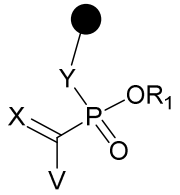
CLAIMS

1. Process for the preparation of a phosphonothiolate or phosphonate comprising the step of:

Reacting a compound of formula (I*)



(I*)

wherein

V represents C_1-C_8-alkyl, preferably methyl, ethyl or propyl, more preferably methyl;

X represents (R_3 R_4)C;

wherein ● represents an aliphatic or aromatic residue;

Y represents S or O;

R_1 represents an optionally substituted aliphatic or aromatic residue;

R_3 represents H or C_1-C_8-alkyl; and

R_4 represents H or

C_1-C_8-alkyl,

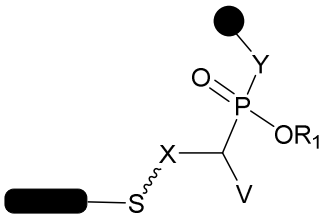
with a thiol-containing molecule of formula (II)



(II)

wherein ▬ represents an amino acid, a peptide, a protein, an antibody, a nucleotide, an oligonucleotide, a saccharide, a polysaccharide, a polymer, an optionally substituted C_1-C_8-alkyl, an optionally substituted phenyl, or an optionally substituted aromatic 5- or 6-membered heterocyclic system;

resulting in a compound of formula (III*)



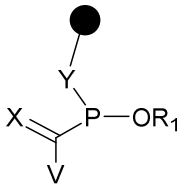
(III*)

wherein ▬, ●, V, R_1, X and Y are as defined above .

2. The process according to claim 1, wherein Y is S.

3. The process according to claim 1 or 2, further comprising a preparation of a compound of formula (I*), said preparation comprising:

reacting a compound of formula (IV*)



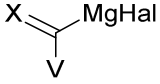
(IV*)

wherein X represents (R_3 R_4)C, and Y, R_1, R_3, R_4, V and ● are as defined in any one of the preceding claims;
with an oxidant, such as e.g. tert-butyl hydroperoxide (*t*Bu-OOH), meta-chloroperoxybenzoic acid (mCPBA), hydrogen peroxide (H_2O_2), iodine (I_2), potassium peroxymonosulphate, or oxygen (O_2), to form the compound of formula (I*).

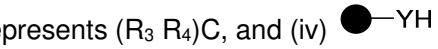
4. The process according to claim 3, further comprising a preparation of the compound of formula (IV*), said preparation comprising:

reacting, in sequential order, a phosphorus trihalide (X), preferably PCl_3, with

(i) R_1–OH (XI), (ii) 

(XII), wherein R_2 independently represents C_1-C_8-alkyl, (iii) 

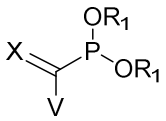
(XIII*), wherein Hal represents a halogen selected from the group

consisting of Cl, Br and I, preferably Br, and X represents (R_3 R_4)C, and (iv)  (XIV) to form the compound of formula (IV*);

wherein R_1, R_3, R_4, V, Y and  are as defined in any one of the preceding claims.

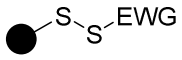
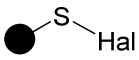
5. The process according to claim 2, further comprising a preparation of a compound of formula (I*), said preparation comprising:

reacting a compound of formula (V*)



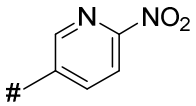
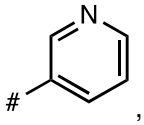
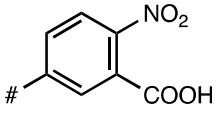
(V*)

with a compound of formula (VIa) or (VIb)

 or 

(VIa) (VIb)

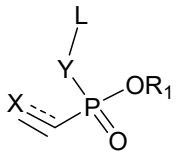
to form a compound of formula (I*);

wherein EWG represents an electron withdrawing group, said electron withdrawing group preferably being selected from the group consisting of , , and , wherein # indicates the position of S; Hal represents a halogen selected from the group consisting of Cl, Br and I, preferably Cl; and

wherein X represents (R_3 R_4)C; and R_1, R_3, R_4, V and are as defined in any one of the preceding claims.

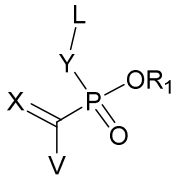
6. Process for the preparation of a compound of formula (I) or formula (I*), said process comprising:

(I) reacting a compound of formula (Ia)



(Ia); or

of formula (I*a)



(I*a),

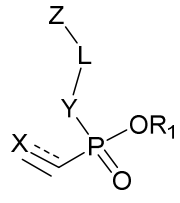
wherein

L represents a linker suitable for binding to an amino acid, a peptide, a nucleotide or an oligonucleotide; and

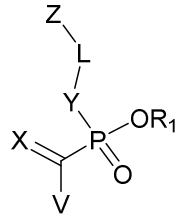
 represents a double bond or triple bond;
X, Y, V and R1 are as defined in any one of the preceding claims,

with an amino acid, a peptide, a nucleotide or an oligonucleotide, wherein the amino acid, the peptide, the nucleotide or the oligonucleotide is bound to a solid support,

resulting in a compound of formula (Ib) or (I*b),



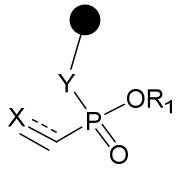
(Ib); or



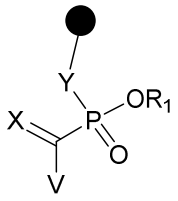
(I*b),

wherein Z represents the amino acid, the peptide, the nucleotide or the oligonucleotide, wherein the amino acid, the peptide, the nucleotide or the oligonucleotide is bound to the solid support; and

(II) cleaving the compound of formula (Ib) or formula (I*b) from the solid support to give the compound of formula (I) or formula (I*):



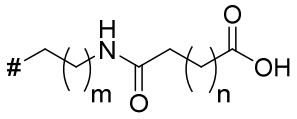
(I); or



(I*),

wherein ● represents the amino acid, the peptide, the nucleotide or the oligonucleotide bound to the Y through the linker L, and

, X, Y, V and R1 are as defined above.

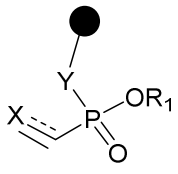
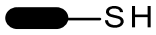
7. The process according to claim 6, wherein the linker L is 

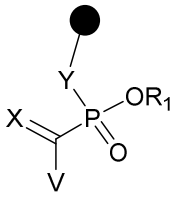
, wherein # indicates the position of the Y, and m and n are each, independently, an integer of from 0 to 20, 0 to 15, 1 to 10, 1 to 8, 1 to 6, 1 to 4, 1 to 3, 1 to 2, or 1, preferably m is 1 and n is 1.

8. The process according to claim 6 or 7, wherein the compound of formula (Ia) or (I*a) is reacted with a peptide bound to a solid support or an oligonucleotide bound to a solid support, preferably with a peptide bound to a solid support.

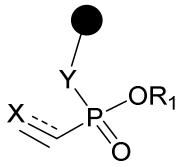
9. The process according to any one of claims 6 to 8, wherein the cleaving is carried out under acidic conditions.

10. The process according to any one of claims 6 to 9, further comprising reacting the compound of formula (I) or formula (I*) with a compound of formula (II) as defined in any one of the preceding claims.

11. The process according to any one claims 1 to 5, wherein the  and the  are in the same molecule.

12. The process according to any one of claims 1 to 5, wherein the  and the  are in the same molecule.

13. A compound of formula (I)



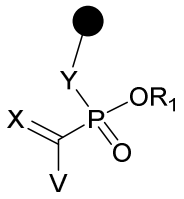
(I)

wherein , , R_1, X and Y are as defined in any one of the preceding claims.

14. The compound according to claim 13, wherein  represents a double bond, X represents $(R_3\ R_4)C$, and R_3 and R_4 independently represent H or C_1-C_8-alkyl.

15. The compound according to claim 13, wherein  represents a triple bond, X represents R_3-C, and R_3 represents H or C_1-C_8-alkyl.

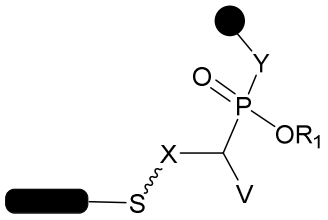
16. A compound of formula (I*)



(I*)

wherein X represents (R_3 R_4)C, and R_1, R_3, R_4, V, Y and ● are as defined in any one of the preceding claims.

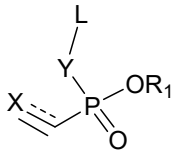
17. A compound of formula (III*)



(III*)

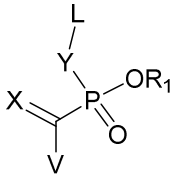
wherein X represents (R_3 R_4)C, and ▬, ●, V, Y, R_1, R_3 and R_4 are as defined in any one of the preceding claims.

18. A kit comprising a solid support, and
a compound of formula (Ia)



(Ia),

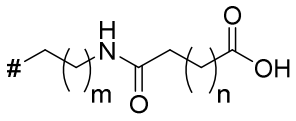
and/or a compound of formula (I*a)



(I*a),

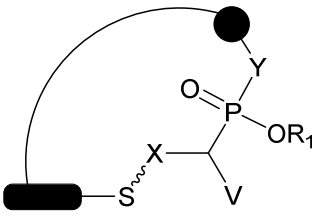
wherein L is a linker suitable for binding to an amino acid, a peptide, a nucleotide or an oligonucleotide; and

wherein , R_1, X, Y, and V are as defined in any one of the preceding claims.

19. The kit of claim 18, wherein the linker L is , wherein # indicates the position of the Y, and m and n are each, independently, an integer of from 0 to 20, 0 to 15, 1 to 10, 1 to 8, 1 to 6, 1 to 4, 1 to 3, 1 to 2, or 1, preferably m is 1 and n is 1.

20. The kit of claim 18 or 19, further comprising one or more of an amino acid, one or more of a peptide, one or more of a nucleotide, and/or one or more of an oligonucleotide.

21. A compound of formula (III*a)



(III*a),

wherein X represents (R_3 R_4)C, and , , V, Y, R_1, R_3, and R_4 are as defined in any one of the preceding claims.