

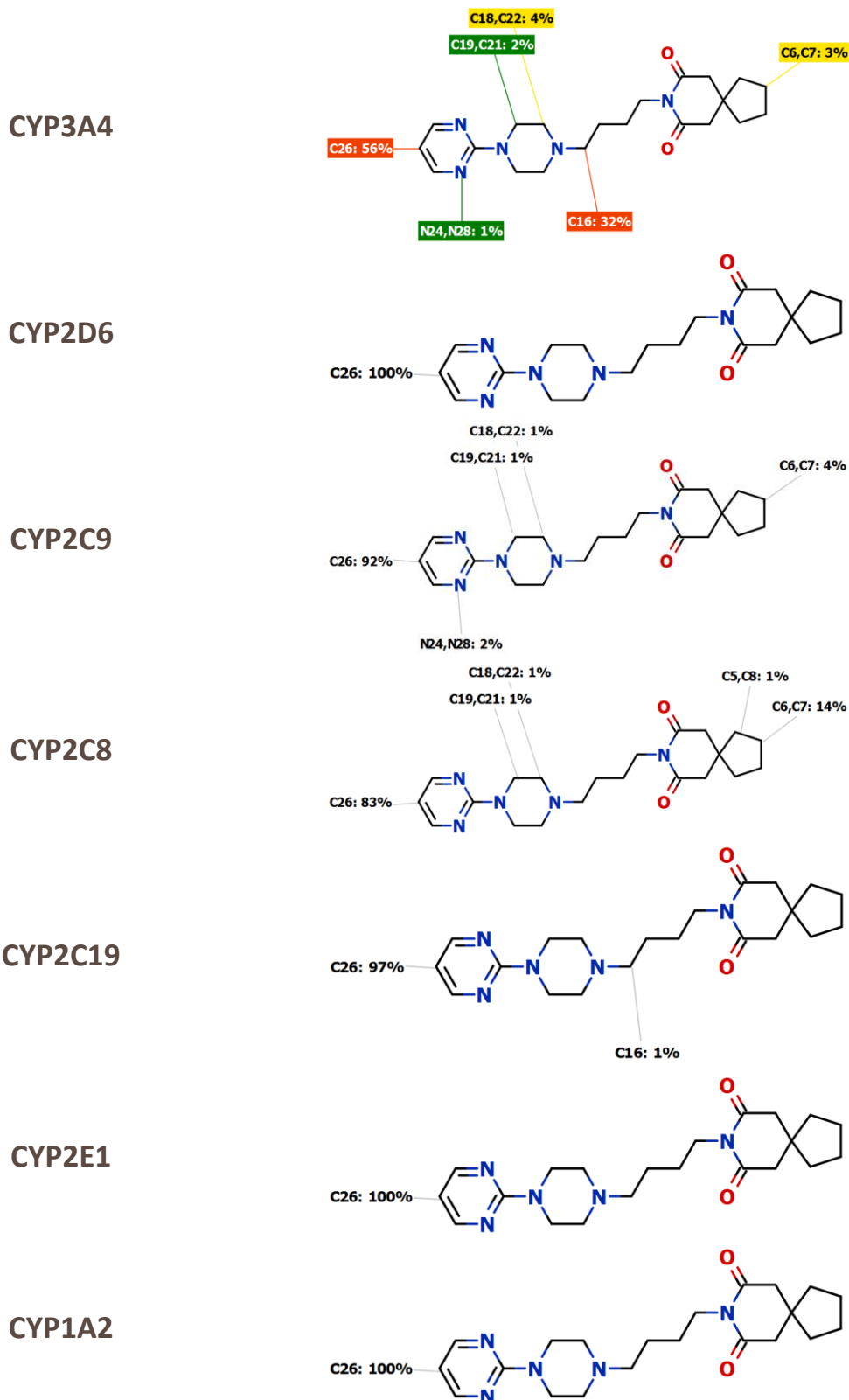
Predicting Regioselectivity and Lability of
Cytochrome P450 Metabolism using Quantum
Mechanical Simulations

SUPPORTING INFORMATION

REGIOSELECTIVITY RESULTS FOR EXAMPLE COMPOUNDS

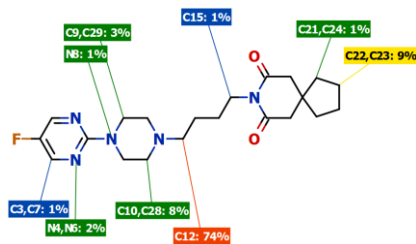
Example 1 - Developing Buspirone analogues with improved metabolic stability

Compound 1

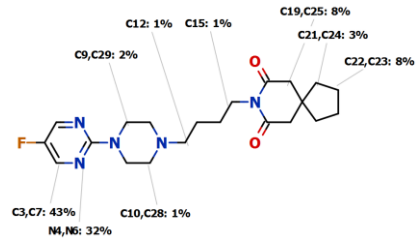


Compound 5

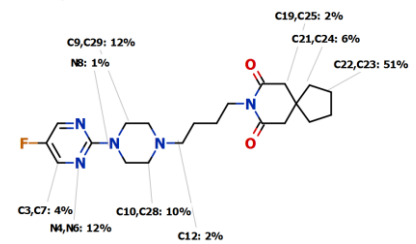
CYP3A4



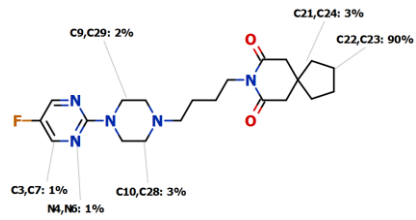
CYP2D6



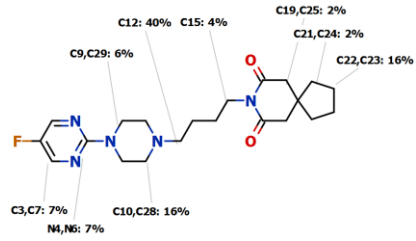
CYP2C9



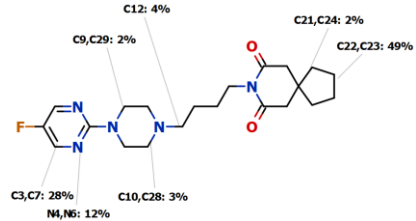
CYP2C8



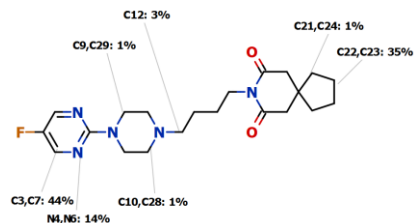
CYP2C19



CYP2E1

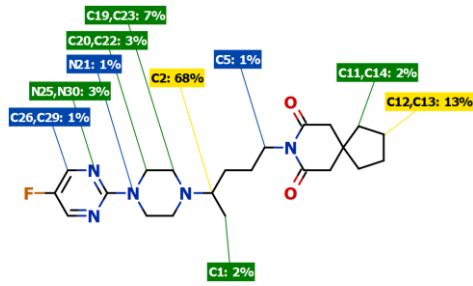


CYP1A2

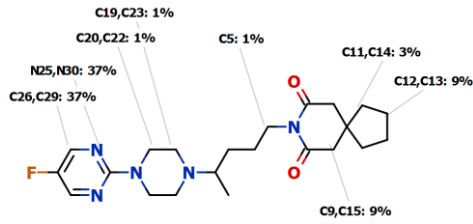


Compound 10

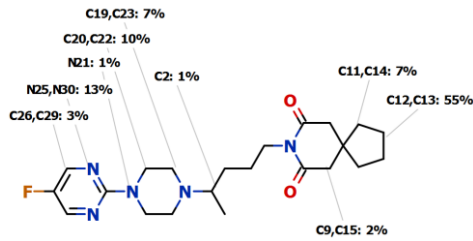
CYP3A4



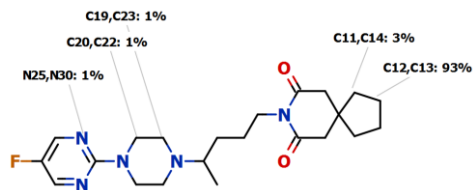
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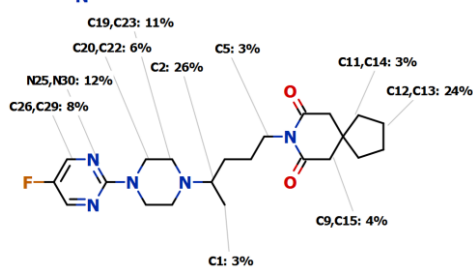
CYP2C9



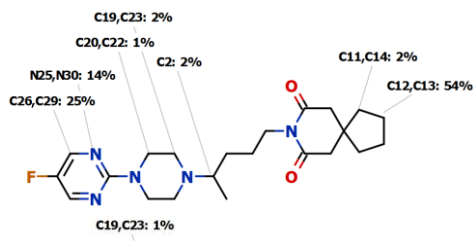
CYP2C8



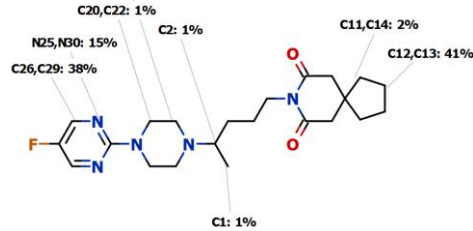
CYP2C19



CYP2E1

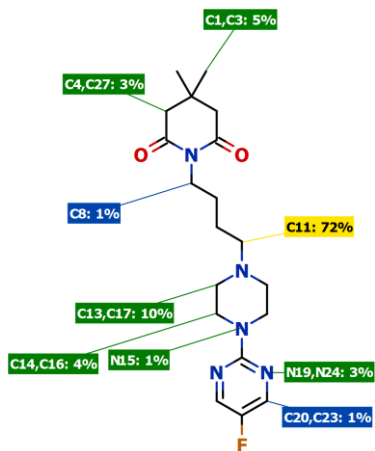


CYP1A2

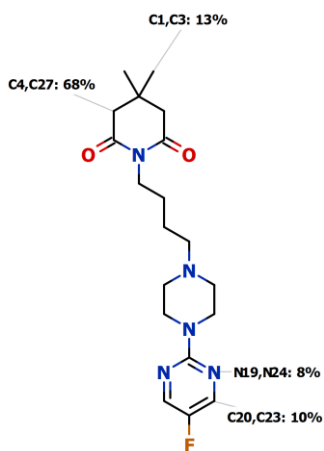


Compound 21

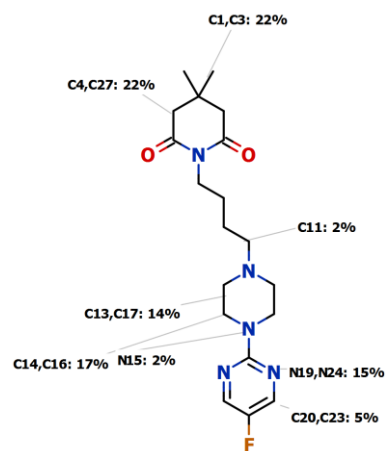
CYP3A4



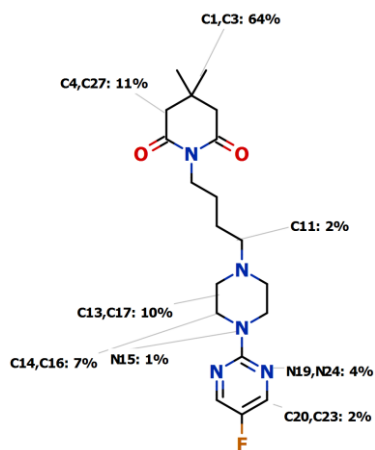
CYP2D6



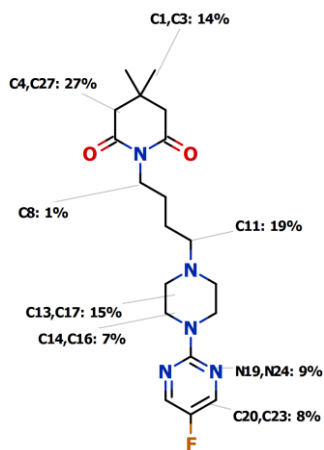
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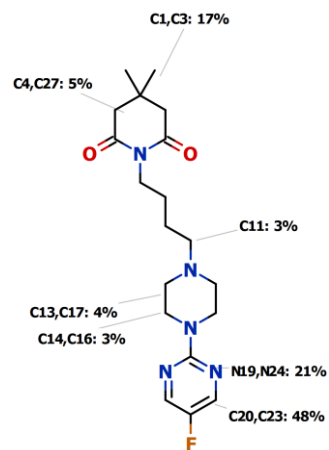
CYP2C8



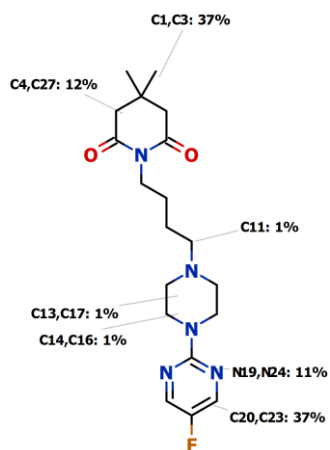
CYP2C19



CYP2E1

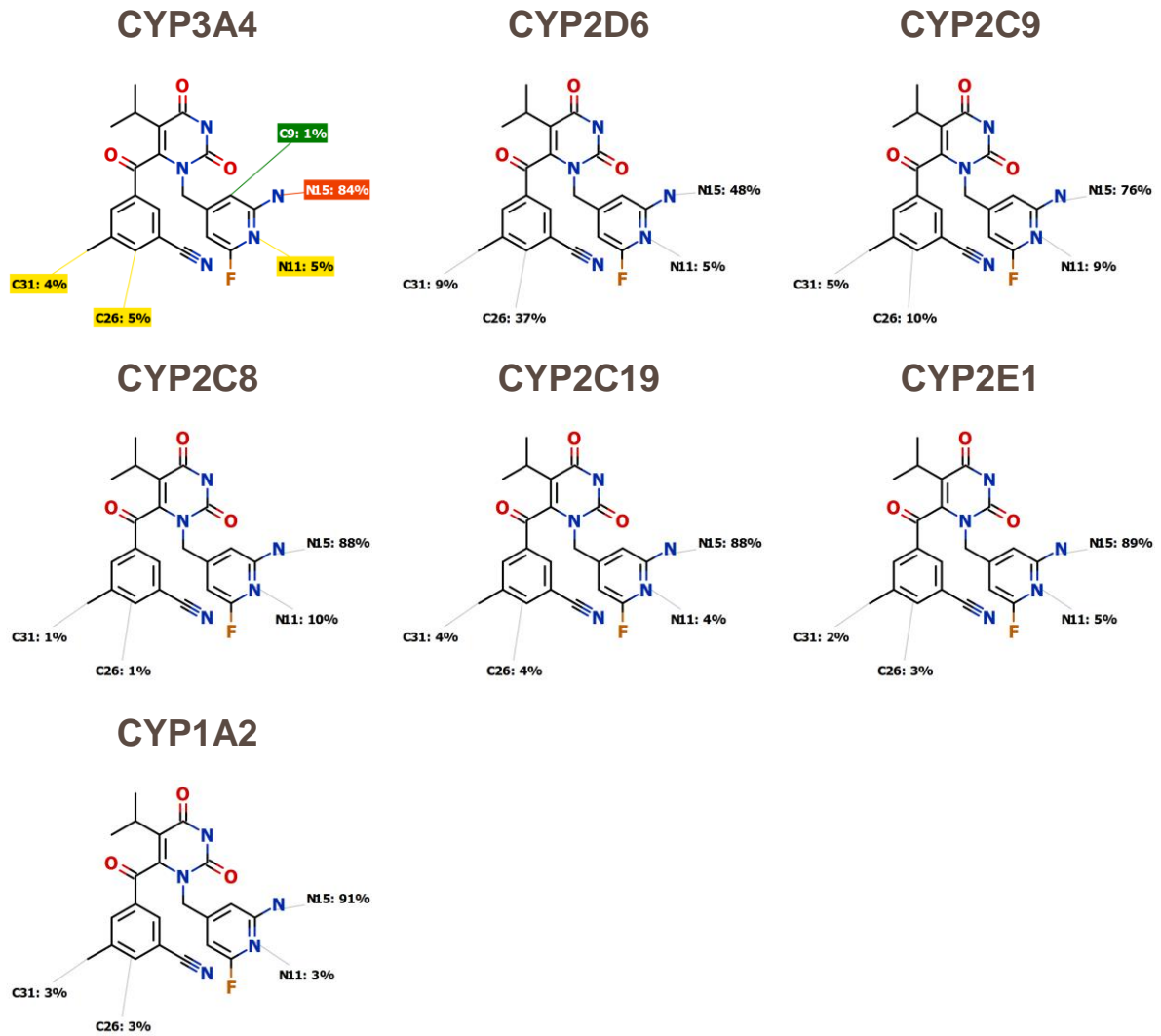


CYP1A2



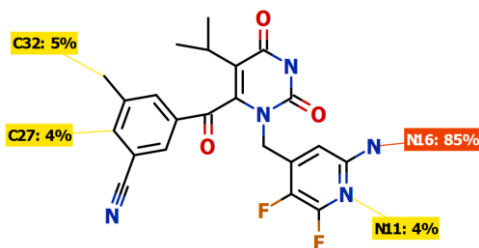
Example 2: Developing HIV-1 reverse transcriptase inhibitors with improved metabolic stability

Compound 1

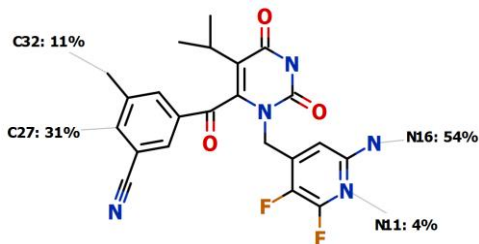


Compound 9

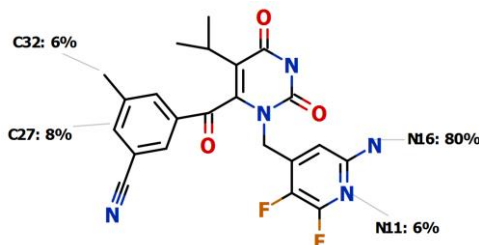
CYP3A4



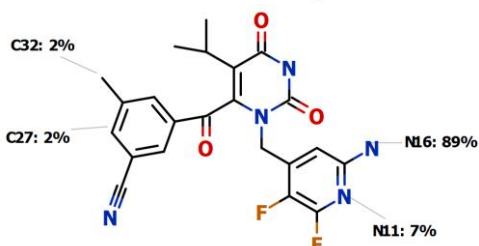
CYP2D6



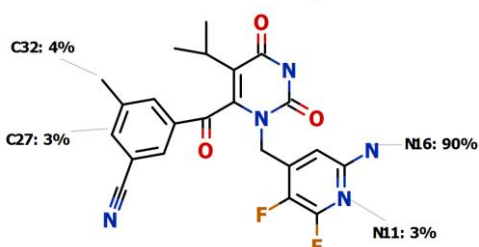
CYP2C9



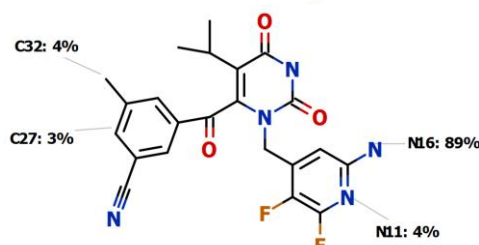
CYP2C8



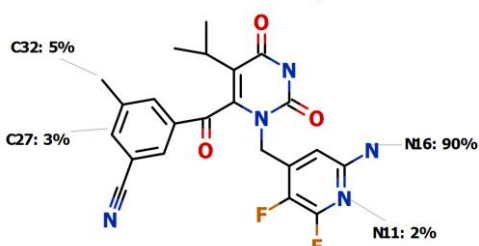
CYP2C19



CYP2E1

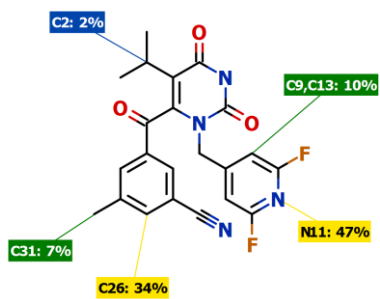


CYP1A2

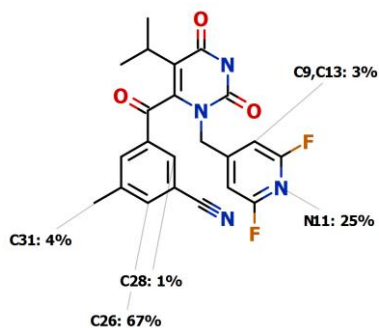


Compound 10

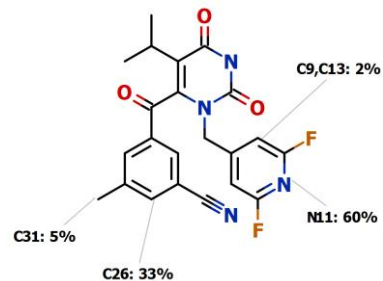
CYP3A4



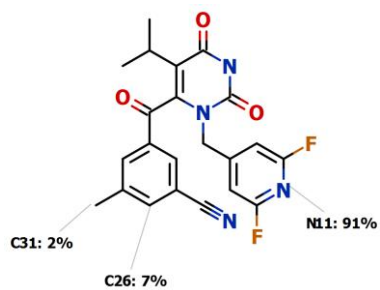
CYP2D6



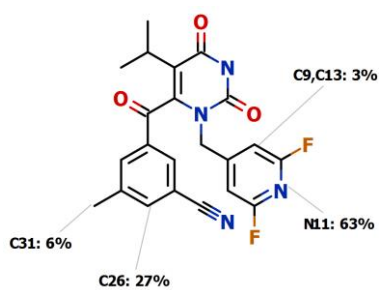
CYP2C9



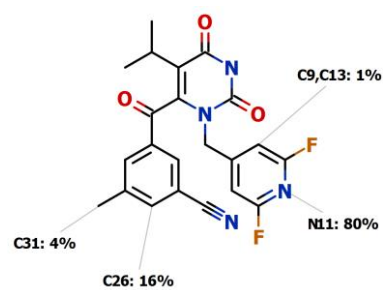
CYP2C8



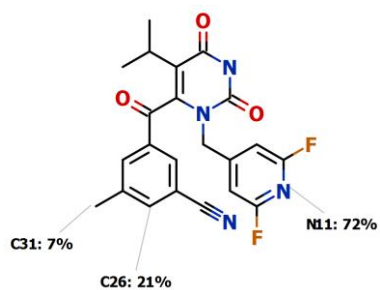
CYP2C19



CYP2E1

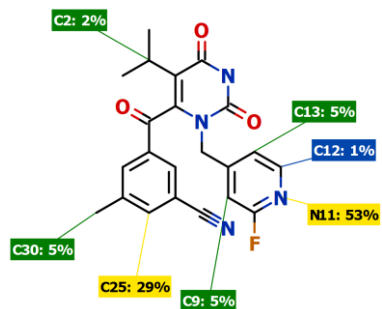


CYP1A2

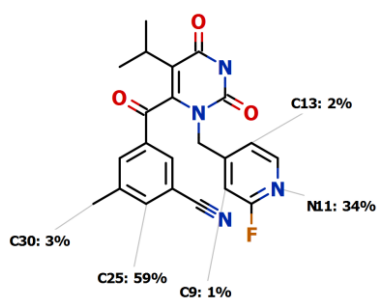


Compound 13

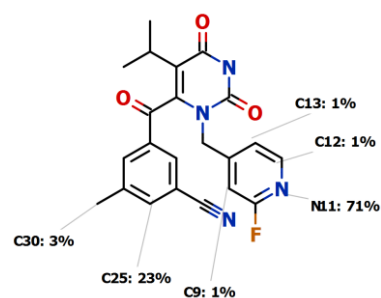
CYP3A4



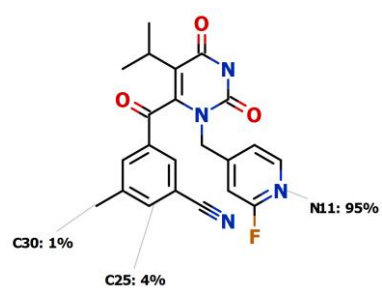
CYP2D6



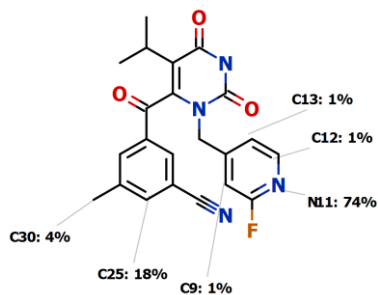
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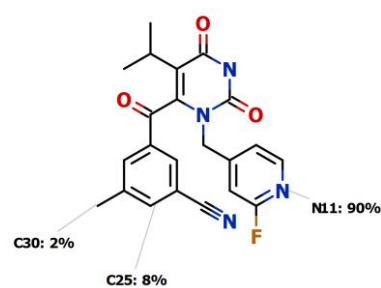
CYP2C8



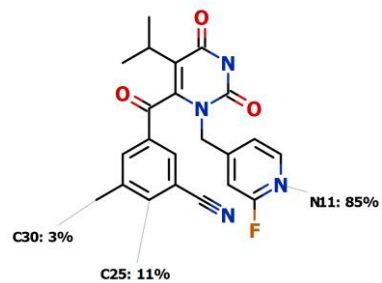
CYP2C19



CYP2E1



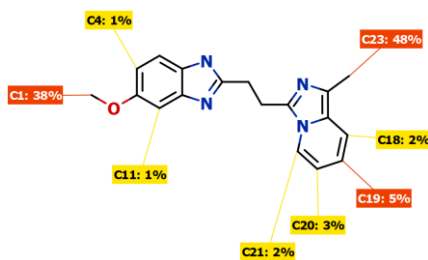
CYP1A2



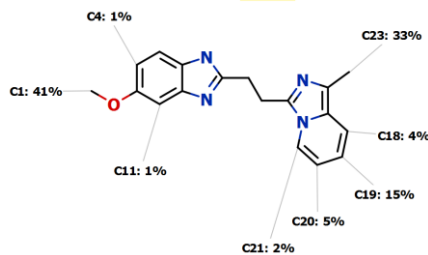
Example 3: Novel benzimidazoles as PDE10A inhibitors with improved metabolic stability

Compound 1

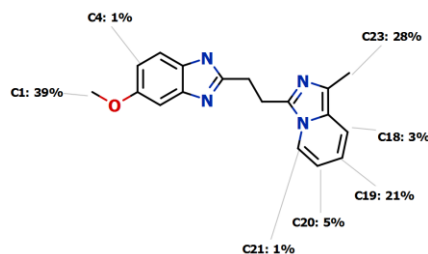
CYP3A4



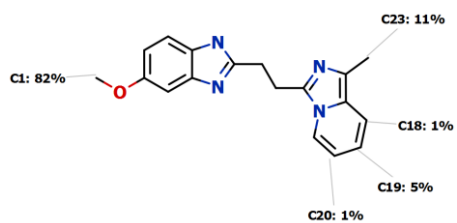
CYP2D6



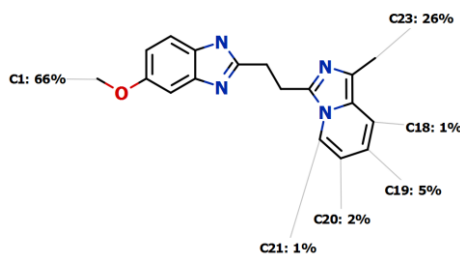
CYP2C9



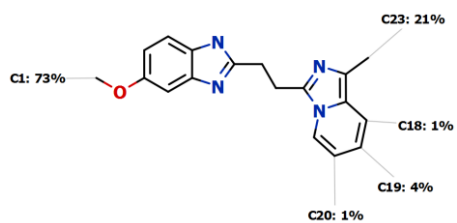
CYP2C8



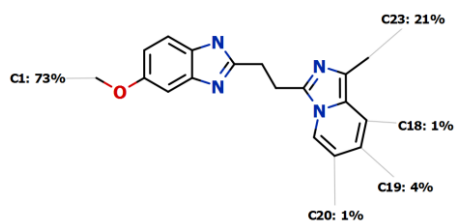
CYP2C19



CYP2E1

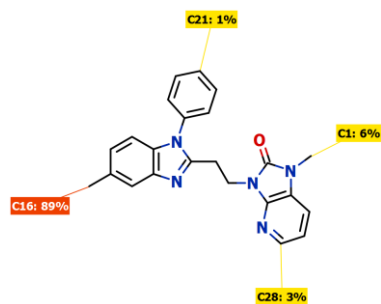


CYP1A2

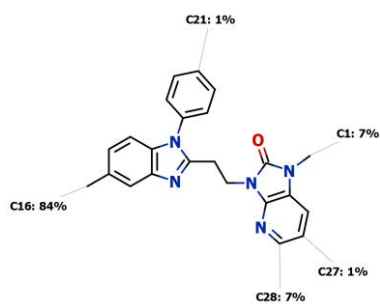


Compound 10b

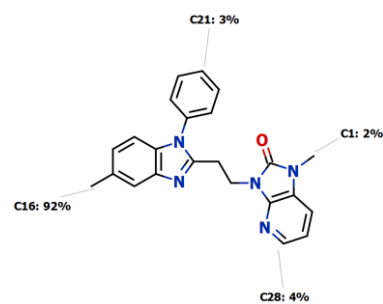
CYP3A4



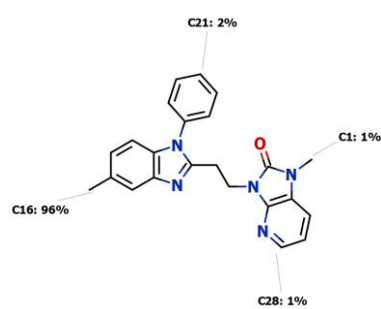
CYP2D6



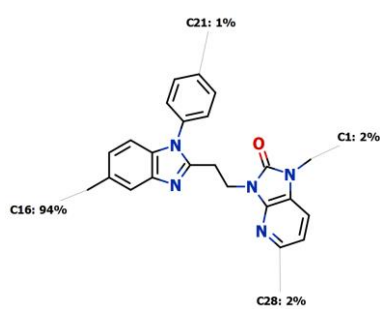
CYP2C9



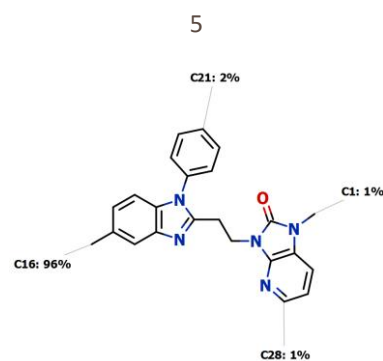
CYP2C8



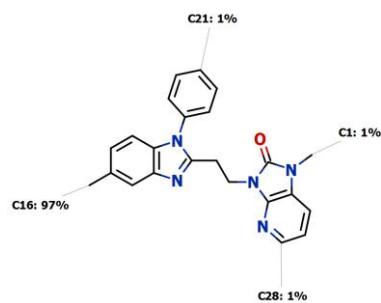
CYP2C19



CYP2E1

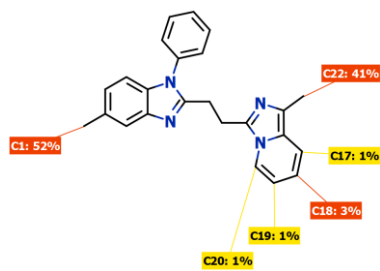


CYP1A2

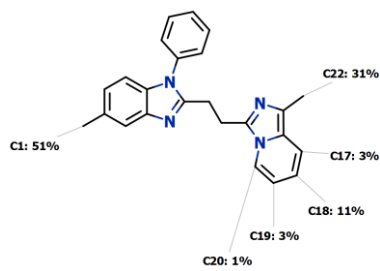


Compound 14a

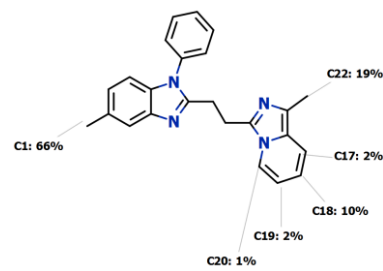
CYP3A4



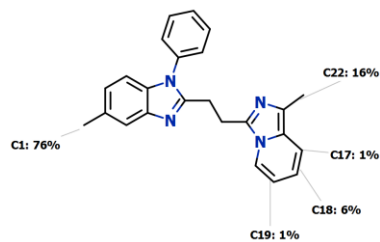
CYP2D6



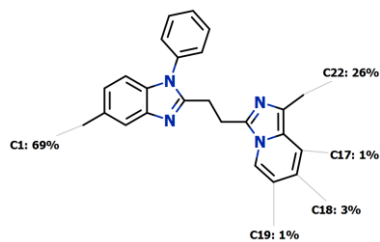
CYP2C9



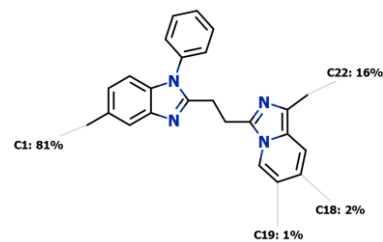
CYP2C8



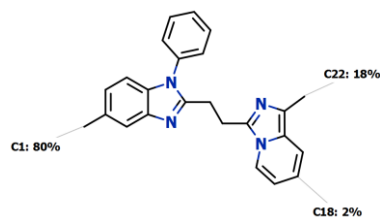
CYP2C19



CYP2E1

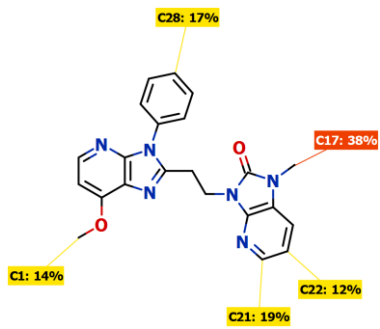


CYP1A2

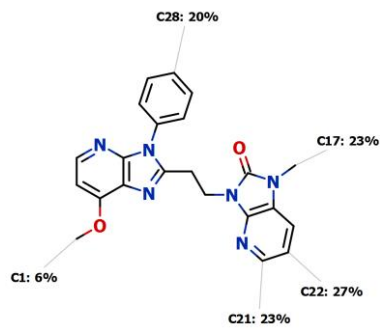


Compound 24a

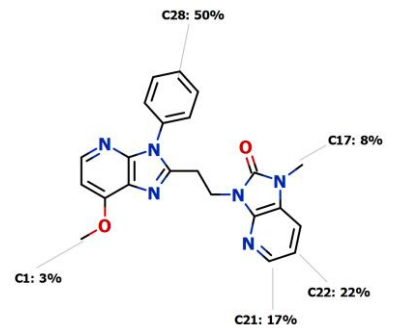
CYP3A4



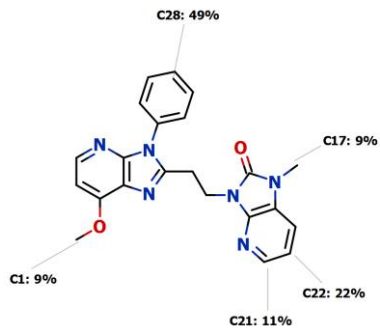
CYP2D6



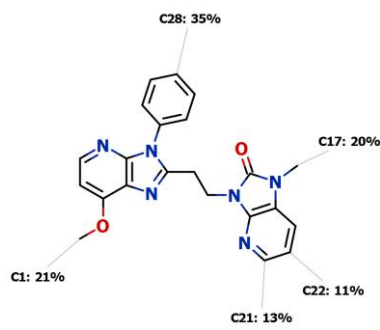
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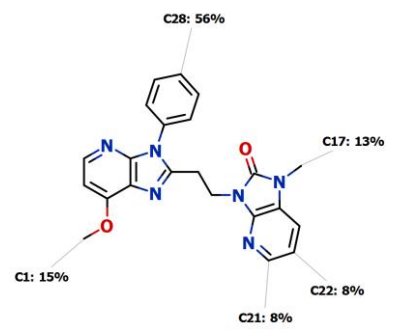
CYP2C8



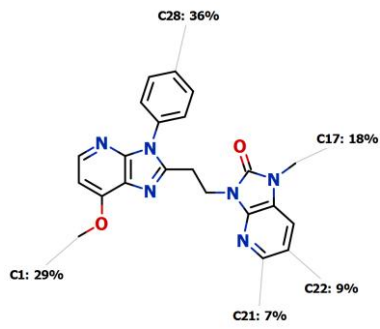
CYP2C19



CYP2E1

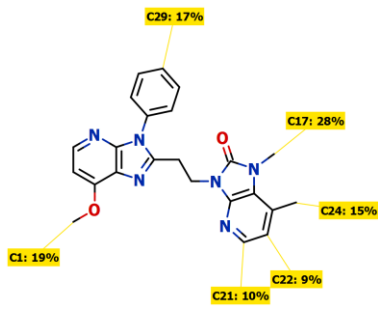


CYP1A2

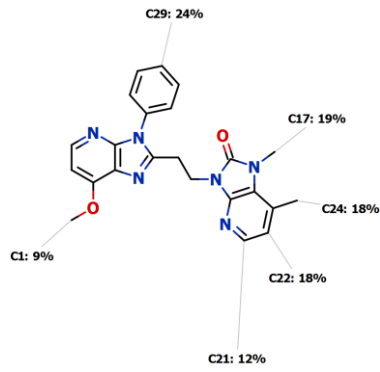


Compound 35

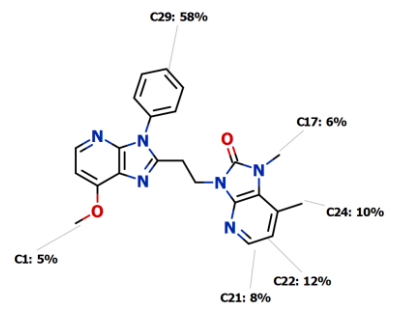
CYP3A4



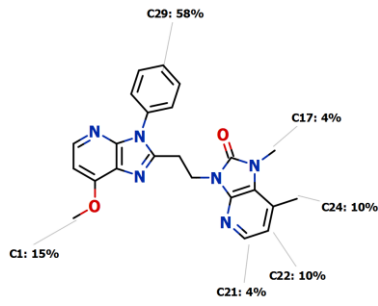
CYP2D6



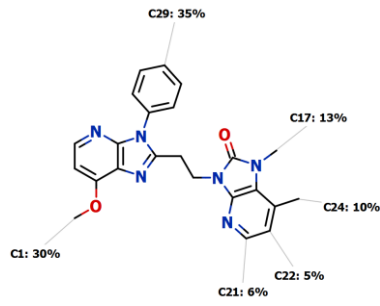
CYP2C9



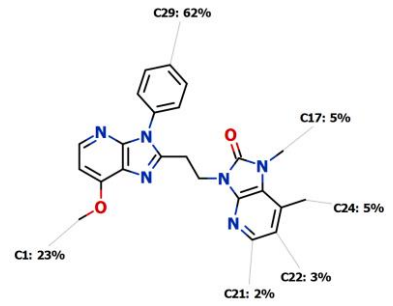
CYP2C8



CYP2C19



CYP2E1



CYP1A2

