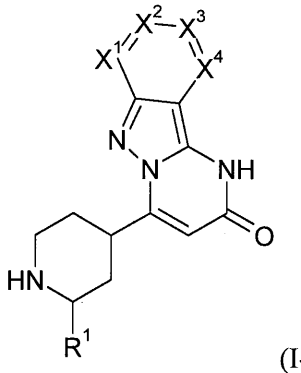
Patent claims

1. Compound of the formula (I-A)



(I-A)

in which

R^1 is selected from hydrogen and C_1-C_4 alkyl;

X^1 is selected from nitrogen and C-R^2;

X^2 is selected from nitrogen and C-R^3;

X^3 is selected from nitrogen and C-R^4;

X^4 is selected from nitrogen and C-R^5;

with the proviso that 0, 1 or 2 of X^1 to X^4 are nitrogen; and

R^2, R^3, R^4, and R^5 are independently from each other selected from hydrogen, halogen, C_1-C_4 alkyl, C_1-C_4 alkenyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, cyano, amino, nitro, mono- or dialkylamino, hydroxy, thiol, carboxyl, C_3-C_7 cycloalkyl, 5 to 6 membered heteroaryl, the 5 to 6 membered heteroaryl being optionally substituted with one, two, or three substituents selected from C_1-C_4 alkyl, and phenyl, the phenyl being optionally substituted with one, two, or three substituents selected from halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy, or

a group of a formula selected from –CO-NR^7R^8, -NH-CO-R^9, -CO-O-R^9, –CO-R^9, -SO_2R^{10}, -$SO_2NR^{11}R^{12}$,–SR^{10}, CH_2CN, -$CH_2NR^{11}R^{12}$, -CH_2OR^{10}, wherein

R^7 and R^8 independently from each other represent hydrogen, C_1-C_4 alkyl, C_6 aryl, and 5-6 membered heteroaryl;

R^9 represents, C_1-C_4 alkyl, C_6 aryl, and 5-6 membered heteroaryl;

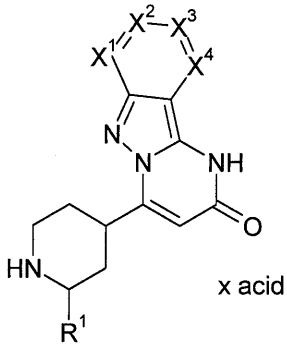
R^{10} represents C_1-C_4 alkyl;

R^{11} and R^{12} independently from each other represent hydrogen, and C_1-C_4 alkyl;

with the proviso that zero, one, two, or three of R^2 to R^5 are different from hydrogen,

and salts, solvates, and solvates of the salts.

2. Compound of the formula (I-B)



(I-B)

in which R^1, X^1, X^2, X^3, and X^4 are as defined in claim 1,

and salts, solvates, and solvates of the salts.

3. Compound of formula (I-A) or (I-B) as defined in claim 1 or 2,

in which

R^1 is selected from hydrogen and C_1-C_4 alkyl;

X^1 is selected from nitrogen and C-R^2;

X^2 is selected from nitrogen and C-R^3;

X^3 is selected from nitrogen and C-R^4;

X^4 is selected from nitrogen and C-R^5;

with the proviso that 0, 1 or 2 of X^1 to X^4 are nitrogen; and

R^2, R^3, R^4, and R^5 are independently from each other selected from hydrogen, halogen, C_1-C_4 alkyl, C_1-C_4 alkenyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, cyano, amino, nitro, mono- or dialkylamino, hydroxy, carboxyl, C_3-C_7 cycloalkyl, 5 to 6 membered heteroaryl, the 5 to 6 membered heteroaryl being optionally substituted with one, two, or three substituents selected from C_1-C_4 alkyl, and phenyl, the phenyl being optionally

substituted with one, two, or three substituents selected from halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy;

with the proviso that zero, one, two, or three of R^2 to R^5 are different from hydrogen,

and salts, solvates, and solvates of the salts.

4. Compound of formula (I-A) or (I-B) according to any of claims 1 to 3 in which

R^1 is selected from hydrogen and methyl;

X^1 is C-R^2

X^2 is C-R^3

X^3 is C-R^4

X^4 is C-R^5; and

R^2, R^3, and R^4, are independently from each other selected from hydrogen and fluorine;

R^5 is selected from hydrogen, halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, cyano, amino, nitro, dialkylamino, hydroxy, carboxyl, C_3-C_7 cycloalkyl, triazolyl (bonded via N), thiazolyl, thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl (bonded via N or C), the pyrazolyl being optionally substituted with one or two substituents selected from C_1-C_4 alkyl, and phenyl, the phenyl being optionally substituted with one or two substituents selected from halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkoxy;

with the proviso that zero, one, or two of R^2 to R^5 are different from hydrogen,

and its salts, solvates, and solvates of the salts.

5. Compound of the formula (I-A) or (I-B) according to any of any of claims 1 to 4 in which

R^1 is hydrogen;

X^1 is C-R^2

X^2 is C-R^3

X^3 is C-R^4

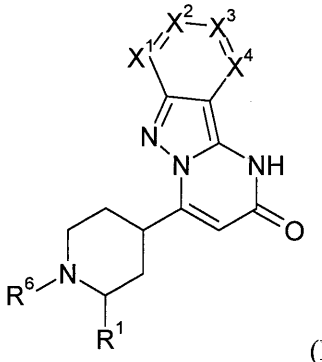
X^4 is C-R^5

R^2 to R^4 are hydrogen, and

R^5 is chlorine;

and its salts, solvates, and solvates of the salts.

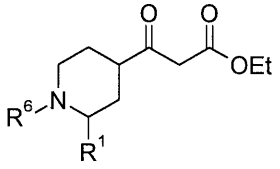
6. Process for preparing a compound of the formula (IV)



(IV)

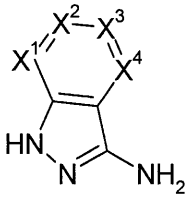
in which R^1, X^1, X^2, X^3, and X^4 each have the meaning as defined in any of claims 1 to 5 and R^6 represents an aminoprotective group, wherein

[A] a compound of the formula (II-A)



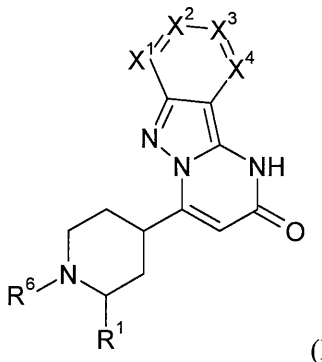
(II-A),

in which R^1 has the meaning given above and R^6 represents an amino protective group, is reacted with a compound of the formula (III)



(III)

in which X^1, X^2, X^3, and X^4 each have the meaning given above in an inert solvent, optionally in the presence of a base, to give a compound of the formula (IV)

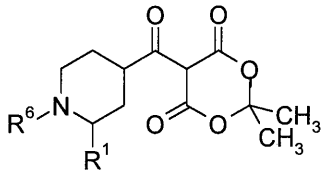


(IV)

in which R^1, R^6, X^1, X^2, X^3, and X^4 each have the meaning given above,

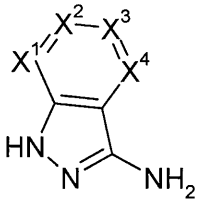
or

[B] a compound of the formula (II-B)



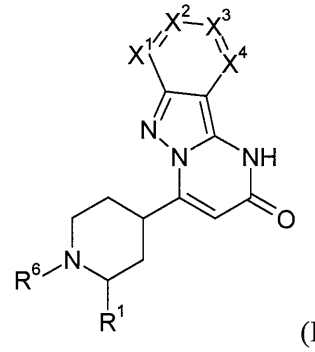
(II-B)

in which R^1 has the meaning given above and R^6 represents an amino protective group, is reacted with a compound of the formula (III)



(III)

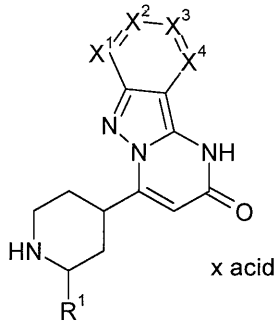
in which X^1, X^2, X^3, and X^4 each have the meaning given above in an inert solvent optionally in the presence of a base, to give a compound of the formula (IV)



(IV)

in which R^1, X^1, X^2, X^3, and X^4 each have the meaning as defined in any of claims 1 to 5 and R^6 represents an amino protective group.

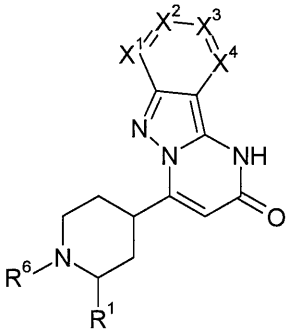
7. Process for preparing compounds of the formula (I-B)



(I-B)

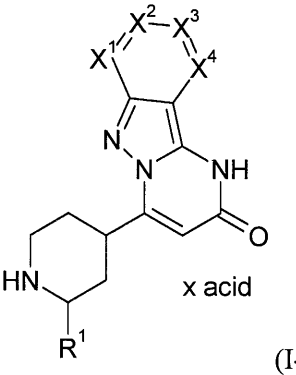
in which R^1, X^1, X^2, X^3, and X^4 each have the meaning as defined in any of claims 1 to 5,

wherein a compound of the formula (IV)



(IV)

in which R^1, X^1, X^2, X^3, and X^4 each have the meaning as defined in any of claims 1 to 5, and R^6 represents an acid cleavable amino protective group, is reacted to the compound of the formula (I-B) by addition of an acid



(I-B).

8. Process for preparing the compound of the formula (I-A) as defined in any of claims 1 to 5, wherein the compound of formula (I-B) as defined in any of claims 2 to 6 is treated with a base.

9. Compound of the formula (I-A) or (I-B) as defined in any of claims 1 to 5 for use in the treatment and/or prophylaxis of acute and recurrent bleeding in patients with or without underlying hereditary or acquired bleeding disorders.

10. Use of a compound of the formula (I-A) or (I-B) as defined in any of claims 1 to 5 in the manufacture of a medicament for the treatment and/or prophylaxis of acute and recurrent bleeding in patients with or without underlying hereditary or acquired bleeding disorders according to claim 9, wherein the bleeding is associated with a disease or medical intervention selected from the group consisting of menorrhagia, postpartum hemorrhage, hemorrhagic shock, trauma, surgery, otolaryngological surgery, dental surgery, urinary surgery, prostatic surgery, gynaecological surgery, cardiovascular surgery, spinal surgery, liver or lung transplantation, stroke, liver diseases, hereditary angioedema, nosebleed, and synovitis and cartilage damage following hemarthrosis .

11. Medicament, comprising a compound of the formula (I-A) or (I-B) as defined in any of claims 1 to 5 in combination with an inert, non-toxic, pharmaceutically suitable auxiliary.

12. Medicament, comprising a compound of the formula (I-A) or (I-B) as defined in any of claims 1 to 5 in combination with a further active compound selected from the group consisting of Factor VIII, Factor IX, Factor VIIa, activated prothrombin complex concentrates (aPCC) or prothrombin complex concentrates (PCCs), ε-aminocaproic acid, ethamsylate, paraaminobutyl benzoic acid, tranexamic acid, desmopressin, danazol, combined oral contraceptive pills (COCPs), progestin intrauterine system, glucocorticoid receptor agonists, analgesics, and nonsteroidal anti-inflammatory drugs (NSAIDs).

13. Medicament according to claim 11 or 12 for use in the treatment and/or prophylaxis of acute and recurrent bleeding in patients with or without underlying hereditary or acquired bleeding disorders.