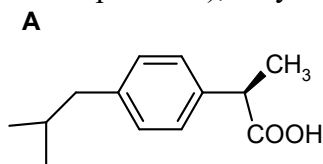


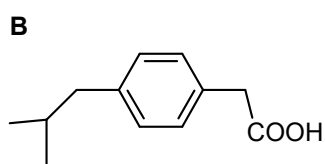
### 5th Assignment

your name:

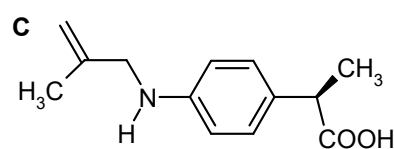
1. The analgesic and anti-inflammatory Ibuprofen faced a series of „me-too“ drugs shortly after its commercial launch, since the corresponding patent claimed the structure of ibuprofen (see compound **A**), only.



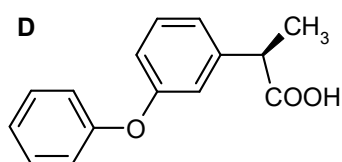
Ibuprofen 1966 Upjohn



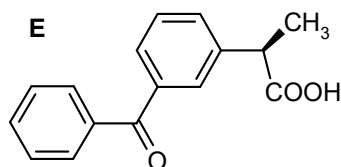
Ibufenac 1968 Boots Pure Drug



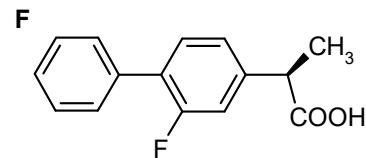
Alminoprofen 1971 Bouchera



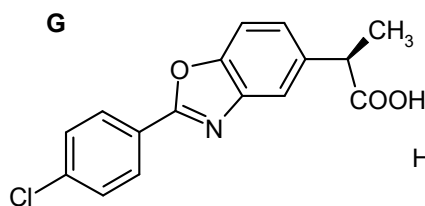
Fenoprofen 1971 Lilly



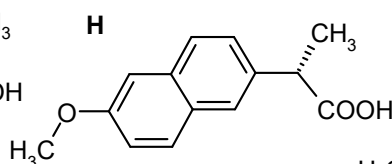
Ketoprofen 1972 AHP



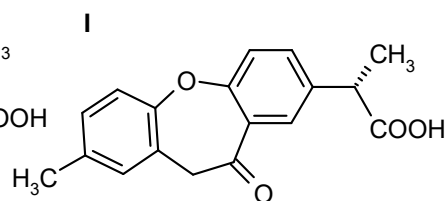
Flurbiprofen 1973 Upjohn



Benoxaprofen 1973 Lilly



Naproxen 1975 Syntec



Bermoprofen 1970 Dainippon

Report the matching compounds(s) (alphabetic character is sufficient) for the given SMARTS 1 to 4. Not all compounds may be matched (5 points for each correct assignment, deduction if more than one is falsely assigned)

1: OC(=O)C(C)c1ccc([C,N])cc1

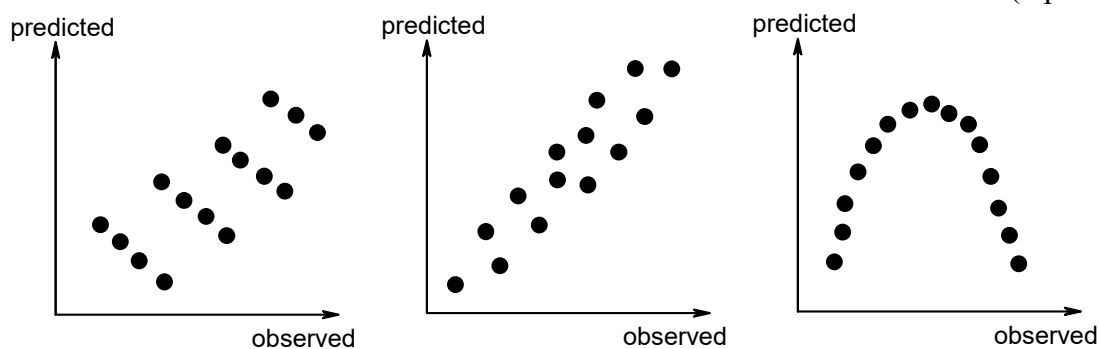
2: OC(=O)C(C)c1cccc([C,O,F])c1

3: OC(=O)C(C)c1cccc([#6])c1

4: OC(=O)C(C)c1cccc([C,O,#7])c1

Which compound is not matched by any of the SMARTS strings? (4 points)

2. Mark the correct value of the linear correlation for each of the plots, respectively (9 points)



$$r^2 = 0.00$$

$$r^2 = 0.60$$

$$r^2 = 0.90$$

$$r^2 = 0.95$$

$$r = -0.98$$

$$r = 0.00$$

$$r = 0.90$$

$$r = 0.98$$

$$r^2 = 0.00$$

$$r^2 = 0.50$$

$$r^2 = 0.60$$

$$r^2 = 0.85$$

3. Which of the QSAR equations (A or B, respectively C or D) is „better“ ? (According to which criteria ?) (10 points)

$n$ : number of molecules;  $r^2$ : squared correlation coefficient;  
 $q^2$ : cross-validated  $r^2$ ;  $s$ : standard error

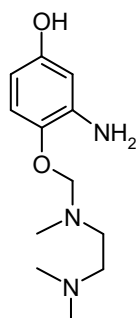
A)  $\log 1/K_i = 0.26(\pm 0.14)\text{ClogP} - 1.36(\pm 0.43)\text{NHB} + 9.66(\pm 0.39)\text{HL}$   
 where  $n = 21$ ,  $r^2 = 0.853$ ,  $q^2 = 0.746$ ,  $s = 0.326$

B)  $\log 1/K_i = 0.34(\pm 0.13)\text{ClogP} - 0.96(\pm 0.27)\text{MR} + 0.85(\pm 0.19)\text{B5Y}$   
 where  $n = 21$ ,  $r^2 = 0.853$ ,  $q^2 = 0.807$ ,  $s = 0.302$

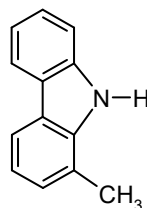
C)  $\log 1/C = 0.26(\pm 0.18)\text{ClogP} - 1.36(\pm 0.43)\text{MR} + 9.66(\pm 0.39)\text{B5Y}$   
 where  $n = 16$ ,  $r^2 = 0.821$ ,  $q^2 = 0.794$ ,  $s = 0.354$

D)  $\log 1/C = 0.23(\pm 0.15)\text{ClogP} - 1.20(\pm 0.56)\text{MR} + 10.74(\pm 0.67)\text{B5Y} - 0.62(\pm 0.12)\text{NN4} + 0.14(\pm 0.05)\text{GEOM6}$   
 where  $n = 16$ ,  $r^2 = 0.892$ ,  $q^2 = 0.632$ ,  $s = 0.325$

4. Chemical alterations shall be carried for the shown compounds. Draw a new structure that includes the suitable modifications. (12 points)



a) suggest a modification that reduces the number of freely rotatable bonds



b) suggest a modification that will lead to increased metabolic stability of the lower benzene ring