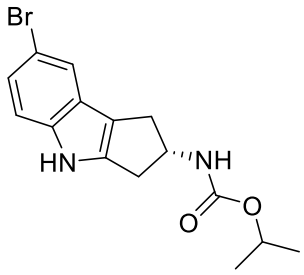
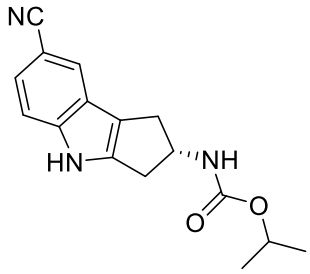
comprising the steps of:

reacting $Zn(CN)_2$ with the compound of Formula II, thereby forming the compound of Formula III

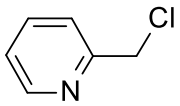


(Formula II)



(Formula III); and

forming the compound of Formula I by reacting the compound of Formula III with the compound of Formula IV



(Formula IV).

~~In another aspect of the present disclosure, there is provided a use of a pharmaceutical composition in the manufacture of a medicament for treating the symptoms of secondary hypogonadism induced by androgen deprivation therapy, wherein the pharmaceutical composition comprises a substantially pure form of (S)-(7-cyano-4-pyridin-2-ylmethyl-1,2,3,4-tetrahydro-cyclopenta[b]indol-2-yl)-carbamic acid isopropyl ester obtained by the process disclosed herein, or a pharmaceutically acceptable salt thereof.~~

~~In a further aspect of the present disclosure, there is provided a substantially pure form of (S)-(7-cyano-4-pyridin-2-ylmethyl-1,2,3,4-tetrahydro-cyclopenta[b]indol-2-yl)-carbamic acid isopropyl ester or a pharmaceutically acceptable salt thereof.~~

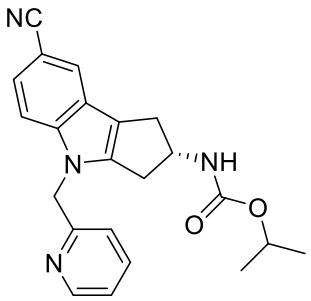
Description

Figure 1 illustrates that Example 1 resulted in no significant accrual of seminal vesicle weight after treatment of 8 weeks in a rat orchidectomized for 8 weeks and which was hyper responsive to any androgenic stimulation.

Figure 2 illustrates that Example 1 resulted in significant accrual of, lumbar vertebra trabecular bone mineral density (LV-TBMD) and showed a trend towards increase in lumbar vertebra trabecular bone mineral content (LV-TBMC), and cross-sectional area (LV-TA) after treatment of 8 weeks in a rat orchidectomized for 8 weeks.

WE CLAIM:

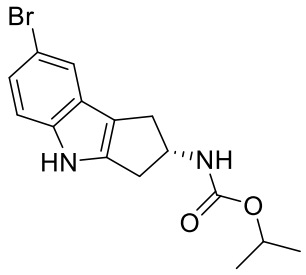
1. A process for the preparation of the compound of Formula I



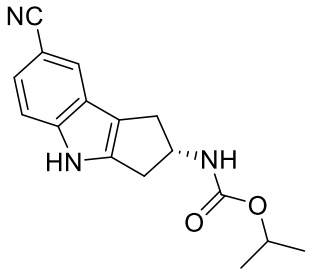
(Formula I)

comprising the steps of:

reacting $Zn(CN)_2$ with the compound of Formula II, thereby forming the compound of Formula III

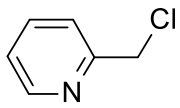


(Formula II)



(Formula III); and

forming the compound of Formula I by reacting the compound of Formula III with the compound of Formula IV



(Formula IV).

2. The process of claim 1, wherein the reaction of the compound of Formula II with $Zn(CN)_2$ to form a compound of Formula III comprises:

(i) reacting the compound of Formula II with $Zn(CN)_2$, $Zn(OAc)_2$, Zn, and $Pd(dppf)_2Cl_2 \cdot CH_2Cl_2$ in DMAC to form a compound of Formula III in solution;

(ii) adding water to precipitate and isolate the compound of Formula III from the solution;

(iii) dissolving the precipitated and isolated compound of Formula III in a mixture of MTBE and acetone to form a slurry;

(iv) filtering the slurry to produce a filtrate having a compound of Formula III; and

(v) treating the filtrate having the compound of Formula III with charcoal, $MgSO_4$, and magnesium metasilicate~~FLORISIL™~~.

3. The process of claim 2, wherein the compound of Formula III is crystalized in the heptane.

4. The process of any one of claims 1-3, wherein the compound of formula I is produced by a process comprising the steps of:

(i) reacting the compound of Formula III with 2-picolyl chloride hydrochloride and K_2CO_3 in DMAC to give a compound of Formula I in solution; and

(ii) isolating the compound of Formula I by adding water to the solution formed in step (i) and filtering.

5. The process of claim 4, further comprising a step of recrystallizing the isolated compound of Formula I in EtOH to produce a crystalline form of a compound of Formula I.

~~6. Use of a pharmaceutical composition in the manufacture of a medicament for treating the symptoms of secondary hypogonadism induced by androgen deprivation therapy, wherein the pharmaceutical composition comprises a substantially pure form of (S)-(7-cyano-4-pyridin-2-ylmethyl-1,2,3,4-tetrahydro-cyclopenta[b]indol-2-yl)-carbamic acid isopropyl ester obtained by the process according to any one of claims 1-5, or a pharmaceutically acceptable salt thereof.~~

~~7. The use according to claim 6, wherein said pharmaceutical composition is in the form of a capsule.~~

~~8. A substantially pure form of (S)-(7-cyano-4-pyridin-2-ylmethyl-1,2,3,4-tetrahydro-cyclopenta[b]indol-2-yl)-carbamic acid isopropyl ester or a pharmaceutically acceptable salt thereof.~~

~~9. The use according to claim 6, wherein the symptoms are the loss in bone mass, bone strength, muscle mass, or muscle strength.~~

~~10. The use according to claim 6, wherein the symptoms are loss of libido and hot flashes.~~

~~11. The process of claim 5, wherein the filtered isolate of the compound of Formula I is recrystallized at least three times in EtOH to produce the crystalline form of the compound of Formula I.~~