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A NOVEL PROCESS S-(-) AMLODIPINE AND THEIR INTERMEDIATES

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ABSTRACT

The present invention relates the new process for preparing for the S-(-) Amlodipine Besylate (S)-3-ethyl 5-methyl 2-[(2-aminoethoxy) methyl]- 4-(2-chlorophenyl)- 6-methyl -1, 4- dihydropyridine-3,5-dicarboxylatebenzenesulphonate) from Amlodipine base using L(+) Tartaric acid using solvent Iso propyl alcohol.

KEYWORDS: Amlodipine base, S-(-) Amlodipine Besylate, L (+) Tartaric acid, Benzene sulfonic acid and Urea.

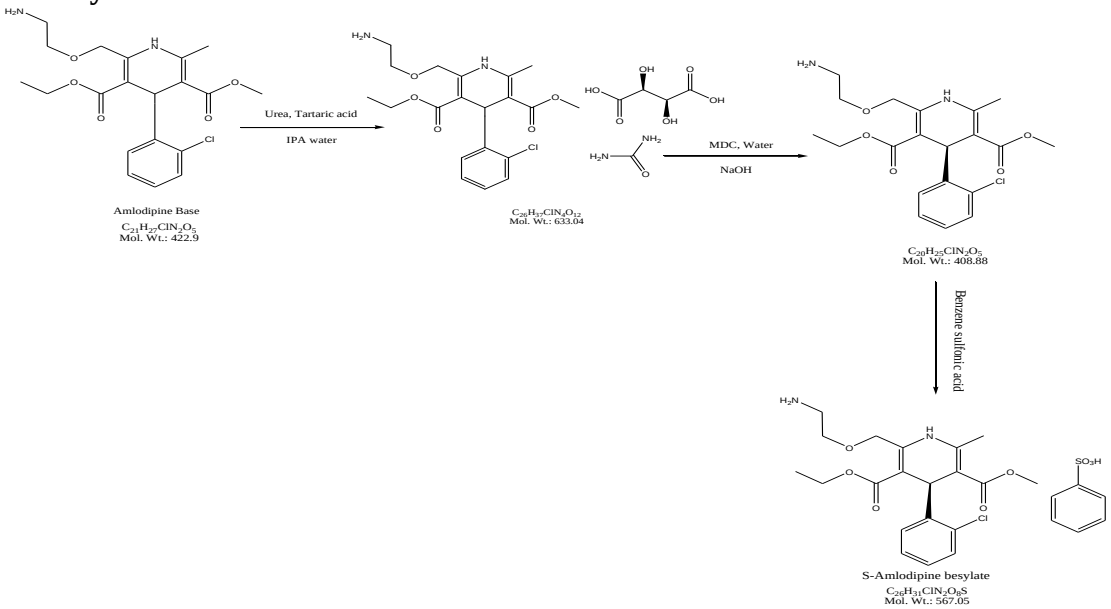
INTRODUCTION

Amlodipine and its salts are long acting calcium channel blockers and its salts are long acting calcium channel blockers and are useful for the treatment of cardiovascular disorders. Racemic Amlodipine is currently being used in the treatment of hypertension and angina. It has also been reported that R (+) Isomer is a potent inhibitor of smooth muscle cell migration. The S (-) Isomer is having calcium channel blocker activity while the R (+) Isomer has little no calcium channel blocking activity.

S-Amlodipine also known as Levoamlodipine. It is pharmacologically active enatiomer of Amlodipine. Dihydro pyridine group of Calcium channel blocker used as an anti hypertensive and antianginal agent.

(S)-Enatiomer of Amlodipine a dihydropyridine calcium channel blocker; activity resides mainly in the (-)-isomer. The present invention take the Amlodipine Besylate converted to free base add to the D (-) Tartaric acid presence of solvent IPA converted to the S (-) Amlodipine Besylate.

Route of synthesis



Method of preparing S-(-) Amlodipine Besylate

Preparation of Amlodipine tartarate salt

Take the urea (67g) was dissolved in water after added Iso propyl alcohol (800ml) after we take the Amlodipine base slowly raise the temperature to 50^{o}C clear solution formed. After we addition of the D (-) Tartaric acid observe the formation of Amlodipine tartarate salt formation. Finally filter the S (-) Amlodipine D (-) tartarate salt.

Preparation of S-(-) Amlodipine

After take this S - (-) Amlodipine D (-) tartarate salt add to the Methylene di chloride and water adjust the P^{H} with 2N NaOH (9-9.5) after the layer separation Take the organic layer washing with the water distillation of MDC layer S-Amlodipine pure base formed. This pure single base isolation in the n-Hexane finally we get pure S-(-) Amlodipine base.

Preparation of S-Amlodipine Besylate

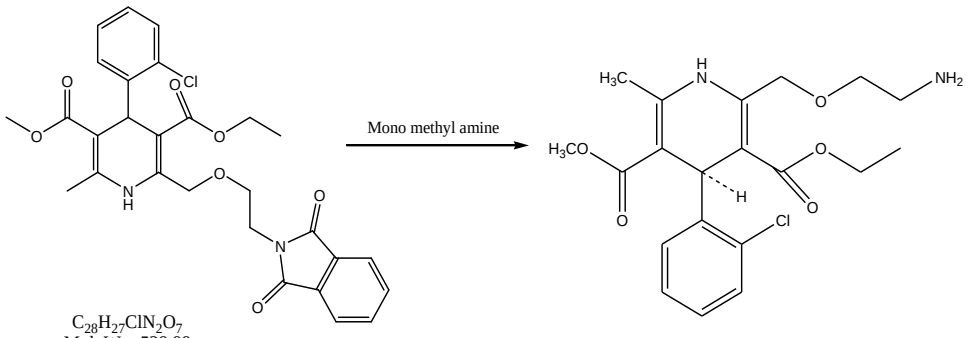
Take the S-(-) Amlodipine base add 4volumes of water heating with 70-75^{o}C. Addition of Benzene sulfonic acid observes the material formation cool and filter the S-Amlodipine Besylate finally dry the material.

Method-II

In this method starting material is Phthaloyl Amlodipine used for the preparation of S-Amlodipine Besylate.

Route of synthesis

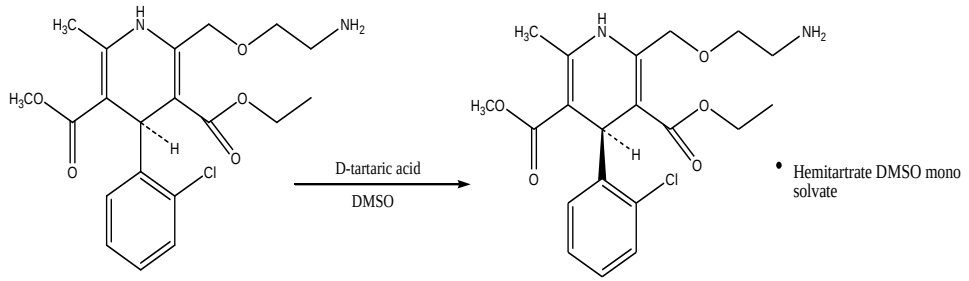
Stage-01



$C_{28}H_{27}ClN_2O_7$
Mol. Wt.: 538.98

$C_{20}H_{25}ClN_2O_5$
Mol. Wt.: 408.88

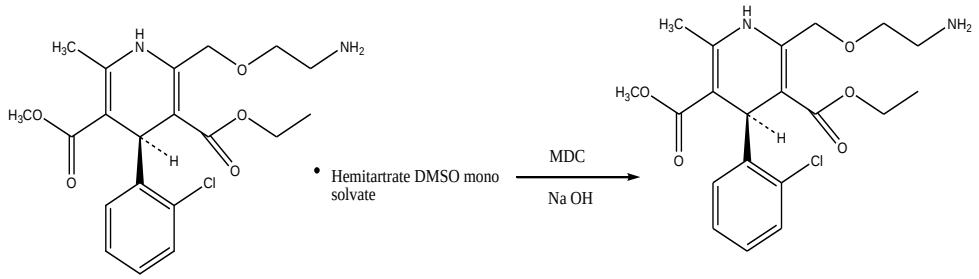
Stage-02



$C_{20}H_{25}ClN_2O_5$
Mol. Wt.: 408.88

S-Amlodipine Hemitartrate
DMSO Monosolvate

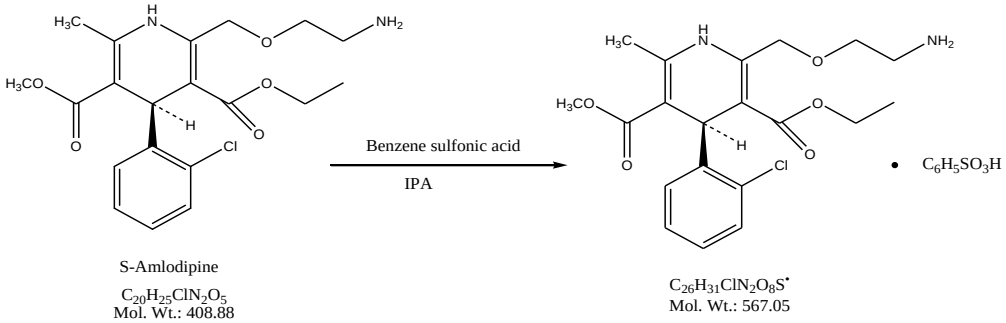
Stage-03



S-Amlodipine Hemitartrate
DMSO Monosolvate

S-Amlodipine
$C_{20}H_{25}ClN_2O_5$
Mol. Wt.: 408.88

Stage-04



S-Amlodipine
$C_{20}H_{25}ClN_2O_5$
Mol. Wt.: 408.88

$C_{26}H_{31}ClN_2O_8S^{\bullet}$
Mol. Wt.: 567.05

CONCLUSION

The present work was undertaken with the aim to preparation of S- (-) Amlodipine Besylate by using the urea and D (-) Tartaric acid using solvent Iso propyl alcohol. This is one alternative method of Preparation of S- (-) Amlodipine Besylate in this first we prepare Amlodipine tartarate salt using the tartaric acid and urea complex. Purify this complex with Iso propyl alcohol after breaking this salt result Amlodipine free base after this reaction with Benzene sulfonic acid in the presence of water to give the Amlodipine Besylate.

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