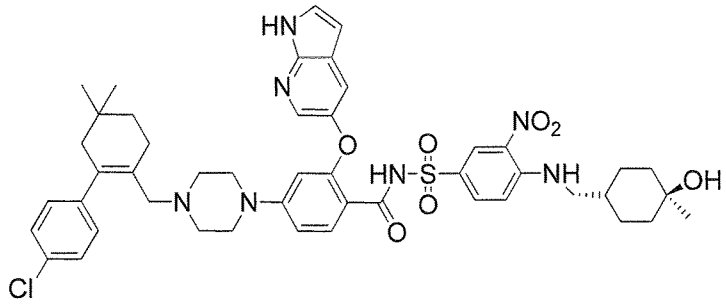
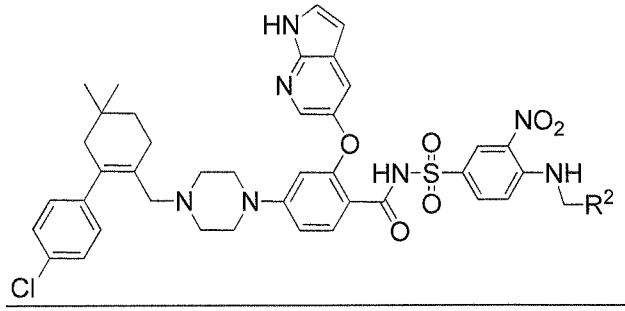


(2)

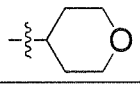
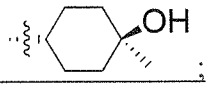
[0006] Compound 1 is currently the subject of ongoing clinical trials for the treatment of chronic lymphocytic leukemia. U.S. Patent Publication No. 2010/0305122 describes Compound 1, Compound 2, and other compounds which exhibit potent binding to a Bcl-2 family protein, and pharmaceutically acceptable salts thereof. U.S. Patent Publication Nos. 2012/0108590 and 2012/0277210 describe pharmaceutical compositions comprising such compounds, and methods for the treatment of neoplastic, immune or autoimmune diseases comprising these compounds. U.S. Patent Publication No. 2012/0129853 describes methods for the treatment of systemic lupus erythematosus, lupus nephritis or Sjogren's Syndrome comprising these compounds. U.S. Patent Publication No. 2012/0157470 describes pharmaceutically acceptable salts and crystalline forms of Compound 1. The disclosures of U.S. 2010/0305122; 2012/0108590; 2012/0129853; 2012/0157470 and 2012/0277210 are hereby incorporated by reference herein in their entireties.

SUMMARY

In one aspect, there is provided a process for the preparation of a compound of formula A1:

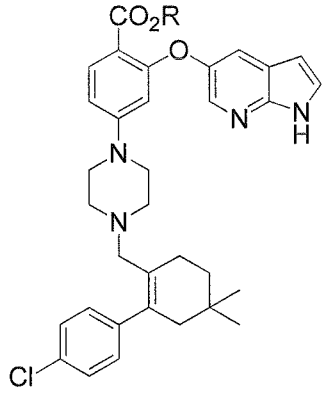


(A1),

wherein R^2 is selected from  and ;

which comprises:

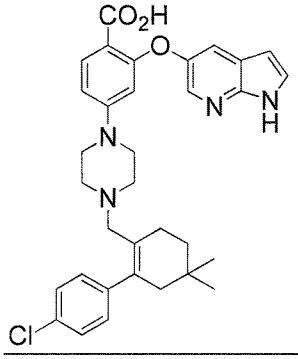
(a) combining a compound of formula (K):



(K)

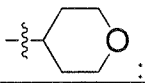
wherein R is C_1 to C_{12} alkyl,

with a tert-butoxide salt, an aprotic organic solvent, and water to provide a compound of formula (L):



(L); and

(b") combining the compound of formula (L) with 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, 4-dimethylaminopyridine, an organic solvent, and either a compound of formula (N), to provide a compound of formula (A1) wherein R^2 is



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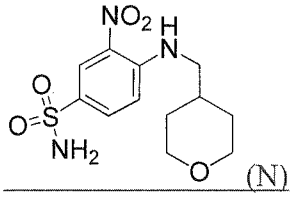
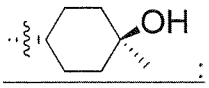
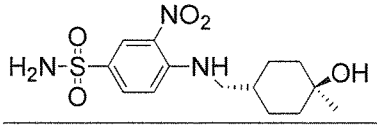


(N)

or a compound of formula (P), to provide a compound of formula (A1) wherein R^2 is



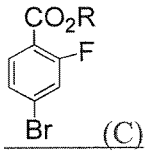
:



(P);

thereby providing a compound of formula (A1).

In one aspect, there is provided a process for the preparation of a compound of formula (C):

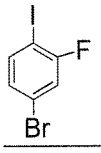


(C)

wherein R is C_1 to C_{12} alkyl,

which comprises:

(a) combining a compound of formula (A):

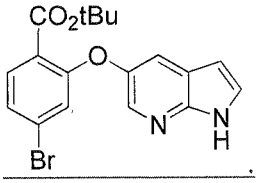


(A)

with R^1MgX in an aprotic organic solvent; wherein R^1 is C_1 to C_6 alkyl and X is Cl, Br or I;

(b) combining a C_1 to C_{12} alkyl chloroformate or a di-(C_1 to C_{12} alkyl)dicarbonate with the product of step (a), to provide the compound of formula (C).

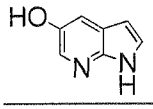
In one aspect, there is provided a compound of the formula:



.

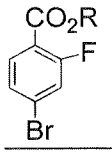
In one aspect, there is provided a process for the preparation of the compound as disclosed herein, wherein the process comprises:

(x) combining a compound of formula (B):



(B);

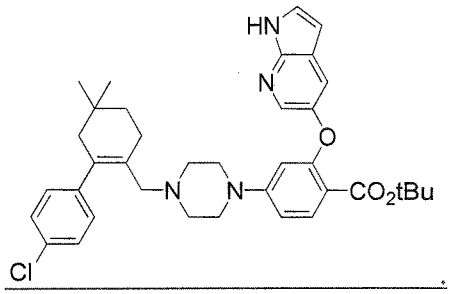
with a compound of formula (C):



(C), wherein R is tert-butyl,

and a *tert*-butoxide salt in an organic solvent to provide the compound as disclosed herein.

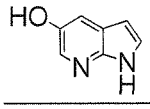
In one aspect, there is provided a compound of the formula:



.

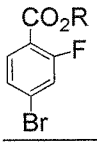
In one aspect, there is provided process for the preparation of the compound as disclosed herein, wherein the process comprises:

(y) combining a compound of formula (B):



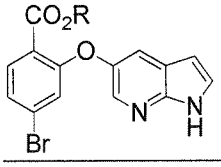
(B);

with a compound of formula (C):



(C), wherein R is tert-butyl,

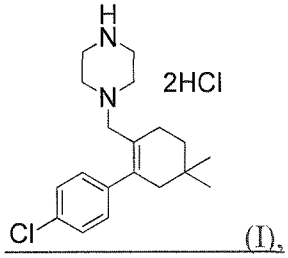
and a *tert*-butoxide salt in an organic solvent to provide the compound of formula (D):



(D), wherein R is tert-butyl;

(z) combining the compound of formula (D), wherein R is tert-butyl;

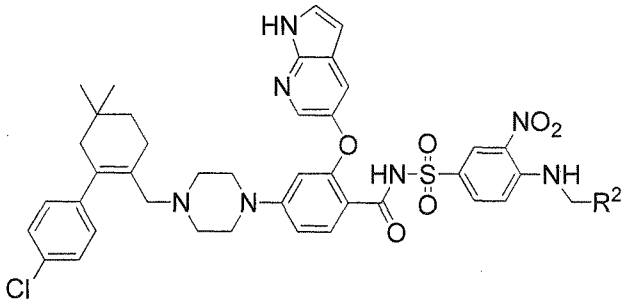
with a compound of formula (I):



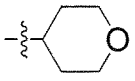
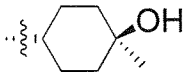
(I),

a source of palladium, a tert-butoxide salt, and a phosphine ligand in an aprotic organic solvent to provide the compound as disclosed herein.

[0007] Provided herein are processes for the preparation of compounds of formula A1:



(A1),

wherein R^2 is selected from  and .

[0008] Also provided herein are compounds of the formulae: