Poster Session I

Retroviruses

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NEW HIGHLY POTENT HIV-1 PROTEASE INHIBITORS

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The human immunodeficiency virus type 1 (HIV-1) encodes an aspartyl protease necessary for viral replication. It has been identified as a major target for the chemotherapeutic treatment of AIDS, because its inactivation leads to the formation of immature non-infectious virions. A number of groups have developed inhibitors of HIV-1 protease[1]. We report a short, efficient enantio- and stereospecific synthesis of new highly active protease inhibitors. The cornerstone of the synthetic strategy is a two step sequence: The diastereospecific epoxidation of 2,3-unsaturated carboxylic esters, derived by Wittig olefination of appropriately protected α- aminoaldehydes and the enantio- and regiospecific opening of these epoxides with N-, S- and O-nucleophiles leading exclusively to 2-hetero substituted statine analogues. Structure activity relationships will be presented, culminating in SDZ 282870, a promising candidate for further development towards an anti-AIDS drug.

1) Graves, M.C. in: Structure and Function of the Aspartic Proteinases (ed. Dunn, B.M.) p395; Plenum Press 1991.