

The most effective process for preparing an antipsychotic drug is olanzapine

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ABSTRACT- Olanzapine is used to treat a number of mental/emotional disorders. In preparation of the drug Malononitrile in, 2-floro nitrobenzene , Stannous chloride & N-methyl piperazine are used in stageA,B,C& D respectively.Maintainnig different temperatures of solvents such as isopropyl alcohol ,Dimethyl formamide,DMSO,Acetone and water is important. Thin layer chromatography should comply at the respective stages. All the solvents used should have the moisture content NMT < 0.2% W/V Index Terms- DMF, RBF, TEA, LOD, TLC

Stage A.2-Amino-5-methylthiophene-3-carbonitrile

I. INTRODUCTION

Olanzapine is used to treat a number of mental/emotional disorders, including bipolar disorder and schizophrenia. It can also be used to treat depression in addition to other medications. With the help of this drug, you may experience fewer hallucinations, think more clearly and positively about yourself, feel less stressed, and engage in daily activities more actively. Olanzapine is a member of the atypical antipsychotic medication class. It functions by assisting in the restoration of the proper ratio of several organic compounds in the brain.



Charge 235 ml DMF into clean dry RBF at 25-30°C & Check MC ensure MC to be less than 0.5% Charge propionaldehyde and sulphur powder at 5-10°, Slowly add 61ml TEA at 5-10°C over a period of ½ hr.Raise temp to 18-20°c over a period of 50 minutes. Slowly add Malononitrile solution at 18-20°c

over a period of 70 minutes (47.5gm malononitrile in 95ml DMF) . Maintain for 45 minutes at 15-20°C. Quench RM into 420g ice+850ml water mix. Below 10°C Air dry the material for 2-3 hrs then dry at 40-45°C.till LOD .5% OUT PUT 70-80 gm.

Stage B. 2-(2-nitroanilino)-5-methylthiophene-3-carbonitrile



Charge IPA and 2-Amino-5-methyl-3thiophenecarbonitrile Charge 2-floro nitrobenzene at 5-10°C KOH powder at 5-10°c Slowly raise temperature to 80-85°c Send sample to QC for TLC Slowly add DM water over a period of 1 hour. Drying of this stage is not required to proceed to next step



Stage C

5-Methyl-2-[(2- nitrophenyl)amino]thiophene-3-carbonitrile hydrochloride



2-(2-nitroanilino)-5-methylthiophene-3-carbonitrile

5-Methyl-2-[(2- nitrophenyl)amino] thiophene-3-carbonitrile hydrochloride

30grams at stage-C add 150ml IPA at 80-85°C for 4 – 8 hours . If Thin Laver Chromatography complies

filter at 5- 10 °C 10.Finally wash with acetone to

obtain wet cake & dry .Output 27gms

Charge DM water and HCL and add Stannous chloride, take up to 150 ml of HCL at 25-30°C and Charge 30g stannous chloride into a round bottom flask at 25-30°C.continiously Stir for 15 minutes at same temperature (25-30°C). Add another

Stage D

Olanzapine



OLANZAPINE

In a clean Round bottom flask add DMSO at stage C along with N-methyl piperazine at 25-35°Cheat the reaction mass to 115-120°C, Maintain at 115-120°C for 24 hours. If TLC ok,add water & filter the mass to 0-5°C to obtain wet cake and dry to get 60gms

II. CONCLUSION

- 1. At Stage A Dimethylformamide moisture content should be maintained as described in stage A &Triethylamine should be added below $10 \ ^{\circ}\text{C}$
- 2. At Stage B Maintain RM reaction temperature reaction mass should be maintained at 80-85 °c
- 3. At Stage C, Wet cake should be washed with acetone
- 4. At Stage D of reaction ,reaction mass temperature should be 115-120 °C, Thin layer chromatography should comply

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