POTENTIAL HIV-1 INTEGRASE INHIBITORS: MOLECULAR STRUCTURES OF SELECTED QUINOLINE DERIVATIVES

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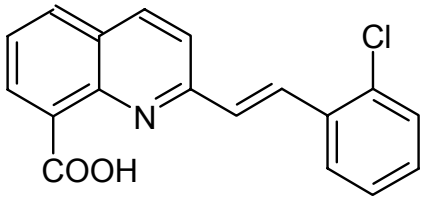
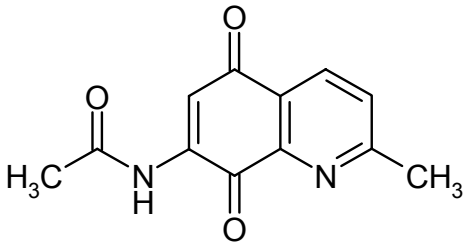
Integrase is the third main HIV enzyme, the first two: reverse transcriptase and protease are used as targets in Highly Active Antiretroviral Therapy (HAART). HIV-1 integrase (HIV-1 IN) is the enzyme that inserts the viral DNA into the host chromosome. There is no mammalian counterpart for that protein, which makes it an attractive target for antiviral drug design [1]. The combination therapy suppresses the replication of HIV-1 and makes the virus level undetectable in the plasma but still the virus exists in peripheral-blood mononuclear cells [2]. This means that discovery of new therapeutic agents is necessary to eradicate HIV-1 infection.

In our experiments we obtained single crystals of compounds, which were postulated to be potential inhibitors of HIV-1 IN.



(1)



(2)

The diffractometer KappaCCD was used for the intensity data collection (MoKα radiation), the phase problem was solved with direct metods.

Both molecules, (1) and (2), are approximately planar. The crystal packing of (1) is dominated by intermolecular non-classical C-H…O hydrogen bonds and short-contact interactions. In (2) the only interactions seem to be π-π stacking of the quinoline rings and week hydrogen bonds.

[1] Goldgur, Y.; Craigie, R.; Cohen, G.H.; Fujiwra, T.; Yoshinaga, T.; Fujishita, T.; Sugimoto, H.; Endo, T.; Murai, H.; Davies, D.R. PNAS **1999**, 96, 12040-13043.

[2] Ouali M.; Laboulais C.; Leh H.; Gill D.; Desmaële D.; Mekouar K.; Zouhiri F.; d'Angelo J.; Auclair Ch.; Mouscadet J.-F.; Le Bret M., J. Med. Chem. **2000**, 43, 1949-1957.