

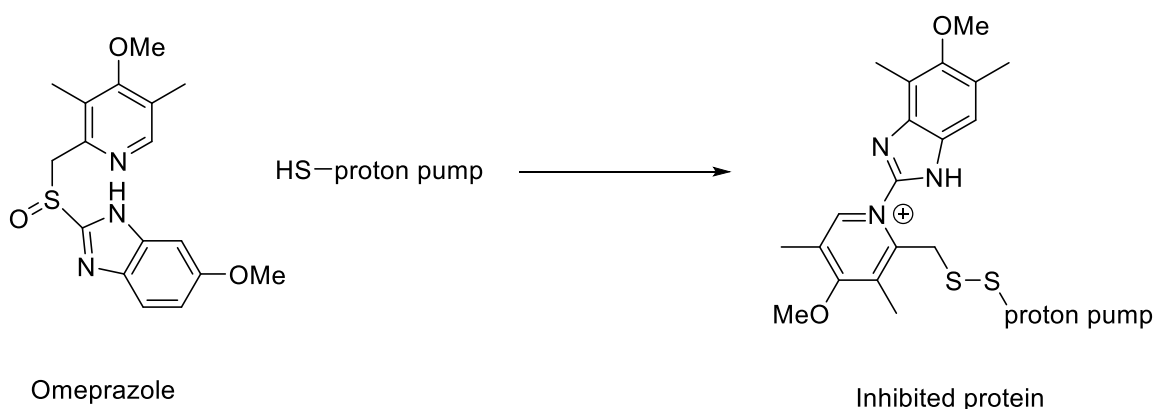
Ana & Nils 09/11/2021

Part 1: Ana

1. Omeprazole is a proton pump inhibitor used to counteract hyperacidity in the stomach.

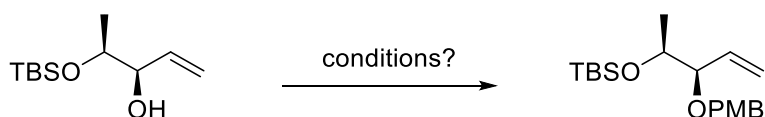
Propose a mechanism by which the drug inhibits the proton pump (HS stands for the sidechain of a Cysteine residue in the protein).

Hint: as a prodrug, Omeprazole only gets activated under the acidic conditions of the parietal cells of the stomach



2. The protection of secondary alcohol A with a PMB group cannot be achieved under standard conditions (PMBCl, NaH) due to the migration of the TBS group.

Suggest alternative reagents to achieve this transformation and propose a reaction mechanism.



3. You have found a random, unlabelled bottle in the back of the fumehood with unknown contents. As a curious and responsible chemist, you carry out several experiments in order to determine the identity of the compound before deciding its fate.

The following data was obtained, use it to determine the structure of the compound.

HRMS [$C_7H_8O_2+H$] expected at 125.0597, found at 125.0599

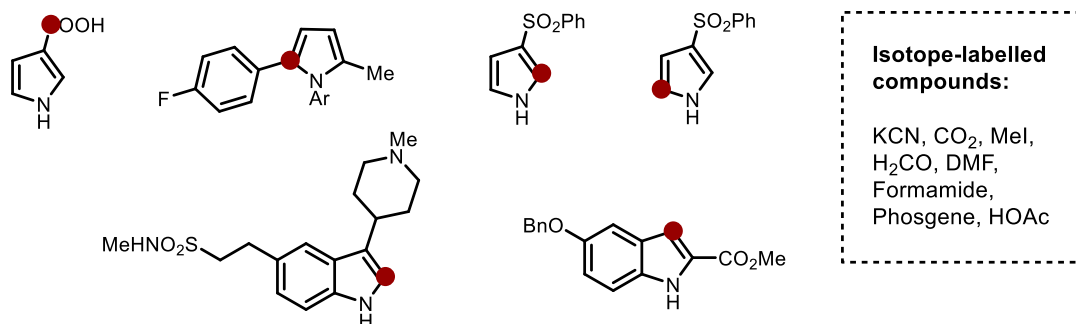
IR 3388.1 (br), 1598.7, 1494.5, 1151.3

1H NMR (400 Mhz, $CDCl_3$) d 7.10 (t, $J=7.5$ Hz, 1H), 6.74 (d, $J=7.5$ Hz, 1H), 6.70 – 6.60 (m, 2H), 5.48 (s, br, 1H), 3.78 (s, 3H).

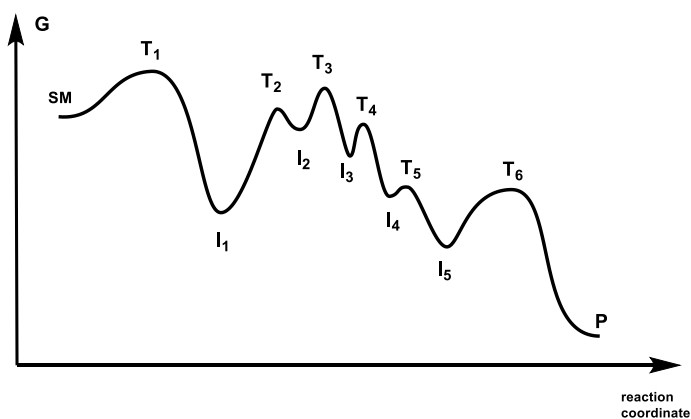
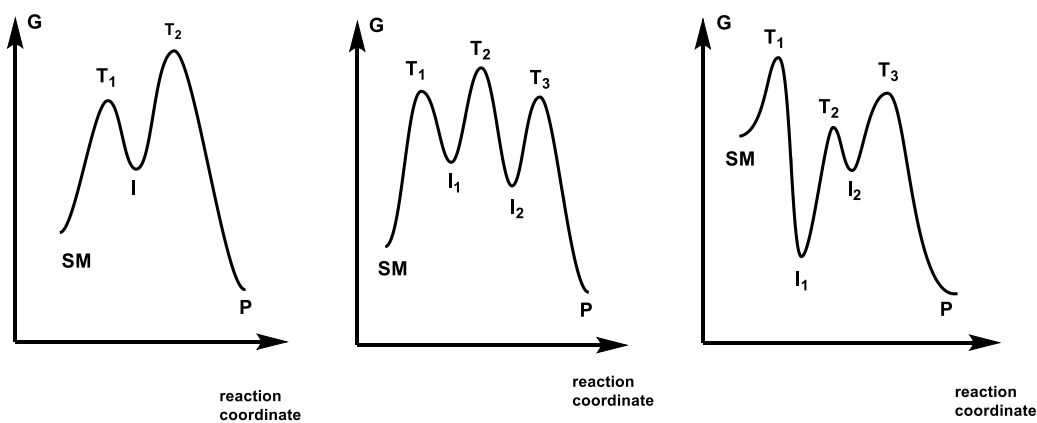
^{13}C NMR (126 Mhz, $CDCl_3$) d 160.9, 156.8, 130.2, 120.2, 114.6, 110.8, 55.9.

Part 2: Nils - Some ticking problems

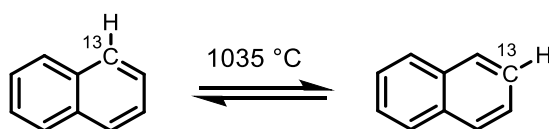
- Propose an efficient synthesis of these carbon isotope-labelled compounds using e.g. the isotope sources given in the box.



- What is the rate-limiting (or rate-determining) step of the following reaction profiles?

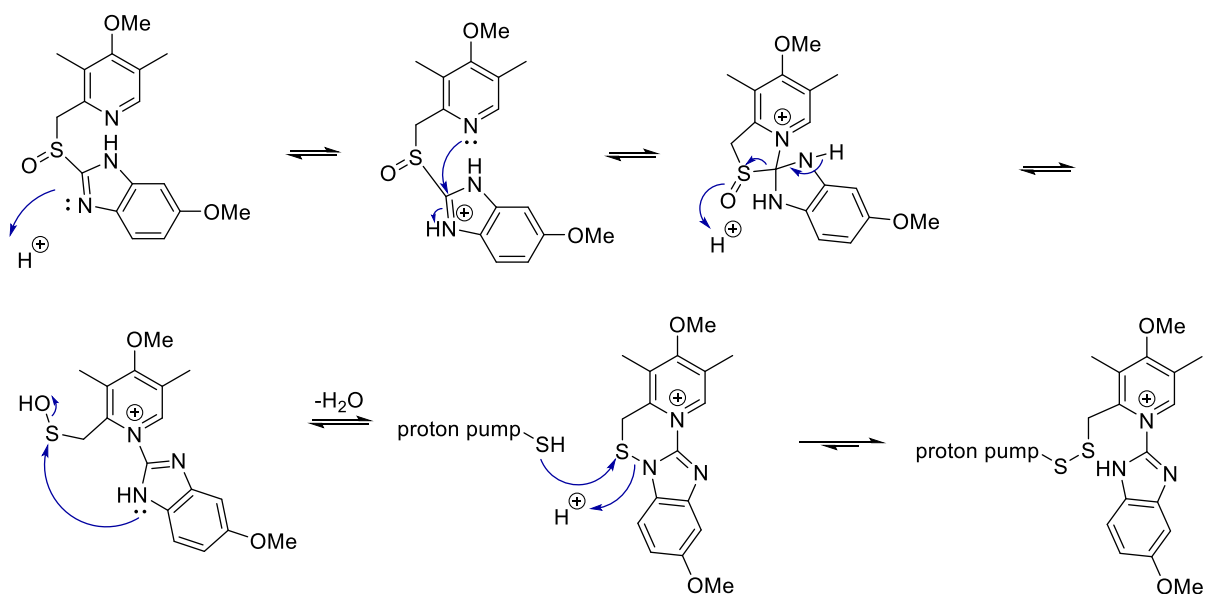


- How would you scramble this ¹³C-labelled Naphthalene?

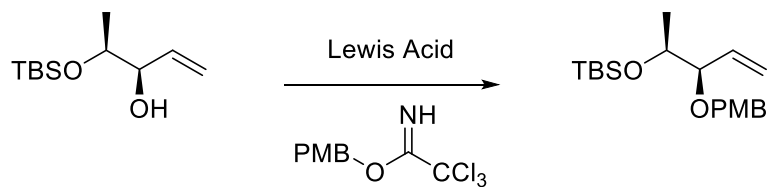


Solutions (Part 1)

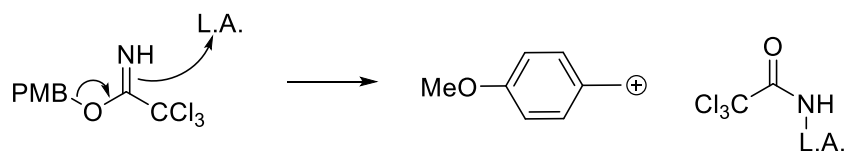
1. Mechanism of inhibition of the proton pump by Omeprazole
(Patrick, Graham. 2017. *An Introduction to Medicinal Chemistry*. 6th ed. London, England: Oxford University Press)



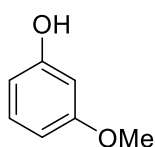
2. Lewis acid catalysed PMB protection – doesn't involve an anionic oxygen intermediate, thus avoids TBS migration



mechanism:

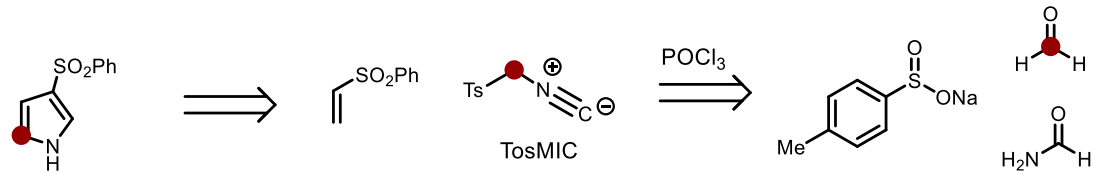
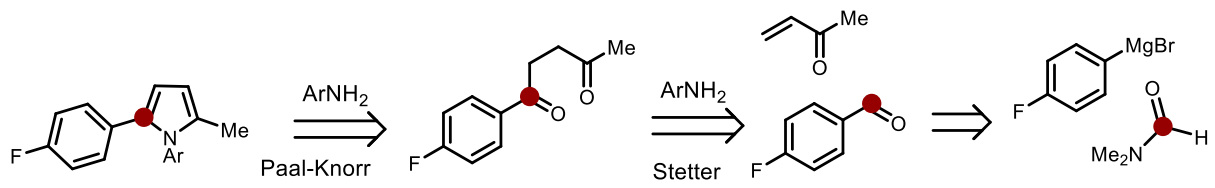


3. 3-methoxyphenol



Solutions (Part 2)

Question 1



both: van-Leusen

