wherein X=F, Cl, Br, I and Y= Li, Na, K, Mg;

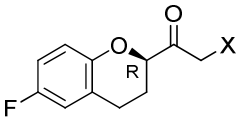
wherein the reaction of said ester with the metal-organic compound is carried out at a temperature between -10°C and +10°C,

wherein the metal-organic compound is an organic magnesium compound of formula RMgX, where X is a halogen and R is a linear or branched, preferably tertiary, C1-C6 alkyl residue.

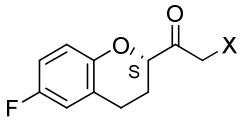
b. carrying out an *in situ* decarboxylation by treatment with an aqueous inorganic acid until reaching a pH equal to or less than 5, to give the corresponding chromanyl haloketone of formula IIIa and/or IIIb in the form of a separate isomer or in racemic form.

CLAIMS

1. A process for the synthesis of chromanyl haloketones of formula IIIa and/or IIIb as separate isomers or as a racemic mixture



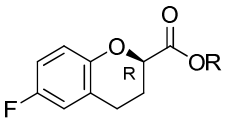
(IIIa)



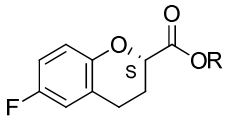
(IIIb)

comprising the following steps:

a. reacting an ester of formula IIa and/or IIb,



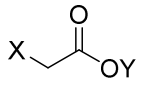
(IIa)



(IIb)

wherein R is a linear C_1–C_6 alkyl group, in form of separate isomer or as a racemic mixture

with a metal-organic compound and a salt of a haloacetic acid of general formula A



Formula A

wherein X=F, Cl, Br, I and Y= Li, Na, K, Mg;

wherein the reaction of said ester with the metal-organic compound is carried out at a temperature between –10°C and +10°C,

wherein the metal-organic compound is an organic magnesium compound of formula RMgX, where X is a halogen and R is a linear or branched, preferably tertiary, C1-C6 alkyl residue.

b. carrying out an *in situ* decarboxylation by treatment with an aqueous inorganic acid until reaching a pH equal to or less than 5, to give the corresponding chromanyl haloketone of formula IIIa and/or IIIb in the form of a separate isomer or in racemic form.

2. The process according to claim 1, wherein said metal-organic compound is *t*-BuMgCl.

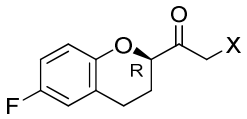
3. The process according to any one of claims from 1 to 2, wherein said haloacetic acid is chloroacetic acid or said salt is sodium chloroacetate.

4. The process according to any one of claims from 1 to 3, wherein the reaction of said ester with the metal-organic compound is carried out at a temperature between -5°C and +5°C, or between -3°C and +3°C.

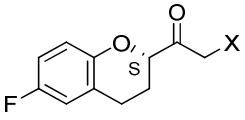
5. The process according to any one of claims from 1 to 4, wherein the solvent used in the reaction of said ester with the metal-organic compound is an ether, preferably selected from tetrahydrofuran, methyl tert-butylether or mixtures thereof.

6. The process according to any one of claims from 1 to 5, comprising the following additional step

c. reducing in an apolar solvent the haloketone of formula IIIa or IIIb

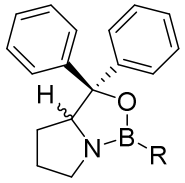


(IIIa)



(IIIb)

with a complex of borane in the presence of an oxazaborolidine catalyst (RCBS) of formula B

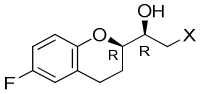


Formula B

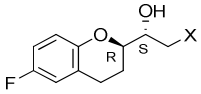
wherein R = methyl or buthyl,

wherein said catalyst has *R* or *S* chirality,

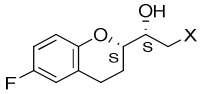
to obtain the respective haloalcohol of formula IV



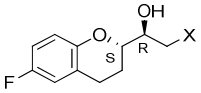
(IVa)



(IVb)



(IVc)



(IVd)

7. The process according to claim 6, wherein said apolar solvent in step c is selected from the group comprising cyclohexane, methylcyclohexane and heptane.

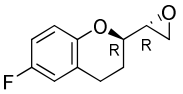
8. The process according to claim 6 or 7, wherein the catalyst is (*R*)MeCBS or (*S*)MeCBS.

9. The process according to claim 6 or 7, wherein the catalyst is (*R*)BuCBS or (*S*)BuCBS.

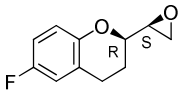
10. The process according to any one of claims from 6 to 9, wherein the complex of the borane is selected from the group comprising borane-diethylaniline (DEA*BH3), borane-dimethylsulfide (BH3*DMS), borane-tetrahydrofuran (BH3*THF).

11. The process according to any one of claims from 6 to 10 comprising the following additional step:

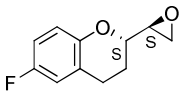
d. carrying out an *in situ* cyclization of the said haloalcohol IVa-IVd with an aqueous solution of an alkaline base, to give the corresponding epoxides of formula Ia-Id in the form of separate optically active isomers:



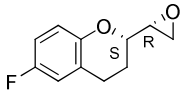
(Ia)



(Ib)



(Ic)

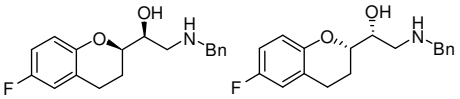


(Id)

12. The process according to claim 11, wherein the alkaline base at step d is a NaOH, LiOH or KOH solution.

13. The process according to any one of claims from 11 to 12, comprising the following additional step:

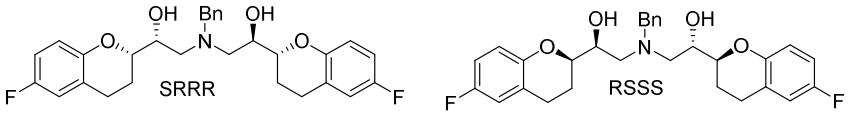
e. reacting separately the SR isomer of the epoxide (Id) and the RS isomer of the epoxide (Ib) with the benzylamine to obtain the RS and SR benzylammine of formula (V)



(V)

14. The process according to claim 13, comprising the following additional step

f. reacting separately the RS amine (V) with the SS epoxide (Ic) and the amine SR (V) with the epoxide RR (Ia) to give separately the SSSR and SRRR isomers of benzylnebivolol of formula (VI)



(VI)

15. The process according to claim 14, comprising the following additional steps :

g. combining the solutions of RSSS and SRRR isomers of benzylnebivolol of formula (VI), and

h. carrying out a crystallization to obtain the SRRR/RSSS benzylnebivolol as a raceme.

16. The process according to claim 15, wherein said crystallization is carried out with a ethyl acetate/cyclohexane mixture and eventual trituration in hot cyclohexane.

17. The process according to any one of claims from 15 to 16, comprising the following additional step:

i. removing the benzyl protecting group and forming a hydrochloride salt, to obtain a product Nebivolol hydrochloride.

18. The process according to claim 17, wherein the benzyl group is removed by catalytic hydrogenation with $Pd(OH)_2$ catalyst.

19. The process according to claim 18, wherein the solvent of the hydrogenation is acetic acid water 7: 1

20. The process according to any one of claims from 17 to 19, in which the hydrochloride salt of Nebivolol is obtained by cation exchange with NaCl solution.