. The first step of the synthesis is a selective monodemethylation:



We will begin with the second step of the synthesis.