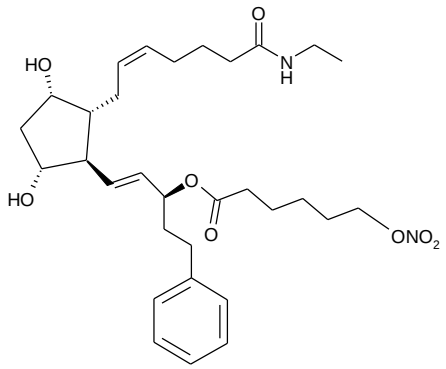
CLAIMS

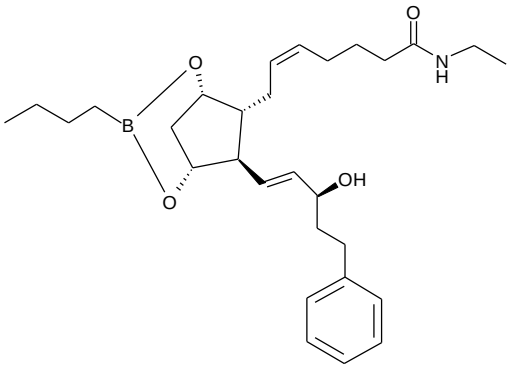
1. A process for the preparation of hexanoic acid, 6-(nitrooxy)-, (1S,2E)-3-[(1R,2R,3S,5R)-2-[(2Z)-7-(ethylamino)-7-oxo-2-hepten-1-yl]-3,5-dihydroxycyclopentyl]-1-(2-phenylethyl)-2-propen-1-yl ester of formula (I):



(I)

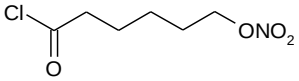
said process comprising the following steps:

a) reacting compound of formula (II):



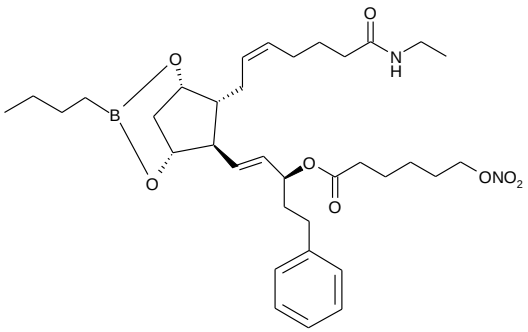
(II)

with 6-(nitrooxy)hexanoyl chloride of formula (IV):



(IV)

in the presence of 4-dimethylaminopyridine in free form, to obtain compound of formula (III):



(III)

b) removing the boronate protective group of compound of formula (III) to obtain compound of formula (I).

2. The process according to claim 1 wherein step a) is carried out in an aprotic organic solvent.

3. The process according to claim 2 wherein the aprotic organic solvent is selected from methyltertbutyl ether, N,N-dimethylformamide or dichloromethane.

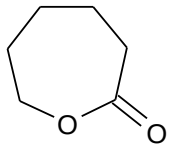
4. The process according to claim 3 wherein the aprotic organic solvent is methyltertbutyl ether.

5. The process according to any one of claims 1 to 4 wherein in step a) the molar ratio of compound of formula (II) to 6-(nitrooxy)hexanoyl chloride of formula (IV) is 1:1.4 to 1:1.6 and the molar ratio of compound of formula (II) to 4-dimethylaminopyridine is 1:2.0 to 1: 2.4.

6. The process according to any one of claims 1 to 5 wherein step a) is carried out at a temperature ranging from 0°C to room temperature.

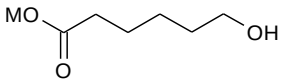
7. The process according to any one of the preceding claims wherein 6-(nitrooxy)hexanoyl chloride of formula (IV) is obtained by a process comprising the following steps:

i) reacting 2-caprolactone of formula (V):



(V)

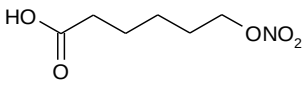
with an inorganic base selected from KOH, NaOH and LiOH to obtain 6-hydroxyhexanoic acid salt of formula (VI):



(VI)

wherein M is K, Na or Li.

ii) nitrating compound of formula (VI) with a mixture of HNO_3 and H_2SO_4 to obtain 6-(nitrooxy)hexanoic acid of formula (VII)



(VII)

iii) converting 6-(nitrooxy)hexanoic acid of formula (VII) with a chlorinating regent to 6-(nitrooxy)hexanoyl chloride of formula (IV).

8. The process according to claim 7 wherein 6-(nitrooxy)hexanoyl chloride of formula (IV) obtained in step iii) is directly used in step a) without further purification.

9. The process according to claim 7 or 8 wherein the inorganic base used in step i) is potassium hydroxide.

10. The process according to any one of claims 7-9 wherein step i) is carried out in a solvent selected from methanol, ethanol or isopropanol.

11. The process according to claim 10 wherein the organic solvent is methanol.

12. The process according to any one of claims 7-11 wherein step ii) is carried out in dichloromethane.

13. The process according to any one of claims 7-12 wherein step iii) is carried out by using oxalyl chloride as chlorinating reagent.

14. The process according to any one of claims 7-13 wherein step iii) is carried out in dichloromethane.

15. The process according to any one of the preceding claims wherein compound of formula (II) is obtained by reacting bimatoprost with butylboronic acid.

16. Hexanoic acid, 6-(nitrooxy)-, (1S,2E)-3-[(1R,2R,3S,5R)-2-[(2Z)-7-(ethylamino)-7-oxo-2-hepten-1-yl]-3,5-dihydroxycyclopentyl]-1-(2-phenylethyl)-2-propen-1-yl ester having a chemical purity above 99% and containing an amount of (S,E)-1-((1R,2R,3S,5R)-2-((Z)-7-(ethylamino)-7-oxohept-2-enyl)-3,5-dihydroxycyclopentyl)-5-phenylpent-1-en-3-yl 6-chlorohexanoate (compound (X)) from 0.15% to 0.26%.