



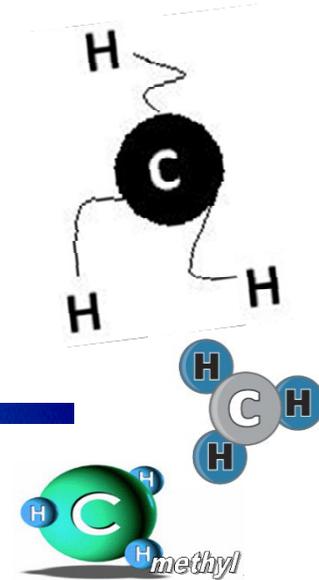
instituto de química

Universidade Federal do Rio de Janeiro

25 de maio de 2016

A metila *aprontando*

Química
na
Medicinal
chem



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Universidade Federal do Rio de Janeiro

Laboratório de Avaliação e
Síntese de Substâncias Bioativas

<http://www.lassbio.icb.ufrj.br/>



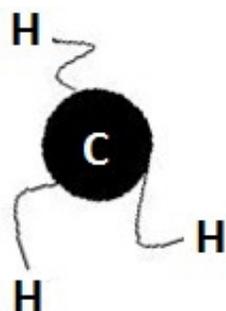
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Pretende-se demonstrar que a simplicidade estrutural do grupamento metila é inversamente proporcional aos efeitos que promove nos fármacos.



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C-H $\mu = 0,4$ D
 δ^+ / R^+
 $\pi = 0,22$
 $\sigma_{\text{meta}} = 0,51 / \sigma_{\text{para}} = 0,52$
 Rekker const = 0,702

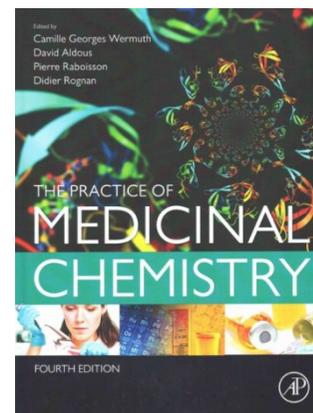
“The methyl group, so often considered as chemically inert, is able to alter deeply the pharmacological properties of a molecule.”

Camille G. Wermuth
(1933-2015)

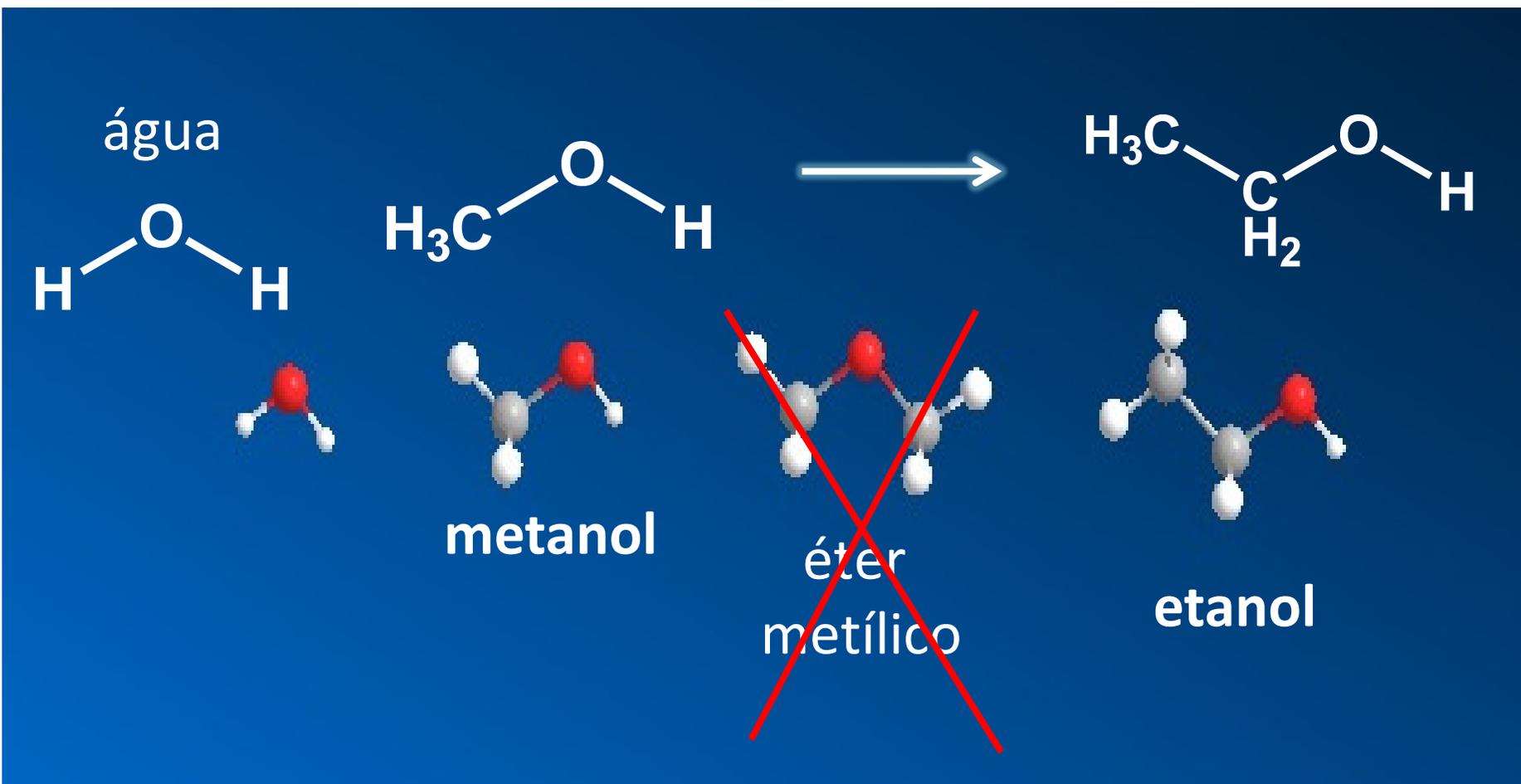
PRESTWICK CHEMICAL
 A medicinal chemistry company



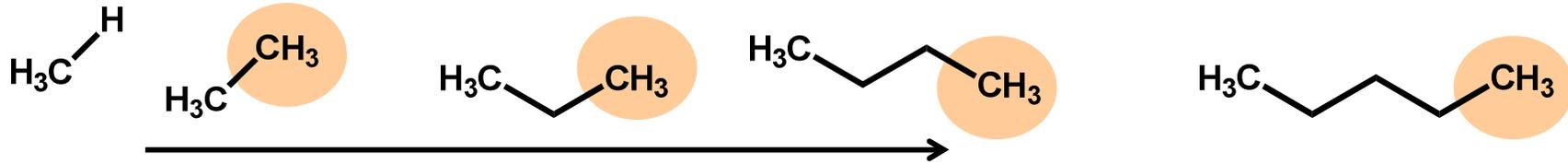
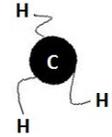
Prestwick Chemical., Ilkirch, FR (2010)



O início: princípio da homologia



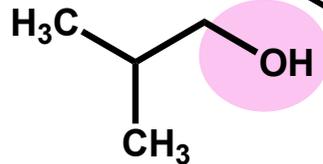
As séries homólogas



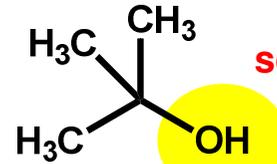
Lipofilicidade



n-butanol
solubilidade em água
8,2 g/100g



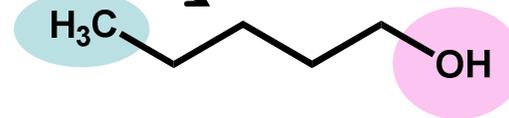
*i*sobutanol
solubilidade em água
12,5 g/100g



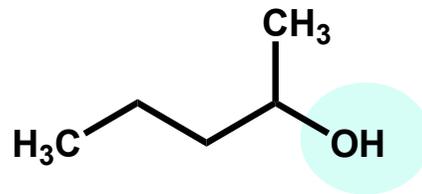
tert-butanol

solubilidade em água
miscível

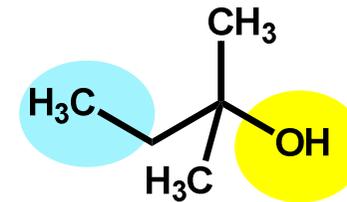
G Némethy, *Angew Chem Int Ed Engl* 1967, 6, 195



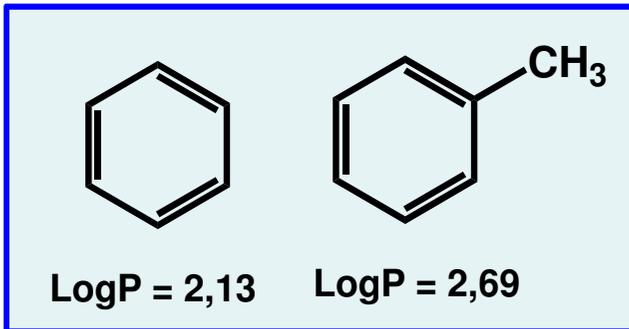
n-pentanol
solubilidade em água
2,4 g/100g



2-pentanol
solubilidade em água
4,9 g/100g



neopentanol
solubilidade em água
12,2 g/100g



CYP

As metilas e a morfina...

Índice de atividade analgésica



morfina
100

codeína
18

isocodeína
25

tebaína
0*

