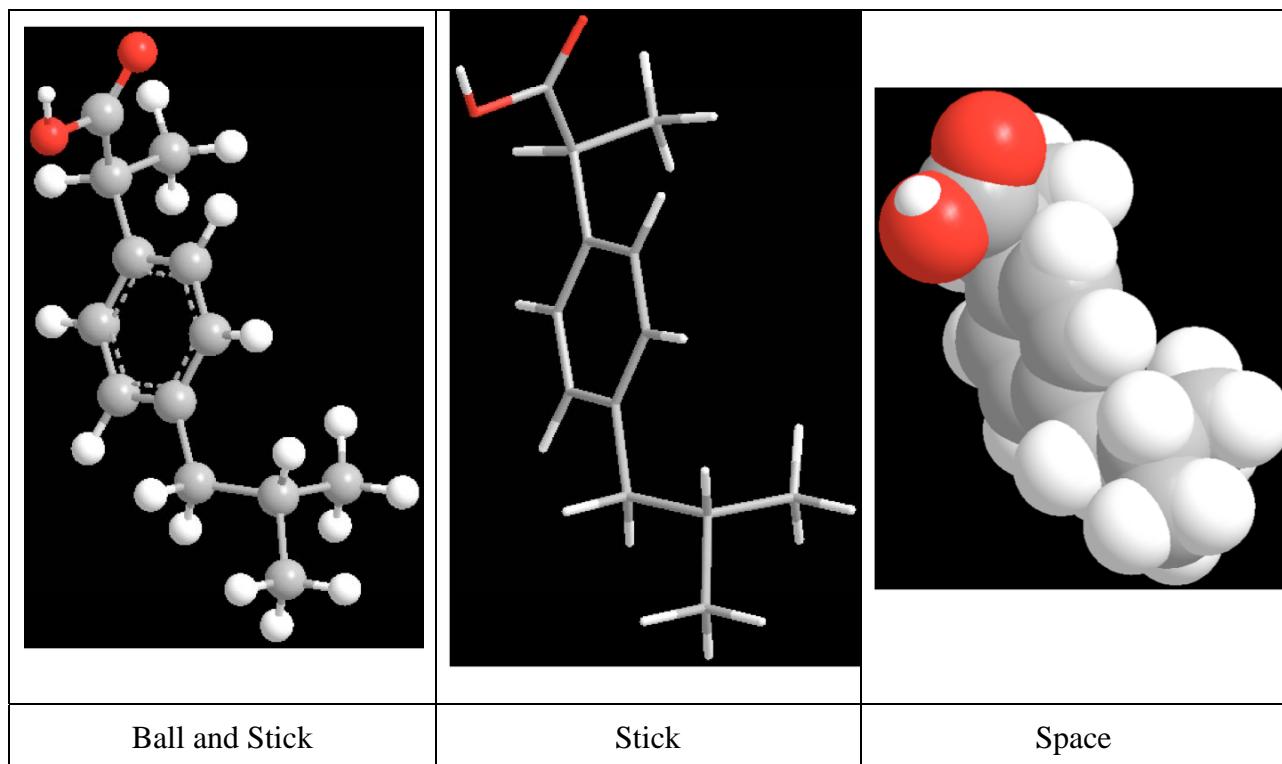


Part A

The structure of advil, 2-[4-(2-methylpropyl)phenyl]propanoic acid, consists of a planar benzene ring with two substituents in para-relation: The ring is attached to an isobutyl group and to the C2-atom of propanoic acid (Figure 1). Important bond angles include the bonds between the benzene and propanoic acid, 120.3° ; between the benzene and the iso-butyl, 120.9° , and between the carboxylic acid and the isopropyl, 111.2° . The dihedral angle between the propanoic acid and the benzene is approximately 101.0° , and the dihedral between the benzene and the isobutyl is 102.0° . Important bond lengths include the bonds from the benzene to propanoic acid, 1.77 \AA and from the first carbon on the propanoic acid to the carboxylic carbon, 1.52 \AA .

Figure 1. Advil, 2-[4-(2-methylpropyl)phenyl]propanoic acid.



Part B

Ibuprofen is an NSAID drug, used to inhibit cyclooxygenase.¹ The active site for cyclooxygenase is located on the interior of the protein and connected to the membrane by a long, non-polar channel. Hydrogen bonding, visible in Figure 2, is the main interaction between ibuprofen and the residues in the active site. Two hydrogen bonds form between the ibuprofen carboxylate and Arg120 and another hydrogen bond forms between the ibuprofen carboxylate and the phenolic hydroxyl of Tyr355. The hydrogen bond between the carboxylate on ibuprofen and Tyr355 is 2.78 Å, while the bonds between ibuprofen and Arg120 are 2.83 Å and 2.91 Å. There are no major changes to the structure when ibuprofen binds to the active site. After the formation of the hydrogen bonds, the amino acid side chains His90, Arg120, Tyr355, and Glu524 lock together to form a blockage in the active site channel, further locking the ibuprofen in place.

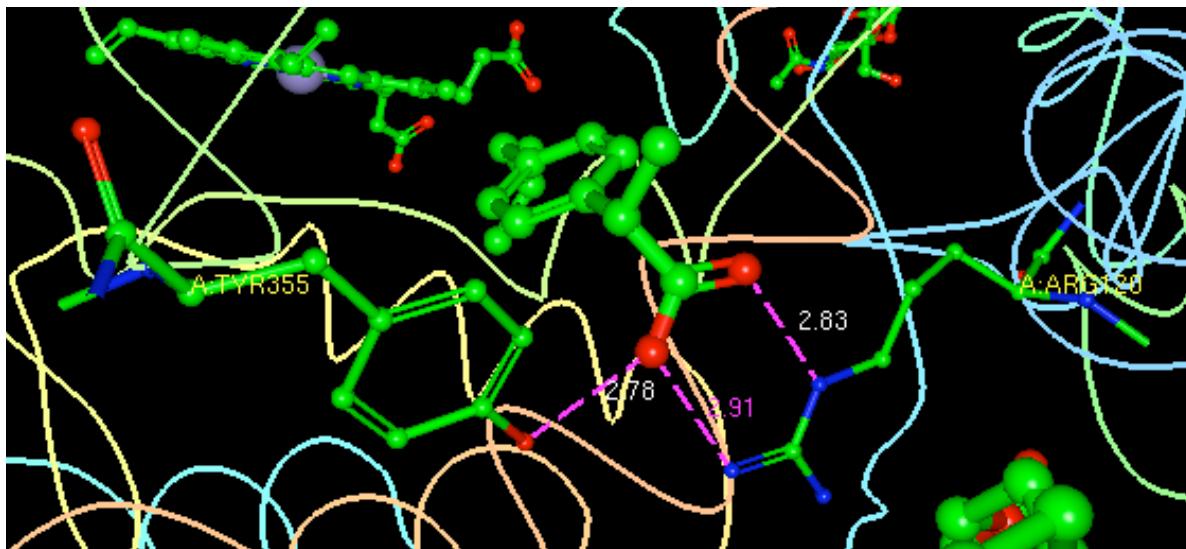


Figure 2. Hydrogen Bonding of Ibuprofen to TYR335 and ARG120.

1 Selinsky, B. S.; Gupta, K.; Sharkey, C. T.; Loll, P. J. Structural analysis of NSAID binding by prostaglandin H2 synthase: time-dependent and time-independent inhibitors elicit identical enzyme conformations. *Biochemistry* **2001**, *40*, 5172-5180.