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Poster Presentation

3-Aryl- and 3-Hetarylcoumarins: Potent HIV Protease Inhibitors

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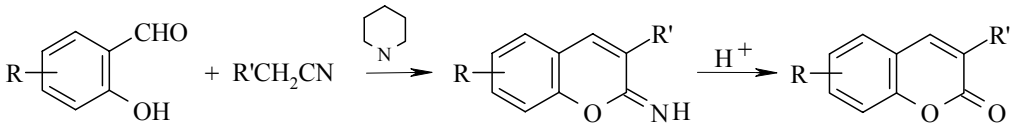
Among the numerous number of highly potent HIV protease inhibitors which have been described in the literature there are many substances with coumarin ring. In present work an activity of coumarins with amino group to HIV protease is estimated by computer modeling method.

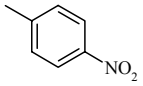
Based on X-ray structure of active centre of HIV-1 protease, the modeling of substrate and HIV-1 protease coordination was carried out by program *Swiss-PDBViewer*. We examined 3-aryl- and 3-(4-phenyl-2-thyazolyl)coumarins **6a,b**, **7a**, **8-10a,b** with NH_2-group in coumarin system and in phenyl substituent. It was shown that the most optimal structures among the selected compounds are **6a, 7a**, that can be bounded by amino group with Gly27 and Gly127 and 8-hydroxy group binds with Gly48 of HIV-1 protease active centre through the hydrohen bond.

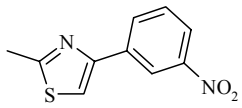
Compounds **6a,b**, **7a**, **8-10a,b** were synthesized at the following scheme:



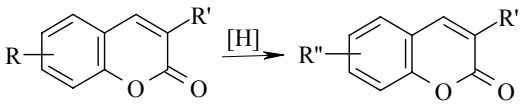
1a,b, 2a, 3-5a,b

1 R = 7-OH, **2** R = 7,8-$(OH)_2$, **3** R = 7-MeO, **4** R = 6-NO_2, **5** R = 6-Br

a R' = 

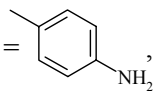
, **b** R' = 

Then NO_2-group had been reduced by ferric powder in acetic acid or by sodium dithionite.



1a,b, 2a, 3-5a,b **6a,b, 7a, 8-10a,b**

6 R" = 7-OH, **7** R" = 7,8-$(OH)_2$,
8 R" = 7-OMe, **9** R" = 6-NH_2, **10** R" = 6-Br,

a R' = 

, **b** R' =