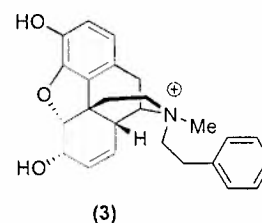
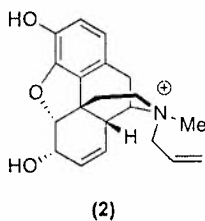
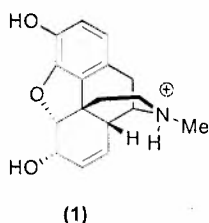
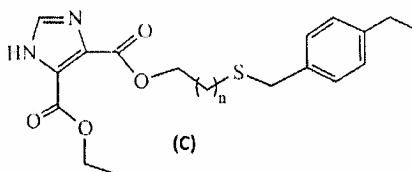
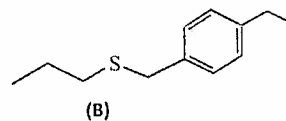
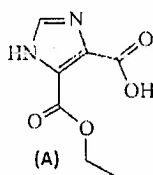


1. For all of the following morphine-based drug candidates, comment on
- What would be the preferred mode of administration (oral/skin/intravenous injection or CNS injection etc.) to the body so that the effect is observed? (no need to write reasons for the preferred mode)
  - What activity (agonist or antagonist) would you predict from them? (no need to write reasons for the activity)

(0.5x3+0.5x3=3 marks)

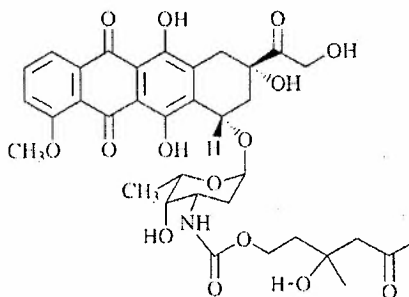


2. Compounds A and B below were leads determined from an SAR by NMR study of a new receptor. Based on this analysis, C was synthesized, and  $n$  was varied, but all the compounds made had much lower potency than either A or B.



- What conclusions can you draw from this result?
  - What structures (show two) would you try next and Why?
3. Catalytic antibody 38C2, an abzyme (not shown here) is capable of catalysing both retro aldol and retro Michael reactions inside human body. Show mechanistically how this abzyme will help in the release of the active drug doxorubicin from the following prodrug.

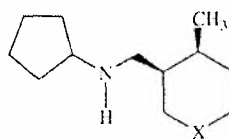
(2.0 marks)



*Doxorubicin*

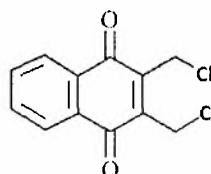
4. An isosteric series of compounds shown below, where  $X = \text{CH}_2, \text{NH}, \text{O}, \text{S}$ , were synthesized. The order of potency was  $X = \text{NH} > \text{O} > \text{S} > \text{CH}_2$ . How can you rationalize these results with reasons for trend in the isosteres?

(3.0 marks)



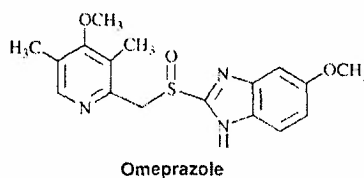
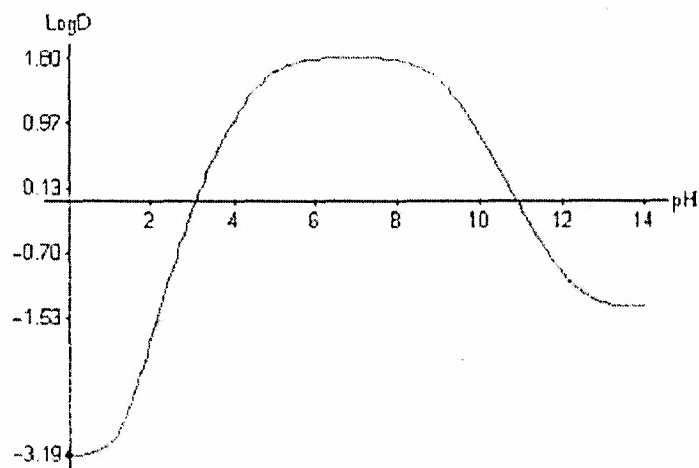
5. The following drug is used in anti-cancer therapy. Predict the mode of action mechanistically.

(1.5 marks)

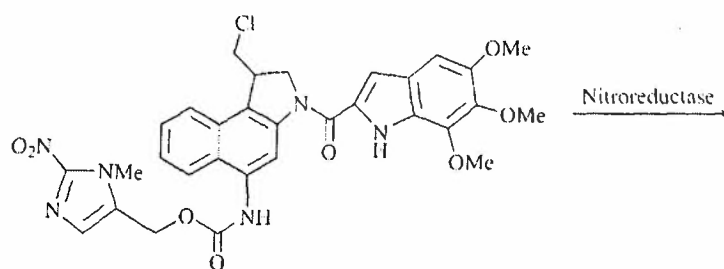


6. Rationalize the change in log D vs pH for omeprazole shown below. Refer to the structure when discussing the log D changes with pH.

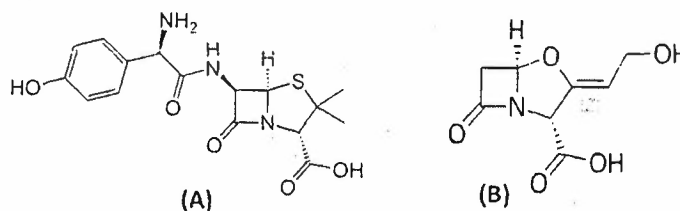
(2 marks)



7. A nitroreductase which catalyses the reduction of aromatic nitro group to the corresponding hydroxylamino group, is used in the following example to trigger the release of anti-cancer drug inside cells. Show mechanistically the release of the drug. Also show mechanistically how the drug acts as anti-cancer agent. (3.0 marks)



8. Amoxicillin, structure **A** (shown below) is a more stable derivative of penicillin and rated as one of the most effective and safest medicines needed in a health system according to WHO. However, it is often used with potassium salt of clavulanic acid (**B**) which has much lower potency. Why we need salt of clavulanic acid (show mechanistically)? Why Amoxicillin is more stable than Penicillin?



(1.5+1 marks)

*Diya*