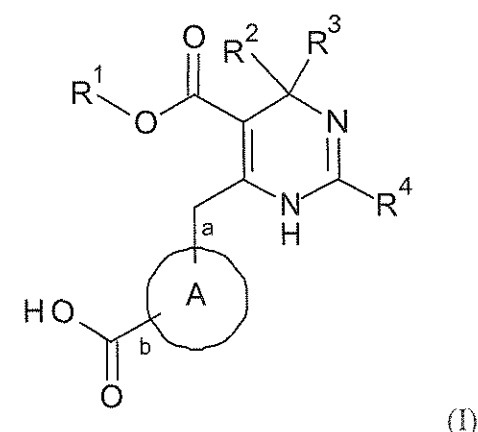


Heteroaryldihydropyrimidines or HAP, including compounds named Bay 41-4109, Bay 38-7690 and Bay 39-5493, were discovered in a tissue culture-based screening (Deres K. et al. *Science* **2003**, 893). These HAP analogs act as synthetic allosteric activators and are able to induce aberrant capsid formation that leads to degradation of the core protein. HAP analogs also
5 reorganized core protein from preassembled capsids into noncapsid polymers, presumably by interaction of HAP with dimers freed during capsid 'breathing', the transitory breaking of individual intersubunit bonds. Bay 41-4109 was administered to HBV infected transgenic mouse or humanized mouse models and demonstrated *in vivo* efficacy with HBV DNA reduction (Deres K. et al. *Science* **2003**, 893; Brezillon N. et al. *PLoS ONE* **2011**, e25096). It was also shown that
10 bis-ANS, a small molecule that acts as a molecular 'wedge' and interferes with normal capsid-protein geometry and capsid formation (Zlotnick A. et al. *J. Virol.* **2002**, 4848-4854).

SUMMARY OF THE INVENTION

15 Objects of the ~~present invention~~embodiments disclosed herein are novel compounds of formula I, their manufacture, medicaments based on a compound in accordance with the ~~invention-disclosure~~invention-disclosure and their production as well as the use of compounds of formula I as HBV inhibitors and for the treatment or prophylaxis of HBV infection. The compounds of formula I show superior anti-HBV activity. In addition, the compounds of formula I also show high
20 selectivity index, better solubility and mouse SDPK profiles.

In one aspect, there is provided compounds of formula (I)

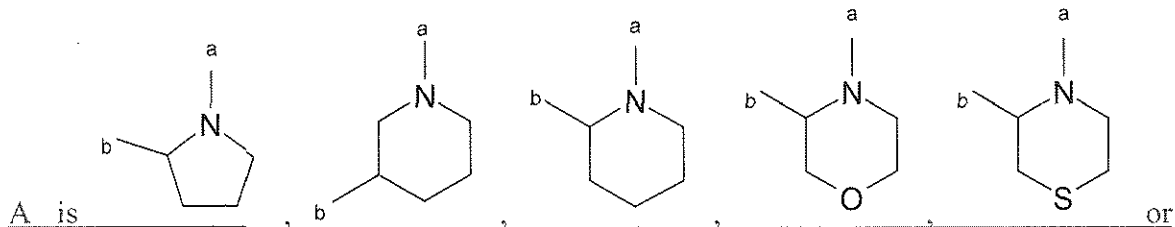
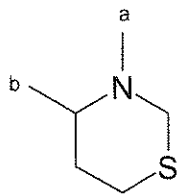


wherein

R¹ is C₁₋₆alkyl or trifluoromethyl-C_xH_{2x}-, wherein x is 1-6;

25 One of R² and R³ is phenyl, which is once or twice or three times substituted by C₁₋₆alkyl, cyano or halogen; and the other one is hydrogen or deuterium;

R⁴ is phenyl, thiazolyl, oxazolyl, imidazolyl, thienyl or pyridinyl, which is unsubstituted or substituted by C₁₋₆alkyl, C₁₋₆alkylsulfanyl, halogen or cycloalkyl, where said C₁₋₆alkyl can be further optionally substituted with halogen;

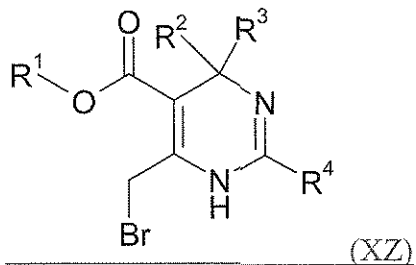
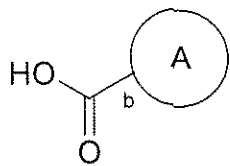


5 , which is unsubstituted or substituted by groups selected from C₁₋₆alkyl, deuterium and halogen;

or pharmaceutically acceptable salts, or enantiomers, or diastereomers thereof.

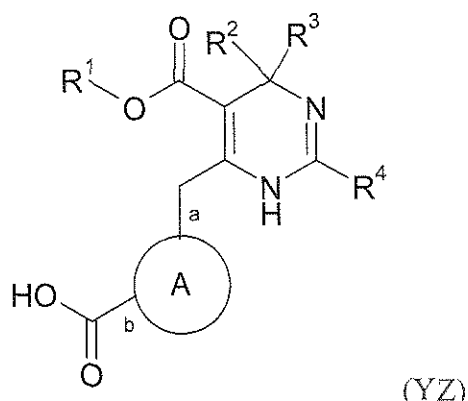
In another aspect, there is provided a process for the preparation of a compound as defined herein comprising the reaction of

10 (a) a compound of formula (XZ)



with in the presence of a base;

(b) a compound of formula (YZ)



under chiral separation condition;

wherein R¹ to R⁴ and A are as defined herein.

5 In another aspect, there is provided use of a compound as defined herein for the preparation of a medicament for the treatment or prophylaxis of hepatitis B virus infection.

 In another aspect, there is provided a compound as defined herein for the treatment or prophylaxis of hepatitis B virus infection.

10 In another aspect, there is provided a compound as defined herein as inhibitors of hepatitis B virus.

 In another aspect, there is provided a compound as defined herein, when manufactured according to a process as defined herein.

DETAILED DESCRIPTION OF THE INVENTION

15 **DEFINITIONS**

 As used herein, the term “C₁₋₆alkyl” alone or in combination signifies a saturated, linear- or branched chain alkyl group containing 1 to 6, particularly 1 to 4 carbon atoms, for example methyl, ethyl, propyl, isopropyl, 1-butyl, 2-butyl, *tert*-butyl and the like. Particular “C₁₋₆alkyl”

20 groups are methyl, ethyl, isopropyl and *tert*-butyl.

 The term “-C_xH_{2x}-” alone or in combination signifies a saturated, linear or branched chain alkyl group containing from 1 to 6 carbon atoms, particularly from 1 to 4 carbon atoms.

 The term “cycloalkyl”, alone or in combination, refers to a saturated carbon ring containing from 3 to 7 carbon atoms, particularly from 3 to 6 carbon atoms, for example,

~~25. The use of a compound according to any one of claims 1 to 21 for the treatment or prophylaxis of hepatitis B virus infection.~~

5 ~~26~~25. The use of a compound according to any one of claims 1 to 21 for the preparation of a medicament for the treatment or prophylaxis of hepatitis B virus infection.

~~27~~26. A compound according to any one of claims 1 to 21 for the treatment or prophylaxis of hepatitis B virus infection.

10

~~28~~27. A compound according to any one of claims 1 to 21 as inhibitors of hepatitis B virus.

~~29~~28. A compound according to any one of claims 1 to 21, when manufactured according to a process of claim 18.

15

~~30. A method for the treatment or prophylaxis of hepatitis B virus infection, which method comprises administering an effective amount of a compound as defined in any one of claims 1 to 21.~~

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