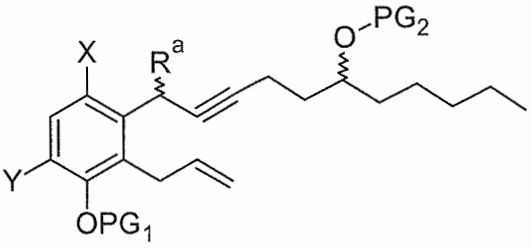
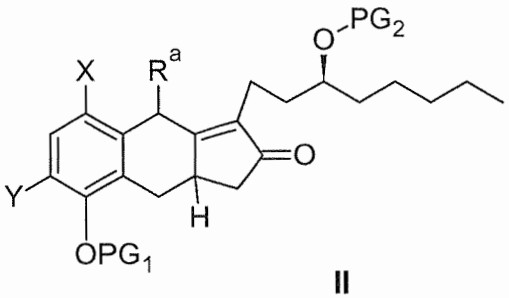
Claims :

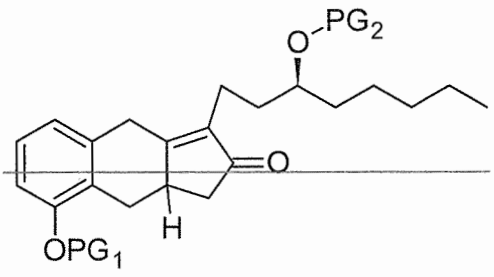
1. A compound of formula I, formula II~~, formula IIb, formula IIIb,~~ or formula IVb



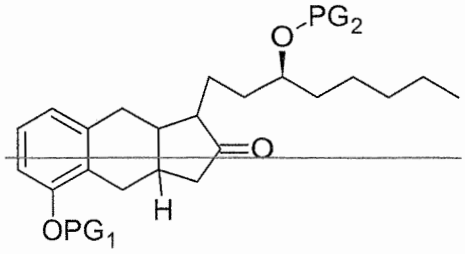
I



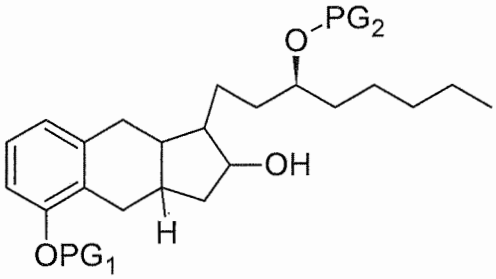
II



IIb



IIIb



IVb

wherein

X is Br and **Y** ~~are independently of one another selected from the group consisting of~~is H~~, F, Cl, Br, I, and benzyl~~; and

PG_1 is selected from the group consisting of methyl, methoxymethyl, benzyloxymethyl, methoxyethoxymethyl, benzyl, 4-methoxybenzyl, 2,6-dichlorobenzyl, 3,4-dichloro-benzyl; $-CH_2COOH$, $-CH_2COOR_x$, and $-CH_2CH_2OPG_2$; and

PG_2 is TBDMS; and

R^a is ~~hydrogen,~~ hydroxy~~, $-OR_x$, $-OCOOR_x$, $-OSO_2R_x$, Cl, Br F, I, $-SR_x$, or $-SO_2R_x$~~; and

R_x is C_{1-4}alkyl or aryl~~; and~~

~~wherein at least one of X or Y is not H~~.

~~2. A compound according to claim 1, wherein~~

~~X and Y are independently of one another selected from H, Br or Cl; and at least one of X or Y is not H.~~

~~3. A compound according to claim 2, wherein~~

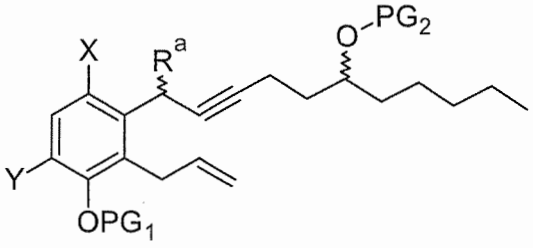
~~X is Br or Cl; and~~

~~Y is H.~~

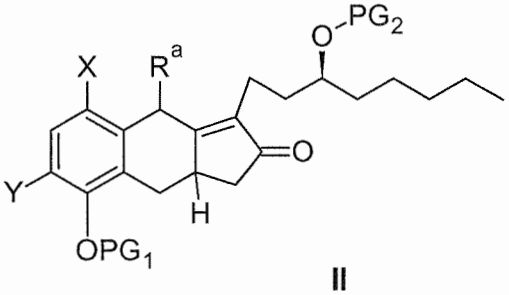
~~4. A compound according to any one of claims 1 – 3, wherein~~

~~X is Br.~~

~~5.~~2. A compound of formula I, or formula II,



I



II

wherein

X is Br and **Y** ~~are independently of one another selected from the group consisting of~~ is H, ~~F, Cl, Br, I, and benzyl~~; and

PG_1 is selected from the group consisting of methyl, methoxymethyl, benzyloxymethyl, methoxyethoxymethyl, benzyl, 4-methoxybenzyl, 2,6-dichlorobenzyl, 3,4-dichloro-benzyl; $-CH_2COOH$, $-CH_2COOR_x$, and $-CH_2CH_2OPG_2$; and

PG_2 is THP, $SiR_1R_2R_3$; or $-CH_2OR_x$; and

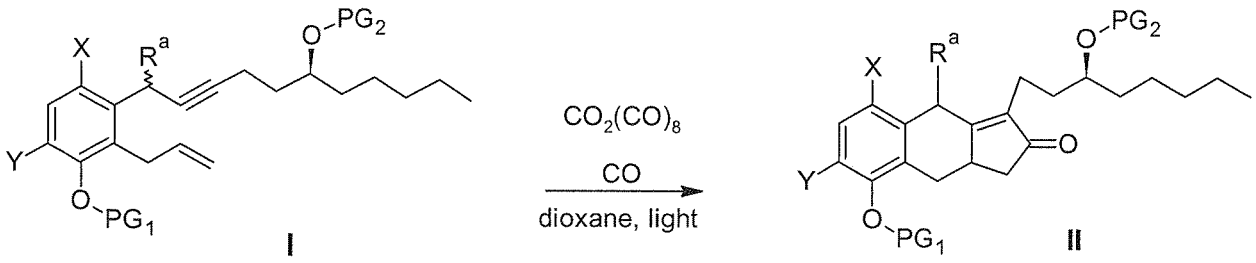
R_1, R_2, and **R_3** are independently from one another selected from the group consisting of methyl, isopropyl, *t*-butyl, and phenyl

R^a is ~~hydrogen,~~ hydroxy ~~$-OR_x$, $-OCOOR_x$, $-OSO_2R_x$, Cl, Br F, I, $-SR_x$, or $-SO_2R_x$~~; and

R_x is $C_{1\text{-}4}$alkyl or aryl~~; and~~

~~wherein at least one of X or Y is not H~~.

~~6.~~3. A process for making a compound of formula (II), comprising the following step:



X, Y, R^a, PG_1 and **PG_2** are as defined in claim 1.

~~7. The process according to claim 36, wherein~~ ~~**PG_2** is TBDMS.~~

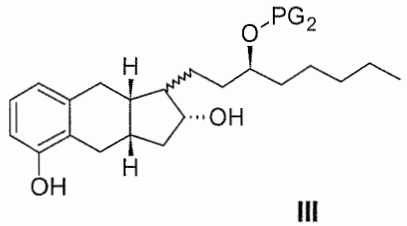
~~8. The process according to claim 36 or 47, wherein~~ ~~**R^a** is hydroxy.~~

~~9.~~4. The process according to claim ~~3~~6, wherein ~~**X** is Br, and~~ **Y** is hydrogen, and **PG_1** is benzyl~~, and **PG_2** is TBDMS; and **R^a** is hydroxy~~.

~~10.~~5. A process for making a compound of formula IV, comprising the steps of a) hydrogenating and reducing a compound of formula II to obtain racemic compound of formula III;

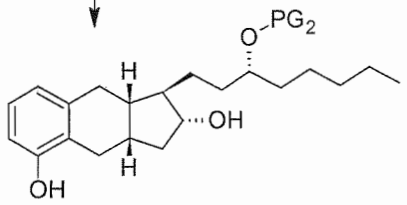
b) contacting racemic compound of formula III with ~~Lipase Ak~~lipase enzyme in the presence of a solvent; and

c) obtaining an optically pure compound IV;



III

lipase enzyme



IV

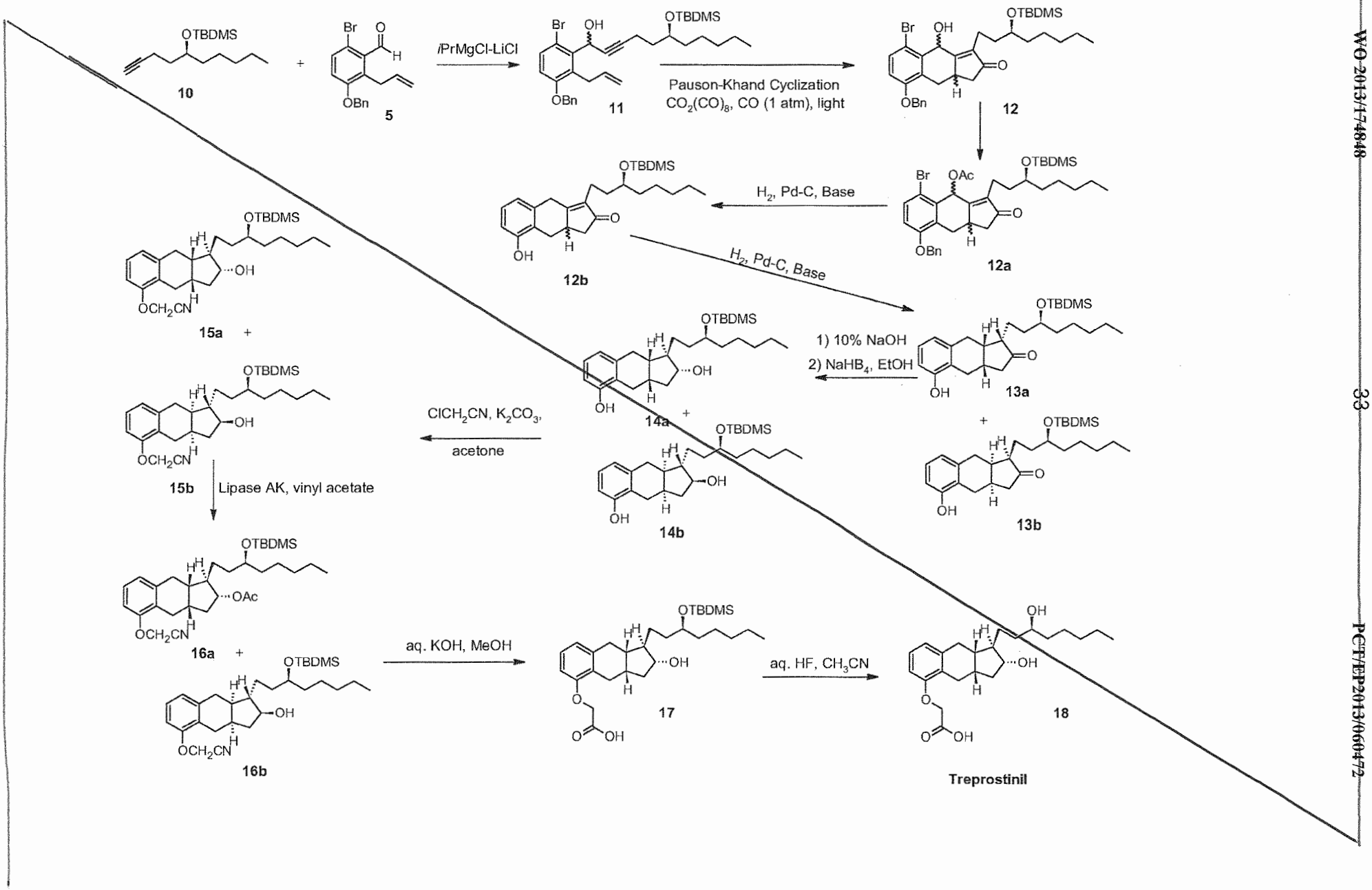
wherein

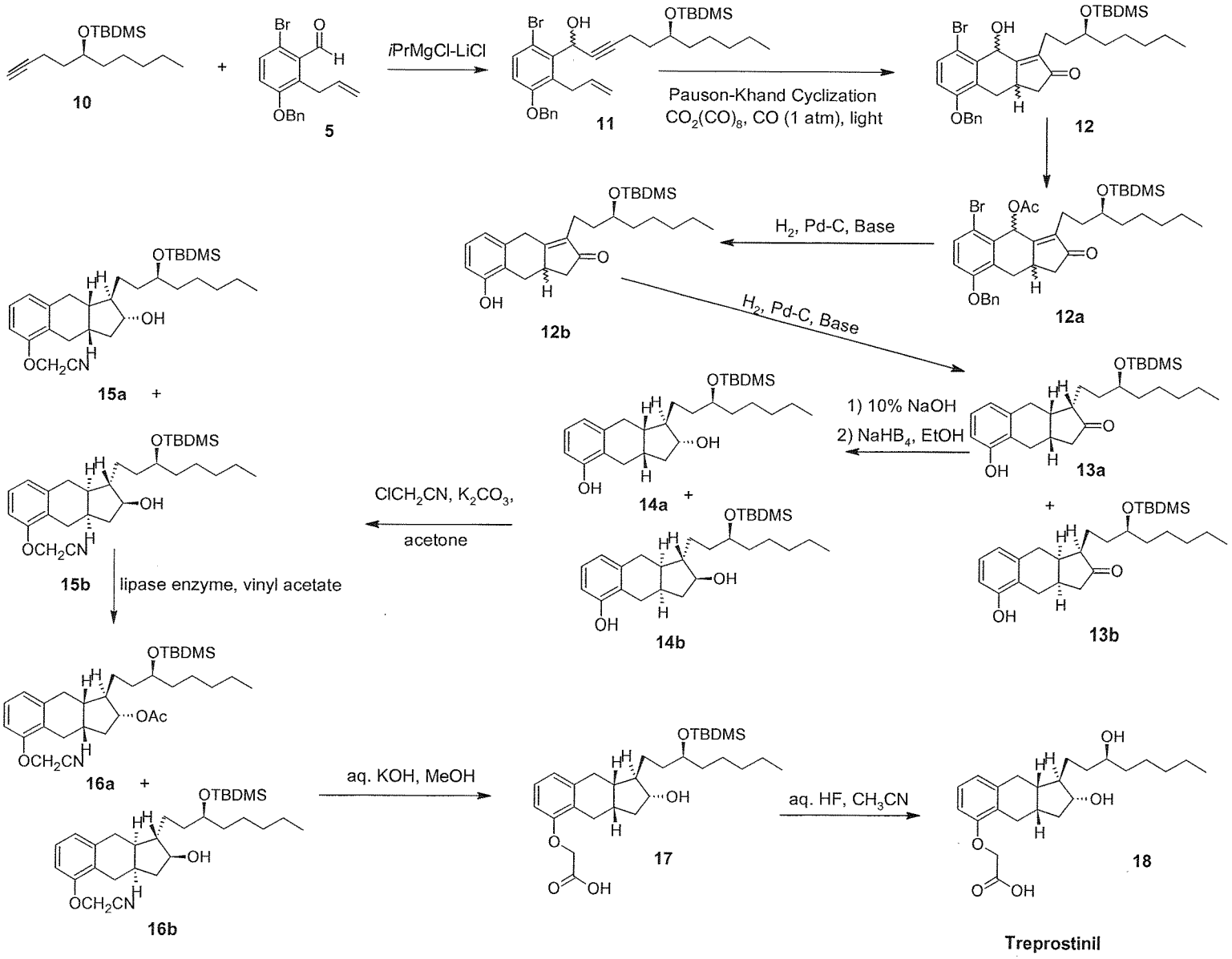
PG_2 is THP or TBDMS.

~~11.~~6. The process according to claim 5~~10~~, wherein the solvent is selected from the group consisting of vinyl acetate, hexane(s), heptane(s), and chloroform

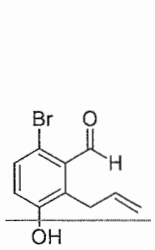
~~12.~~7. The process according to claim 5~~10~~ or 6~~11~~, wherein the hydrogenation is performed at a pH of about 8 to 12, preferabl at pH about 9 to 10.

~~13.~~8. A process for making treprostinil (**18**) comprising the following steps:

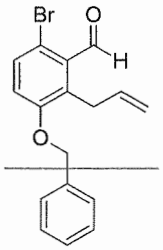

OTBDMS
Br
O
H
OBn
10
5
iPrMgCl-LiCl
OH
11
Pauson-Khand Cyclization
$CO_2(CO)_8$, CO (1 atm), light
12
OAc
12a
H_2, Pd-C, Base
12b
H_2, Pd-C, Base
1) 10% NaOH
2) $NaHB_4$, EtOH
13a
13b
14a
14b
$ClCH_2CN$, K_2CO_3,
acetone
15a
15b
Lipase AK, vinyl acetate
16a
16b
aq. KOH, MeOH
17
aq. HF, CH_3CN
18
Treprostinil


OTBDMS
10
Br
O
H
OBn
5
iPrMgCl-LiCl
OH
11
Pauson-Khand Cyclization
CO2(CO)8, CO (1 atm), light
12
OAc
12a
H2, Pd-C, Base
12b
H2, Pd-C, Base
1) 10% NaOH
2) NaHB4, EtOH
13a
13b
14a
14b
ClCH2CN, K2CO3,
acetone
15a
15b
OCH2CN
lipase enzyme, vinyl acetate
16a
16b
aq. KOH, MeOH
17
aq. HF, CH3CN
18
Treprostinil

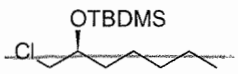
~~14.~~9. A new intermediate compound selected from the group consisting of



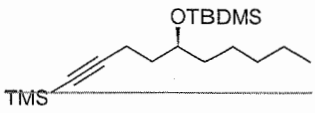
4a



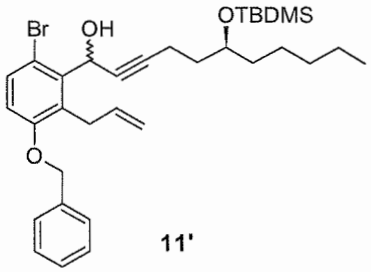
5



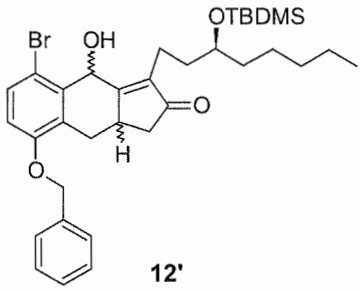
8



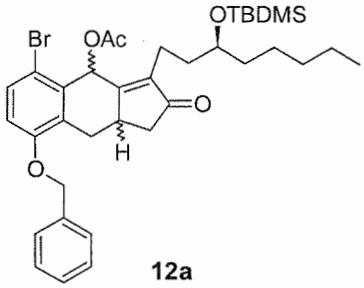
9



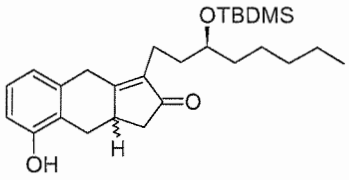
11'



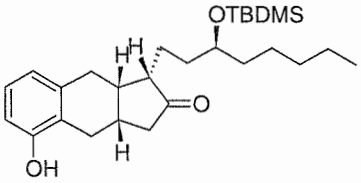
12'



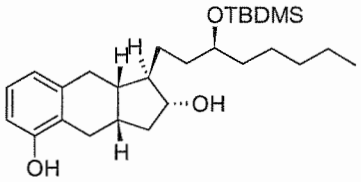
12a



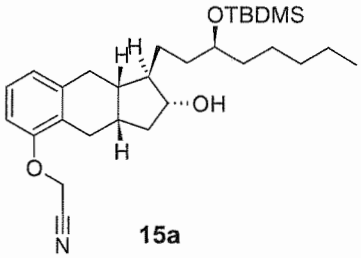
12b



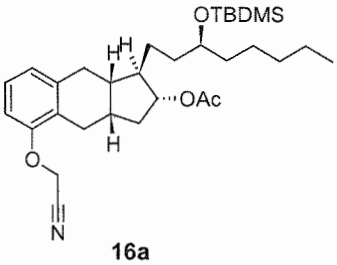
13a



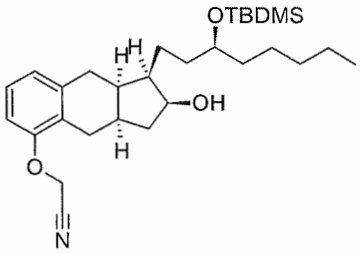
14a



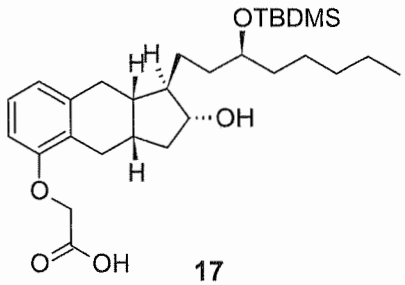
15a



16a



16b



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