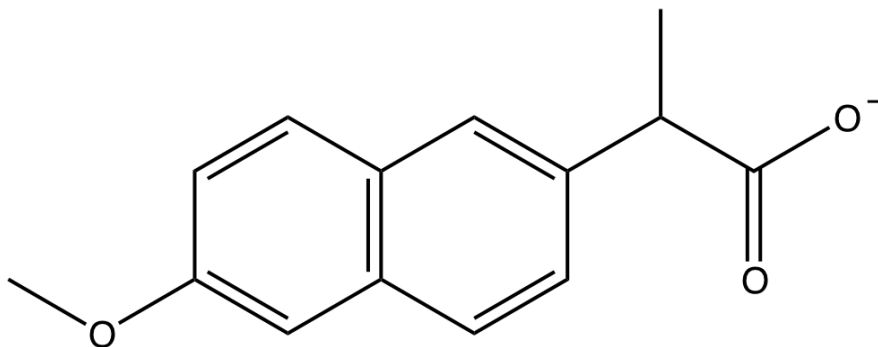


Cyclooxygenase II (COX-2) is an important protein that participates in the inflammatory response in humans. Regulation of COX-2 has become an important method of pain, swelling, and fever management among humans. One such regulator of human COX-2 activity is *naproxen*, which is the active ingredient in the over-the-counter medication Aleve™. Naproxen interacts with COX-2 and blocks its function, which can lessen the inflammatory response.

### Chemical Structure of Naproxen

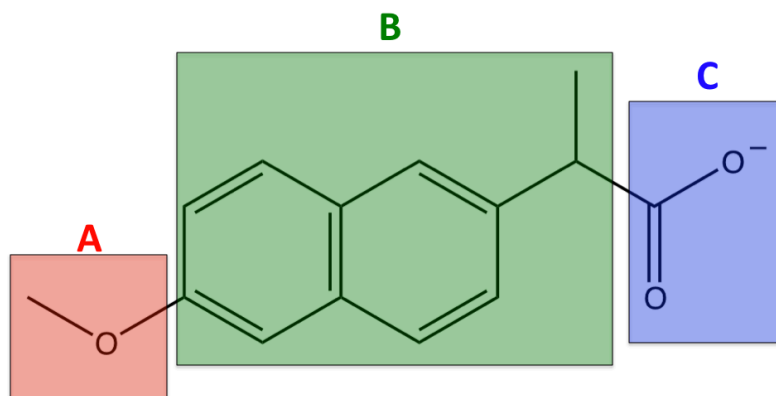


1. Add lone pairs of electrons to the above structure to convert it to an acceptable Lewis-dot form.
2. Label on the above structure:
  - a. Hydrogen bond donors (HD)
  - b. Hydrogen bond acceptors (HA)
  - c. Proton donors (PD)
  - d. Proton acceptors (PA)
3. The pK<sub>a</sub> of naproxen is 4.15. An initial oral dose of Aleve™ to manage pain will contain 550 mg (or 2.39 mmole) of naproxen.
  - a. Draw the chemical structure or structures of naproxen that are present in the stomach when a person has taken an Aleve™ tablet and the stomach is at of pH of 3.8.
  - b. Indicate the number of moles of each form that are present. (Show your work).

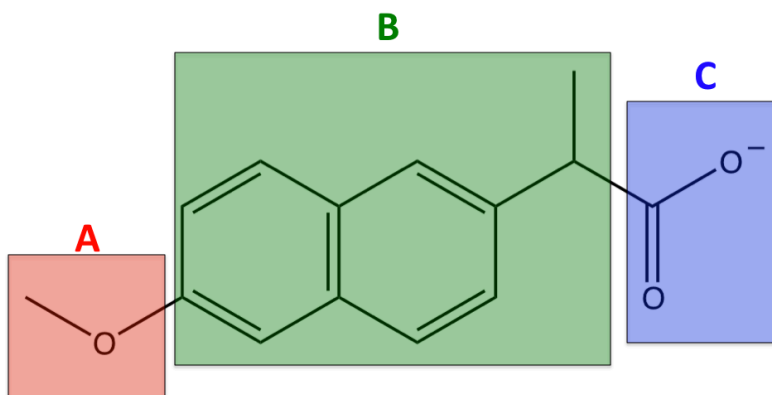
4. The sidechains of the following amino acids on COX-2 interact with naproxen:

R120	V349	L352	Y355	Y385
W387	A527	L531	S530	G526

Below, the structure of naproxen is divided into three chemical regions (A, B, and C). Predict to which chemical region of naproxen each of the amino acid sidechains of COX-2 listed above will interact. List each amino acid below only one box of the image.



5. Use a computer to investigate the high resolution structure of naproxen:COX-2 complex. Indicate the chemical region of naproxen (abbreviated "NPS" in Pymol) to which each of the amino acid sidechains listed in #4 actually interacts. List each amino acid below only one box of the image.



**6. Are there any surprising results when you compare your predictions in #4 to the molecular structure in #5? Justify these discrepancies with chemical reasoning.**