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# Synthesis and characterization of novel 2,2-di(pyridin-2-yl) hexahydropyrimidine and its derivative5,5-dimethyl-1,3-bis[(methylsulfonyl)oxy]-2,2-dipyridin-2-ylhexahydropyrimidine

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**ABSTRACT**

*2,2-di(pyridin-2-yl) hexahydropyrimidine heterocyclic compound was prepared by condensation reaction of 1,3-propanediaminewith di(pyridin-2-yl)methanone1.5,5-dimethyl-1,3-bis[(methyl sulfonyl)oxy]-2,2-dipyridin-2-ylhexahydropyrimidine2 was prepared by protection of both N-H groups in2 using $MeSO_3Cl$ reagent in pyridine/THF media.The prepared compounds revealed good thermal stability, and simple one step decomposition mechanism. The condensation reaction to prepare 1has been monitored by IR.The structures of the desired compounds were characterized by elemental analysis, EI-Ms, UV-Vis, FT-IR, TG and NMR.*

**Keywords:** Hexahydropyrimidine;di(pyridin-2-yl)methanone;2,2-di(pyridin-2-yl)hexahydropyrimidine, NMR.

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## INTRODUCTION

Hexahydropyrimidine nucleus is present in some natural compounds such as tetraponerines, verbamethine and verbametrine [1-3]. Hexahydropyrimidines are pharmaceutically used as antiinflammatory and analgesic agents, fungicides, antibacterials, parasiticides and antivirals [3-9]. Several hexahydropyrimidine derivatives have been prepared and evaluated for many biological activities [10-16]. In additionhexahydropyrimidine are classified as good polydentate ligand for transition metal complexes coordination [5, 8].

Hexahydropyrimidine compounds classically synthesized by condensation both propane-1,3-diamines and aldehydes/ketones [2, 5, 9]. Due to their facile cleavage under mild acidic conditions, it has been employed in organic synthesis as protective groups [5].

In connection with previous research of our group on the characterization of nitrogen-containing heterocycle compounds [9], here in this work, 2,2-di(pyridin-2-yl)hexahydropyrimidineand 5,5-dimethyl-1,3-bis[(methyl sulfonyl)oxy]-2,2-dipyridin-2-ylhexahydropyrimidine were prepared.The reaction was monitored by IR and NMR, the structures like derivatives were previously published by our group [5,9, 17, 18].

## MATERIALS AND METHODS

2.1. Experimental section

The Uv-visible spectrum was measured by using a TU-1901 double-beam UV–visible spectrophotometer. The IR spectra for samples were recorded using Perkin Elmer Spectrum 1000 FT-IR Spectrometer. High-resolution $^1$H, and

$^{13}C\{^{1}H\}$ were recorded on Bruker DRX 250 spectrometer (Bruker, Mainz, Germany) ($^{1}H$, 250 MHz and $^{13}C$, 62.5 MHz frequency) at 298 K. EI-MS data was obtained on a Finnigan 711A (8 kV) (PerkinElmer Inc., Waltham, MA, USA). TG spectrum was measured by using a TGA-7 PerkinElmer thermogravimetric analyzer (PerkinElmer Inc., Waltham, MA, USA).

*Synthesis of 2,2-di(pyridin-2-yl)hexahydropyrimidine1*

A solution of 2-dipyridlketone 2.0mmoL in dichloromethane (20 mL) was mixed with 2,2-dimethyl-1,3-propanediamine 2.1 mmoL and allowed to stand for 1h at RT. The resulting mixture was concentrated under reduced pressure and the title compound was precipitated by the addition of 70 mL of n-hexane. The precipitates were filtered off, washed three times with 80 mL of distilled water.

Yield 92%, Colorless, Mp: 98 $^{o}$C; Molecular formula $C_{16}H_{20}N_4$; $^{1}H$ NMR (250 MHz, $CDCl_3$): (ppm) 1.69 (br, 2H, $CH_2$), 3.55 (br, 2H, NH), 3.67 and 3.68 (2br, 4H, $CH_2$), 7.09–8.58 (3m, 10H, Py–H), $^{13}C$ NMR (62.5 MHz, $CDCl_3$): (ppm) 28.34 ($CH_2$), 53.42 ($2CH_2$),76.92 (N-C-N) 122.14-162.23(complex five group-12C-Py). Calcd. For $C_{14}H_{16}N_4$: C, 69.97; H, 6.71; N, 23.32. Found: C, 69.85; H, 6.51; N, 23.45). [$M^+$] = 240 *m/z*. IR: 3380 $cm^{-1}_{N-H}$, 3060 $cm^{-1}_{C–H\ Py}$, 2970-2750 $cm^{-1}_{C\text{-}H\ aliphatic}$.

*Synthesis of 5,5-dimethyl-1,3-bis[(methylsulfonyl)oxy]-2,2-dipyridin-2-ylhexa-hydropyrimidine **2***

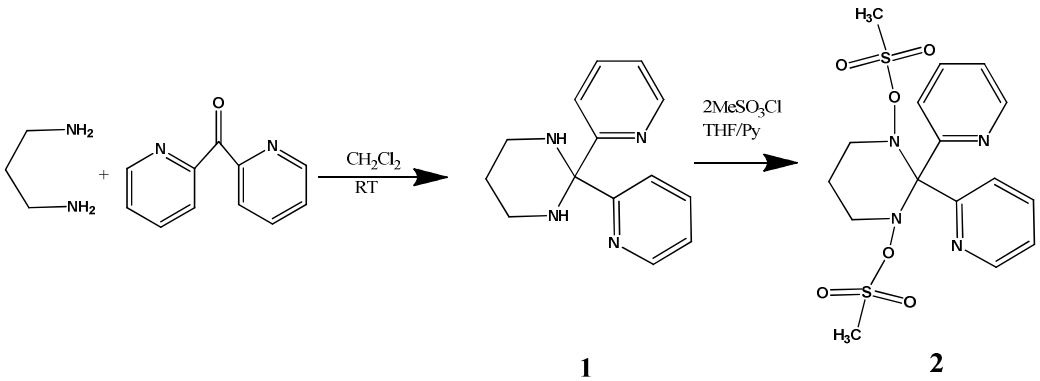
5% excess of methanesulfonyl chloride (4.0mmol) was dissolved in 10 mL dry THF then added slowly to a stirred solution of 2,2-di(pyridin-2-yl)hexahydropyrimidine(1.5 mmol) in 20 mL dry THF, the reaction mixture was lifted to stand under stirring for 24h until the white precipitate appeared. The PyHCl salt was filtrated, then the volume of the solution was concentrated under reduced pressure then transferred to a separating funnel and washed with 40 mL dichloromethane and 100 mL of distilled $H_2O$. By extracting the organic layer and evaporating the solvent in vacuum white solid powder product was collected in good yield.

Yield 78%, Colorless, m.p: 45 $^{o}$C; $^{1}H$ NMR (250 MHz, $CDCl_3$): (ppm) 1.90 (br, 2H, $CH_2$), 3.15 (br, 6H, $2CH_3$), 3.80 and 3.95 (2br, 4H, $CH_2$), 7.10–9.30 (4m, 10H, Py–H), $^{13}C$ NMR (62.5 MHz, $CDCl_3$): (ppm) 30.50 ($CH_2$), 40.82 ($CH_3$), 55.52 ($2CH_2$),80.12 (N-C-N) 120.00-168.00 (complex five group-12C-Py). Calcd. form $C_{16}H_{20}N_4O_6S_2$: C, 44.85; H, 4.70; N, 13.08 Found: C, 44.65; H, 4.61; N, 13.25). EI-MS =[$M^+$] *m/z* = 428. IR: 3480 $cm^{-1}_{O-H}$, 3020 $cm^{-1}_{C–H\ Py}$, 2950-2770 $cm^{-1}_{C\text{-}H\ aliphatic}$. 1150 $cm^{-1}_{S=O.}$

## RESULTS AND DISCUSSION

***3**.1 Synthesis of 1 and 2*

2,2-di(pyridin-2-yl)hexahydropyrimidine1was synthesized by mixing equimolar amounts of 2,2-dimethylpropane-1,3-diamine and di(pyridin-2-yl)methanone in dichloromethane at room temperature, as shown in Scheme 1. 5,5-dimethyl-1,3-bis[(methyl sulfonyl)oxy]-2,2-dipyridin-2-ylhexahydropyrimidine 2 was prepared from 1 using two equivalent amount of $MeSO_3Cl$in basic media. Both 1 and 2are colorless and soluble partially in ROH, insoluble in water and non-polar solvents like *n*-hexane. The structure of the desired compound has been deduced from elemental analysis, infrared spectroscopy, EI-mass spectrometry, Uv-visible, TG and$^{1}H$-NMR spectra




**1** **2**

Scheme 1. Synthesis of 2,2-di(pyridin-2-yl)hexahydropyrimidine1 and5,5-dimethyl-1,3-bis[(methylsulfonyl)oxy]-2,2-dipyridin-2-ylhexahydropyrimidine 2.

***3.2 Elemental analyses and EI-MS***

The elemental analysis of 1is consistent with the proposed molecular formula, (Calcd. for $C_{14}H_{16}N_4$: C, 69.97; H, 6.71; N, 23.32. Found: C, 69.85; H, 6.51; N, 23.45). EI-MS of the compound is in good agreement with the assigned structure and shows the experimental molecular ion [$M^+$] *m/z* = 240 (240.3 theoretical).

The elemental analysis of 2 is also consistent with the proposed molecular formula, (Calcd. for $C_{16}H_{20}N_4O_6S_2$:C, 44.85; H, 4.70; N, 13.08 Found: C, 44.65; H, 4.61; N, 13.25). EI-MS =[$M^+$] *m/z* = 428.0 (428.5 theoretical).

*3.3 Thermal analysis*

The thermal properties TG of 1 was investigated under an open atmosphere in the range of 0–400 °C and heating rate of 10 °C/min. Figure 1 showed one broad step typical decomposition started from ~ 95°C and end at ~ 200°C, with weight loss ~100% and without any intermediate decomposition steps.

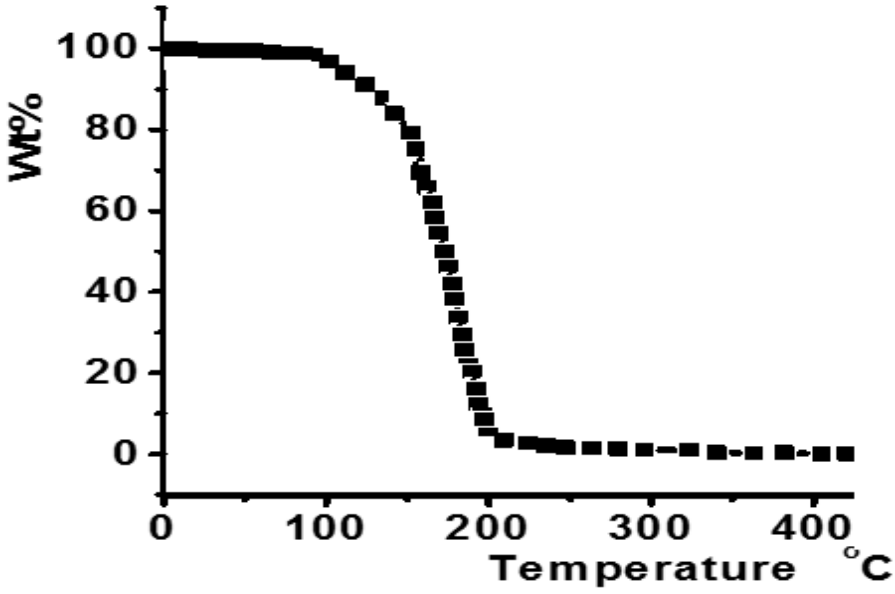



**Figure 1. TG thermal curve of the *2,2-di(pyridin-2-yl)hexahydropyrimidine***

***3.4 FT-IR Spectral Analysis***

The starting materials were subjected to IR before/and after it mix to produce1 and 2, this empowered us to monitor their condensation reaction through FT-IR.The formation of the 1 was confirmed by the ketone C=O disappearance (at 1745 $cm^{-1}$) as seen in Figure 2a, and N-H stretching vibration shiftedfrom 3460 and 3390 $cm^{-1}$doublet (see Figure 2b) to single at 3280 $cm^{-1}$, as seen in Figure 2c. The formation of the 2 from 1 was confirmed by N-H stretching vibration disappearance at 3280 $cm^{-1}$and new S=O stretching vibration appeared at 1150 $cm^{-1}$, as seen in Figure 2d.

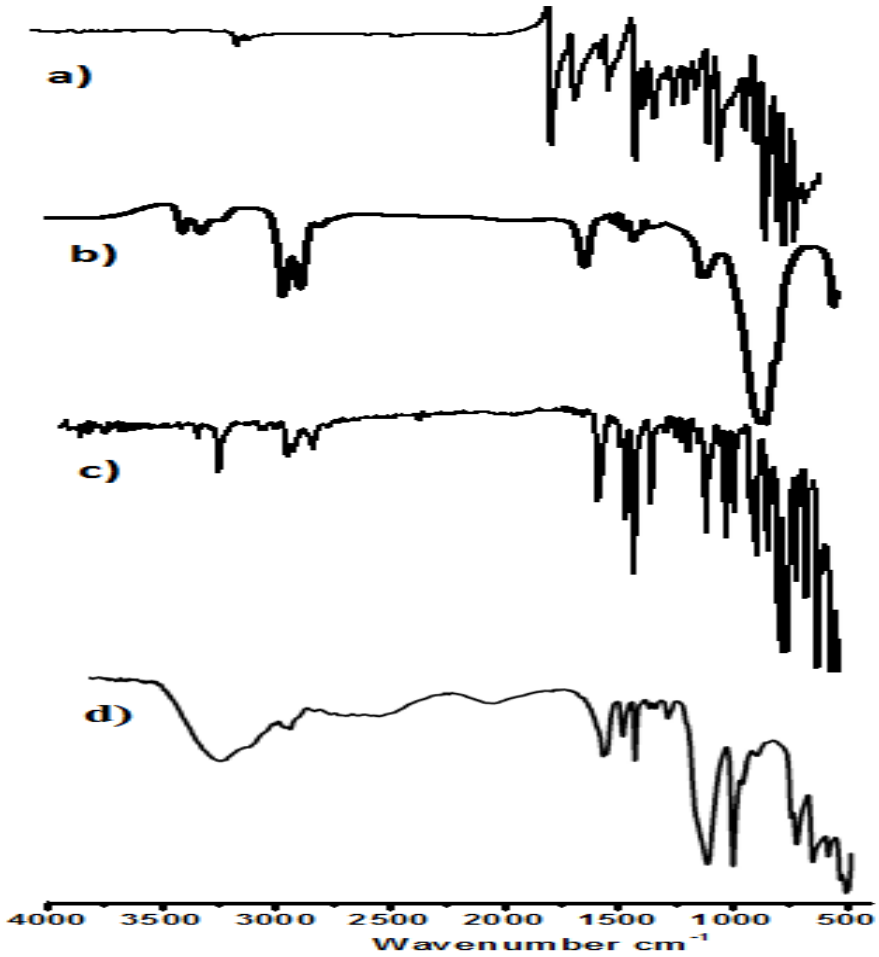



**Figure 2. IR spectra of: a) 2-dipyridlketone (starting material), b) 2,2-dimethyl-1,3-propanediamine(starting material) and c) 2,2-di(pyridin-2-yl)hexahydropyrimidine (product) d) and5,5-dimethyl-1,3-bis[(methylsulfonyl)oxy]-2,2-dipyridin-2-ylhexahydropyrimidine**

***3.5 UV-Vis Spectral Analysis***

The electronic absorption spectrum of the compoundswere acquired in $CH_2Cl_2$ at RT. Figure 3 showed the UV electronic absorption as expected for both compounds. **1** revealed two absorption maxima at $\lambda_{max}$ = 240 and 275 nm a),while **2** gave only one signal at $\lambda_{max}$ = 260 nm b)which assigned to intra-ligand π-π* transitions in both compounds.

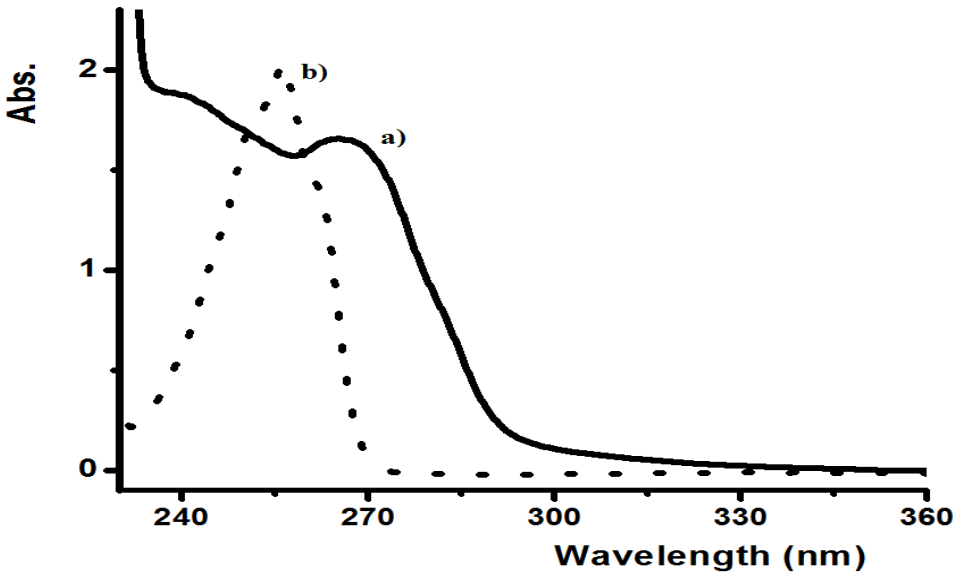



**Figure 3. UV–Vis spectrum of 1 x $10^{-5}$ M in $CH_2Cl_2$ at RT a) 2,2-di(pyridin-2-yl)hexahydropyrimidine and b) and5,5-dimethyl-1,3-bis[(methylsulfonyl)oxy]-2,2-dipyridin-2-ylhexahydropyrimidine**

### *3.6 $^1$H NMR Spectral Analysis*

$^1$H-NMR spectra data are in a good agreement with its assigned structures, signals of aromatic and aliphatic protons are cited to their positions (see experimental section). Figure 4 and 5 showed typical $^1$H-NMR of **1**and **2** respectively.

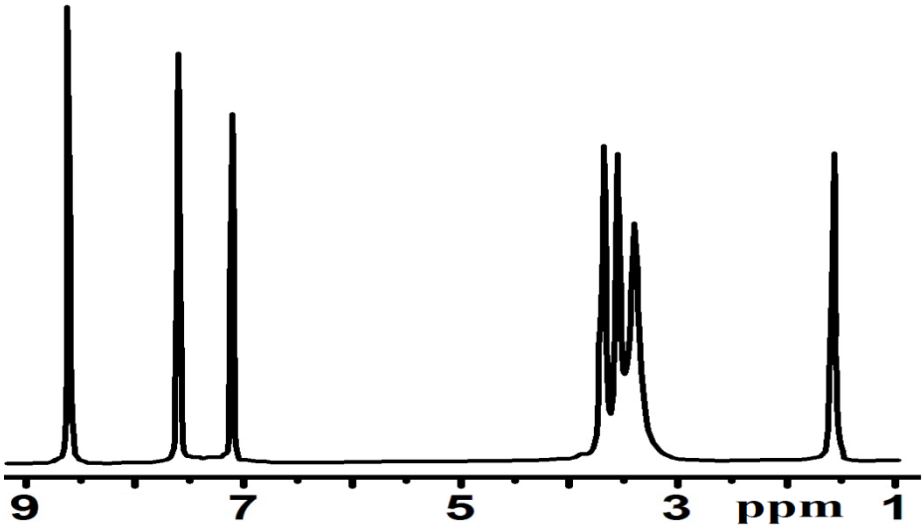



**Figure 4. $^1$H NMR spectrum of 2,2-di(pyridin-2-yl)hexahydropyrimidinein $CDCl_3$ at RT**

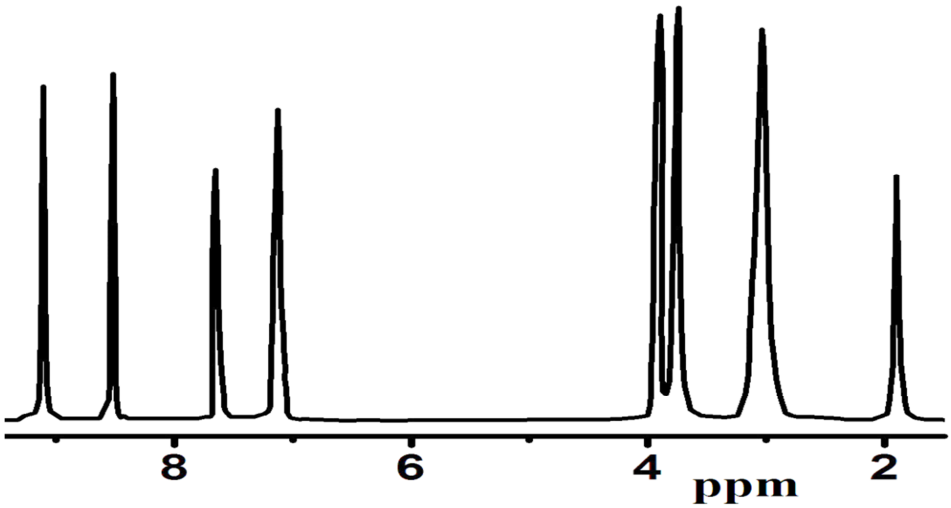



**Figure 5. $^1$H NMR spectrum of and5,5-dimethyl-1,3-bis[(methylsulfonyl)oxy]-2,2-dipyridin-2-ylhexahydropyrimidine in $CDCl_3$ at RT**

## CONCLUSION

In conclusion, we have described the design and synthesis of novelhexahydropyrimidine compound **1** through simple condensation process. Both the polar N-H function groups in **1** was protected by $MeSO_3Cl$ to prepare compound **2** for the first time. Simple one step thermal decomposition mechanism was observed when **1** was subjected to TG.FT-IR found to suitable technique to follow up such reactions. The structures of the desired compounds were successfully characterized by elemental analysis, EI-Ms, UV-Vis, FT-IR, TG and NMR.

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