CHAPTER 4

Ionic liquid catalyzed, microwave assisted synthesis of Pyrido[2,3-*d*:6,5-*d*] dipyrimidine-2,4,6,8-tetraones

4.1 Introduction

Strategic synthetic manipulation towards fused heterocycles in general and fused pyrimidines in particular has always been considered as active and never ending area of research in the field of organic and medicinal chemistry. Synthetic and medicinal chemists throughout the globe have consistently been putting their best efforts to synthesize variably fused pyrimidine derivatives and subsequent evaluation of their medicinal values. A plethora of reports published every year is a mere reflection of existing demand and importance in this regard. Although a wide spectrum of fused pyrimidines have been covered by these reports, however a few pyrimidine derivatives have somehow managed to be less focused and so remain less explored. Pyrido[2,3-*d*:6,5-*d*]dipyrimidine-2,4,6,8-tetraones(**1**, **Fig. 1**) constitute one class of such kind. The first report describing the synthesis of the oldest member (**2**, **Fig. 1**) of this family was published in 1967 [1]. Only a few reports had been published [2] thereafter before the moiety somehow lost the

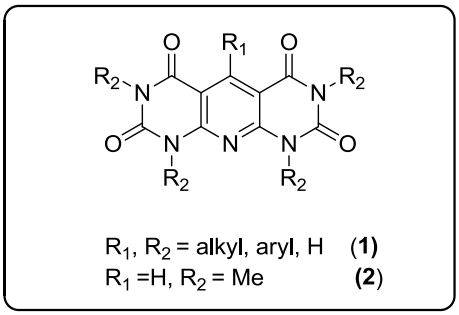


Fig. 1: Structure of pyrido[2,3-*d*:6,5-*d*]dipyrimidine-2,4,6,8-tetraones

attraction of the scientific community. All these described methods were restricted to the synthesis of a few particular pyrido[2,3-*d*:6,5-*d*]dipyrimidine-2,4,6,8-tetraones and clearly lack generality. The moiety came out of hibernation in 2007, when Dabiri, M. et al. reported [3] synthesis of pyrido[2,3-*d*:6,5-*d*]dipyrimidine-2,4,6,8-tetraones via direct condensation of aldehydes and 6-amino-1, 3-dimethylpyrimidine-2, 4(1*H*, 3*H*)-dione (**3**) in ionic liquid media. A very recent report [4] describes a methodology to synthesize pyrido[2,3-*d*:6,5-*d*]dipyrimidine-2,4,6,8-tetraones from the same substrates as in the work of Dabiri, M. et al. and is

observed to be quite general. However, both of these possess their own demerits like lower yield, longer reaction time, lack of generality, use of AcOH as reaction media etc. As such, development of an efficient protocol for the synthesis of pyrido[2,3-*d*:6,5-*d*]dipyrimidine-2,4,6,8-tetraones has remained as a decent task for the synthetic chemists.

With the 'go green' movement everywhere, ionic liquids and microwave irradiation have been able to occupy special places in the field of development of greener synthetic methodology. Due to their unique properties like low volatility, non-flammability, high thermal stability, negligible vapor pressure and ability to dissolve a wide range of materials, ionic liquids have got considerable importance as eco-friendly solvents [5]. Designing of Brønsted acidic ionic liquids to replace solid as well as mineral acids has already been grown up as an interesting field of research [6]. As far as 'green chemistry' is concerned, microwave assisted reactions also attract one's attention due to their ability to reduce reaction times, improve yields and cleaner reaction in comparison to conventional thermal processes [7].

In this chapter, a novel methodology towards the synthesis of pyrido[2,3-*d*:6,5-*d*]dipyrimidine-2,4,6,8-tetraones via condensation of 6-amino-1, 3-dimethylpyrimidine-2, 4(1*H*, 3*H*)-dione (**3**) and aldehydes using Brønsted acidic ionic liquid as reusable catalyst under microwave irradiation (MWI) has been described.

4.2 Results and discussion

To start with, seven ionic liquids bearing -SO_3H as Brønsted acid site (**Fig. 2**) were chosen and their catalytic activity were screened by carrying out a model reaction (**Scheme 1**) between 6-amino-1, 3-dimethylpyrimidine-2, 4(1*H*, 3*H*)-dione (**3**) and benzaldehyde (**4a**) under MWI. For this, 6-amino-1, 3-dimethylpyrimidine-2, 4(1*H*, 3*H*)-dione (**3**, 1 mmol), benzaldehyde (**4a**, 2 mmol) and ionic liquid (20 mol% with respect to **3**) were mixed well in a round bottom flask which was then exposed to MWI (450 W) for 2 minutes. The results are summarized in a bar diagram (**Fig. 3**).

It clearly reveals the suitability of Brønsted acidic ionic liquids for the purpose as full consumption of **3** was observed in every case. **Fig. 3** also reflects that yields of **5a** could be varied with the ionic liquid used and it was observed that ionic liquids with more number of -SO_3H groups serve better. As such, [Dsim]Cl and [Dsim]CH_3SO_3 with two -SO_3H groups are found to be more effective than the others with single -SO_3H group. However, [Dsim]Cl is observed to be marginally more preferable than [Dsim]$CH_3SO_3$and so it was used in the rest of our study.

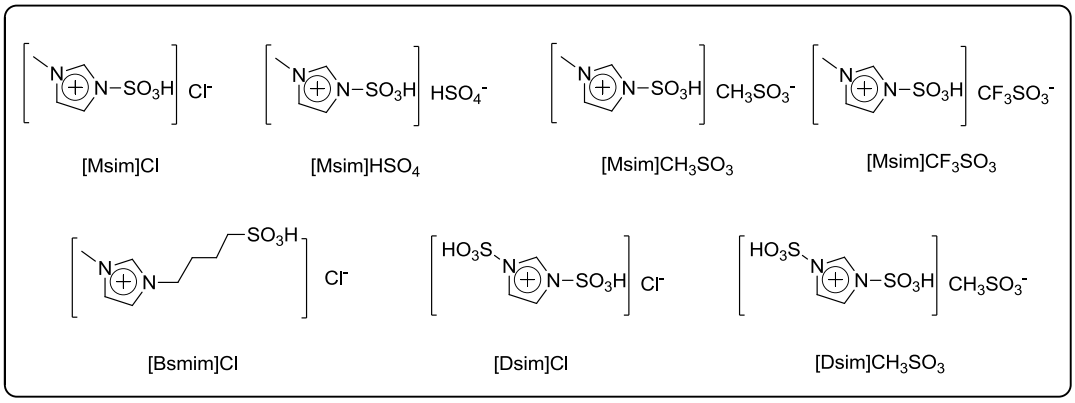
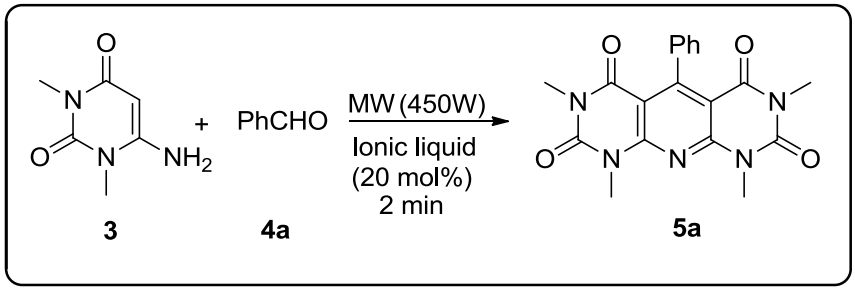


Fig. 2: Selected ionic liquids with Brønsted acid site



Scheme 1: Model reaction for synthesizing **5a**

Optimization of the reaction condition was done by carrying out the same reaction in presence of different amount of [Dsim]Cl under MWI and 15 mol% catalyst loading (with respect to **3**) was found to be optimal for synthesis of **5a** under microwave power of 450 W within 2 minutes. The reaction was attempted with simple mechanical grinding (using mortar and pestle) also without exposing to any MWI which concluded with the neat formation of a new product possessing R_f value distinctly different from **5a**. This new product was identified as 6-amino-5

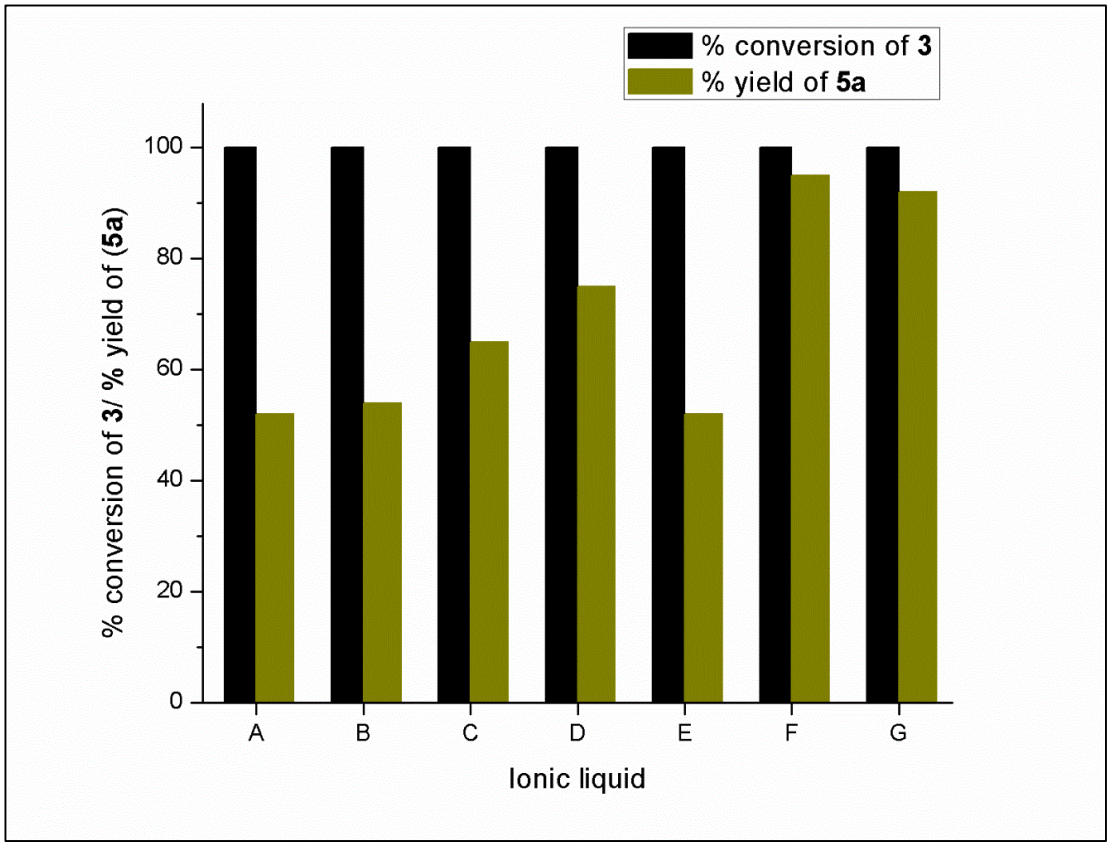


Fig. 3: Screening of ionic liquids for **Scheme 1**. Here, A=[Msim]Cl; B=[Msim]HSO_4; C=[Msim]CH_3SO_3; D=[Msim]CF_3SO_3; E=[Bsmim]Cl; F=[Dsim]Cl; G=[Dsim]CH_3SO_3(% yield were isolated yield)

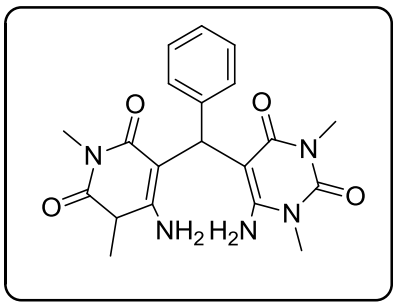
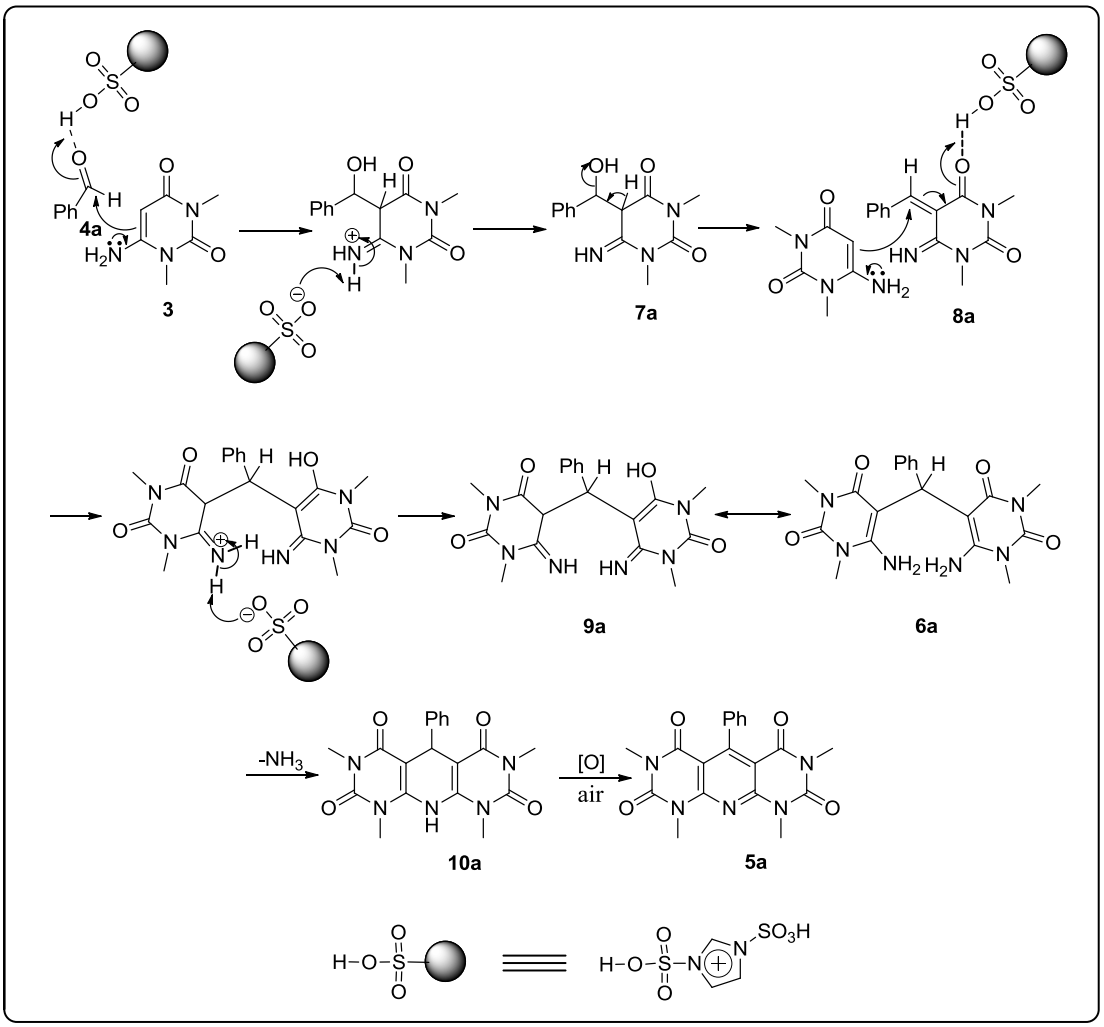


Fig. 4: Structure of 6-amino-5-((4-amino-1,5-dimethyl-2,6-dioxo-1,2,5,6-tetrahydropyridin-3-yl)(phenyl)methyl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (**6a**)

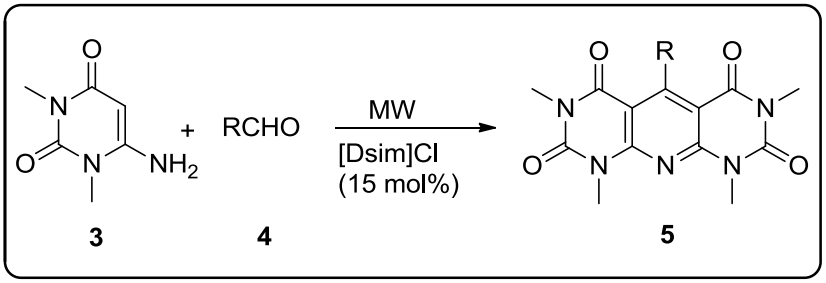
-((4-amino-1,5-dimethyl-2,6-dioxo-1,2,5,6-tetrahydropyridin-3-yl)(phenyl)methyl)-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (**6a**, **Fig. 4**) by NMR

study as well as melting point and R_f comparison with authentic compound [8]. To have some insight into the mechanism, we isolated **6a** and then exposed to MWI (450 W) in presence of [Dsim]Cl (15 mol%) which led to the formation of **5a** within 1 minute only. This observation was an expected one, and implied the possibility of involvement of **6a** as an intermediate in the reaction. Although a detailed mechanistic study was not performed, a plausible mechanism (**Scheme 2**) has been suggested for the reaction based on formation of **6a** as an intermediate. The rule of [Dsim]Cl is to activate the carbonyl group. The final step is the aerial oxidation of **10a** to its aromatized counterpart **5a** and is supported by the fact that the reaction results **10a** as ultimate product when the reaction is carried out in N_2 atmosphere under an otherwise similar condition.



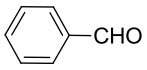
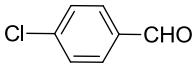
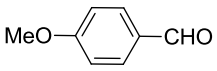
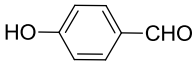
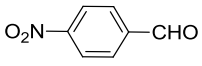
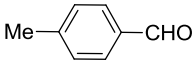
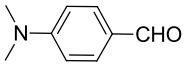
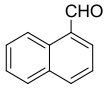
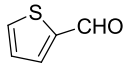
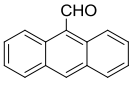
Scheme 2: Plausible mechanism for the synthesis of **5a** via **Scheme 1**

To access the generality of the developed protocol, a series of aldehydes were screened via **Scheme 3** and the results obtained are summarized in **Table 1**. **Table 1** clearly reflects the suitability of the protocol for a wide spectrum of aromatic aldehydes. Effect of electron withdrawing and electron releasing groups



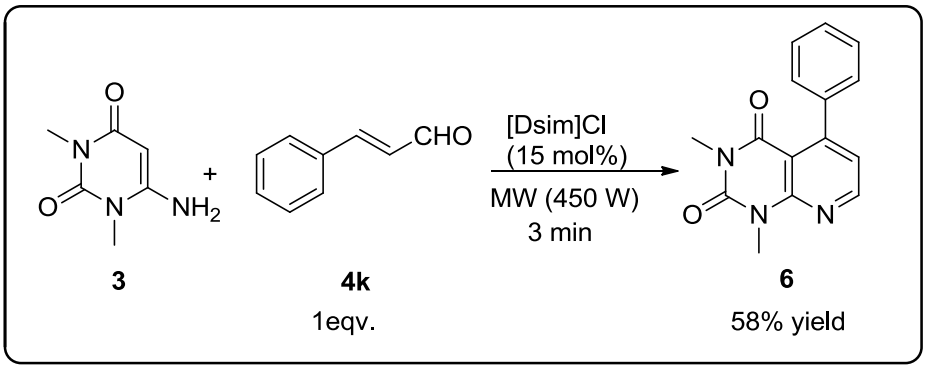
Scheme 3: [Dsim]Cl catalyzed, microwave assisted synthesis of **5**

Table 1: Synthesis of **5** via **Scheme 3**

Entry	Structure of **4**	MW power (W)	Time (min)	Yield of **5** [%][a]	mp of **5**
a		450	2	95	247
b		450	6	80	281
c		450	6	82	263
d		450	6	75	352
e		450	3	85	343
f		450	5	68	328
g		600	10	32	287
h		450	7	85	238
i		450	3	96	247
j		450	3	--	--[b]

[a]Isolated yield
[b] Unidentified product

(Entries b-f, **Table 1**) in the aromatic ring of aldehydes towards their reactivity is not found to follow a general trend and so is not very conclusive. However, aldehyde with strongly electron donating group (Entry g, **Table 1**) is found to be reluctant towards the reaction. 9-Anthraldehyde (Entry j, **Table 1**) is found to result unidentified product under the reaction condition. While an attempt to extend the protocol for ketone using $(CH_3)_2CO$, $PhCOCH_3$ and $(Ph)_2CO$ went in vain, aliphatic aldehydes are not also found suitable for synthesis of their corresponding pyrido[2,3-*d*:6,5-*d*]dipyrimidine-2,4,6,8-tetraones resulting unidentified products under the reaction condition. Pyrido[2,3-*d*]pyrimidine, rather than pyrido[2,3-*d*:6,5-*d*]dipyrimidine is found to be formed when the reaction is carried out with cinnamaldehyde (*α*,*β*-unsaturated aldehyde) under similar condition (**Scheme 4**).



Scheme 4: Synthesis of pyrido[2,3-*d*]pyrimidine (**6**)

All the new synthesized compounds were characterized by FTIR, ^1H & ^{13}C NMR spectroscopy, HRMS and CHN analysis. Structure of **5f** was further confirmed by single crystal X-ray analysis and the ORTEP diagram of the molecule is as shown in **Fig. 5**.

The synthesized compounds (**5a-j**) were screened for their preliminary antimicrobial activity against both the Gram positive (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram negative (*Klebsilla pneumonia*, *Escherichia coli* & *Pseudomonas aeruginosa*) bacterial strains at a concentration of 1 mg/mL. The bacterial zones of inhibition (mm) values were evaluated using the well diffusion method (**Table 2**) taking ampicillin (2 μg/mL) as positive control while sterilized

DMSO as negative control. It is observed from **Table 2** that the synthesized compounds show modest activity against *S. aureus* and *K. pneumoniae* only and are inert to other bacterial strains tested.

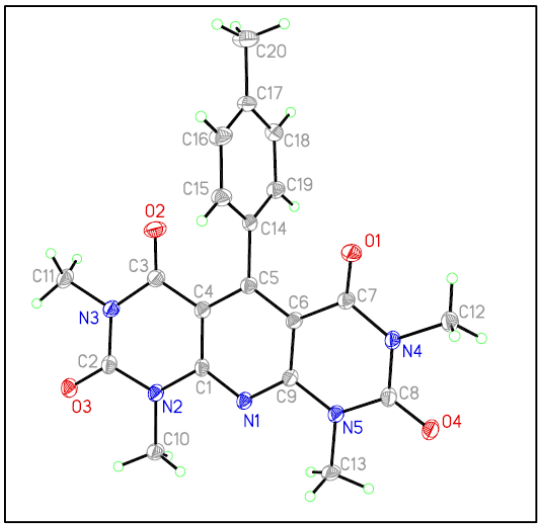


Fig. 5: ORTEP diagram of **5f**

4.3 Recovery and reusability of [Dsim]Cl

To check the worth of the catalyst further, recovery and reusability of the catalyst were studied. For this, the reaction was carried out in comparatively large scale taking 0.02 mol of **3** and 0.04 mol of **4a** as substrates. After completion of the reaction, H_2O (6 mL) was added to the reaction mixture and the content was stirred for 5 min and then filtered. The water soluble ionic liquid was recovered from the filtrate by evaporation. The recovered catalyst thus obtained was used for the next batch of reaction. Activity of the reused catalyst was tested up to the fourth cycle and the results are presented in **Fig. 6**. Although only a slight decrease in activity is observed in the 2^{nd}cycle as compared to fresh catalyst, activity drops sharply with further run as indicated by **Fig. 6**. The loss in activity of the catalyst can be attributed to the loss of active sites during the process. In the aqueous media, a quantity of [Dsim]Cl gets hydrolyzed to imidazole which is supported by existing reports [9].

Table 2: Bacterial zones of inhibition (in mm) by synthesized pyrido[2,3-*d*:6,5-*d*]dipyrimidine

Entry	Compounds	Microorganisms				
		Gram positive		Gram negative		
		B. subtilis	*S. aureus*	*K. pneumonia*	*E. coli*	*P. aeruginosa*
1	**5a**	**--**[a]	**10**	**12**	**--**	**--**
2	**5b**	--	14	12	--	--
3	**5c**	--	13	12	--	--
4	**5d**	--	14	12	--	--
5	**5e**	--	14	13	--	--
6	**5f**	--	14	12	--	--
7	**5g**	--	13	14	--	--
8	**5h**	**--**	**13**	**12**	**--**	**--**
9	**5i**	--	13	13	--	--
10	**6**	**--**	**13**	**13**	**--**	**--**
11	Ampicillin	14	16	23	18	23

[a] No activity

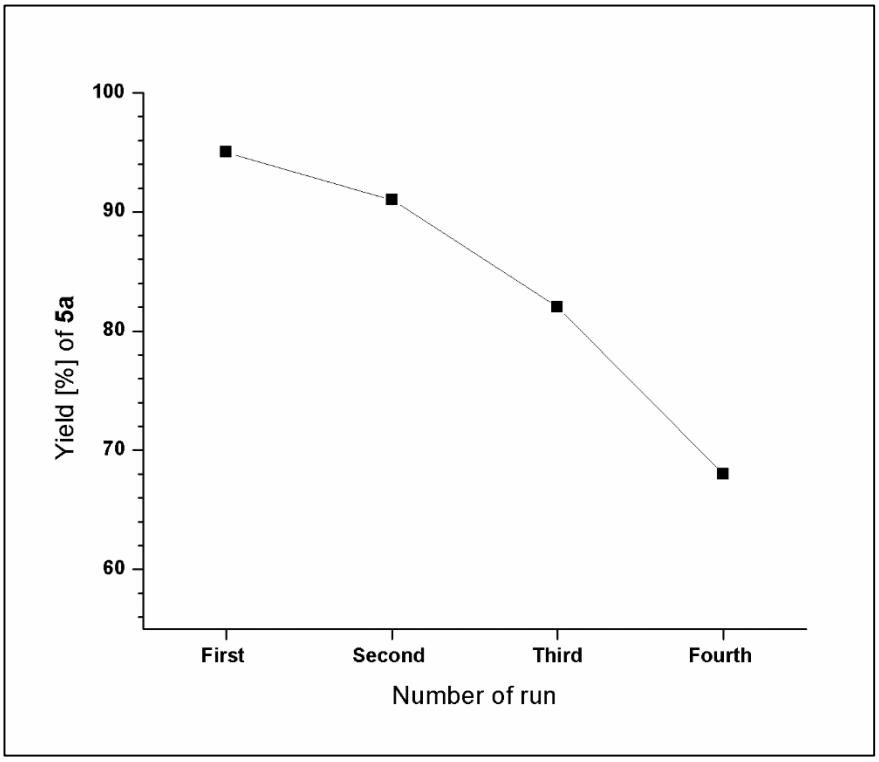


Fig. 6: Reusability of [Dsim]Cl for synthesis of **5a** via **Scheme 3**

4.4 Conclusion

In conclusion, an ionic liquid catalyzed microwave assisted synthesis of pyrido[2,3-*d*:6,5-*d*]dipyrimidine-2,4,6,8-tetraones via condensation of 6-amino-1,3-dimethylpyrimidine-2,4(1*H*, 3*H*)-dione and aldhehydes has been developed. Brønsted acidic ionic liquid, [Dsim]Cl serves the purpose sufficiently well in absence of added acids within a short time and the protocol is found to be quite general covering a wide variety of aldehydes. The methodology is superior to the existing method [3] in terms of time economy and resulting yield. Although, the reusability of the catalyst is not so great, the catalyst can be used however for the second run without any remarkable change in activity. We believe that the methodology is the first to carry out the transformation using ionic liquid catalyst coupled with microwave irradiation. The synthesized compounds are found to have modest activity against *S. aureus* and *K. pneumoniae.*

4.5 Experimental section

4.5.1 General information

One of the starting materials 6-amino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (**3)** was prepared by the procedure as described in **Chapter 3**. The ionic liquid [Dsim]Cl was prepared and characterized by following a standard procedure mentioned in the work of Zolfigol, M. A. et al [9a]. All other reagents and chemicals were of reagent grade (AR grade) and were used as purchased without further purification. Reactions were carried out in a 'Microwave Synthesis System' (model CAT-2R) from Catalyst TM systems. Melting points were determined with a Büchi 504 apparatus and are uncorrected. IR spectra were recorded as KBr pallets with a Nicolet (Impact 410) FT-IR spectrophotometer with frequencies expressed in wave numbers (cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded with a JNM ECS 400 MHz NMR spectrophotometer (JEOL) using tetramethylsilane (TMS) as the internal standard. Chemical shift and coupling constant values are expressed in ppm & Hz respectively. X-ray intensity data were collected with a Bruker SMART APEX CCD area-detector diffractometer with Mo-*K*α radiation (λ = 0.71073 Å). The structures

were solved by SHELX97 and refined by full-matrix least-squares on F^2(SHELX97) (Sheldrick, G. M. *Acta Crystallogr., Sect. A* 2008, *64*, 112-122). Reactions were monitored by thin-layer chromatography (TLC) using aluminium sheets with silica gel $60F_{254}$ (Merck). UV light and Iodine vapour were used as visualizer. Elemental analyses were carried out with a Perkin-Elmer CHN analyzer (2400 series II). Mass spectrometric analysis were performed using a Waters Q-TOF Premier & Aquity UPLC spectrometer.

4.5.2 Procedure for the preparation of ionic liquid [Dsim]Cl

To a round-bottomed flask (100 mL) containing imidazole(0.340 g, 5 mmol) in dry CH_2Cl_2 (50 mL), was added chlorosulfonic acid (1.19 g, 10.2 mmol) dropwise over a period of 20 min at room temperature. After the addition was completed, the reaction mixture was stirred for 12 h under nitrogen atmosphere. Then, it was allowed to stand for 5 min and then CH_2Cl_2 was decanted. The residue was washed with dry CH_2Cl_2 (3×50 mL) and dried under vacuum to give [Dsim]Cl as a viscous pale yellow oil (1.257 g, Yield= 95%).

4.5.3 General procedure for Scheme 3

6-amino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (**3**, 1 mmol), aldehydes (**4**, 2 mmol) and ionic liquid (15 mol % with respect to **3**) were mixed well in a round bottom flask which was then exposed to microwave irradiation (with microwave power as mentioned in **Table 1**). The reaction was monitored using TLC. After completion of the reaction, the reaction mixture was allowed to cool and then H_2O was added to dissolve the catalyst. Filtration was done and the residue (after complete drying) was purified by column chromatography using silica gel (100-200 mesh) as adsorbent and EtOAc-Hexane as eluent.

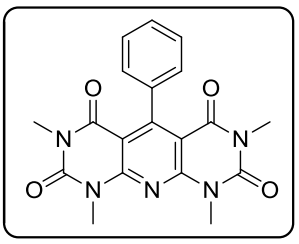
4.5.4 Screening of pyrido[2,3-*d*:6,5-*d*]dipyrimidine-2,4,6,8-tetraones towards preliminary antibacterial studies

The well diffusion methods was used to evaluate the antimicrobial susceptibility of compounds. All bacterial strains were cultured in Luria-Bertani (LB) broth at 37 ^{0}C

on a shaker at 200 rpm for 24 h. 10^5 to 10^6 colony-forming units per mL (CFU mL^{-1}) of microorganism were spread on Muller Hinton Agar plates and a concentration of 1mg/mL of compounds (**5a-i, 6**) was loaded into the corresponding wells. Ampicillin was used as standard control. Zones of growth inhibition were determined by measuring the diameter (mm) of bacterial clearance after 24 h of incubation at 37 ^{0}C. All assays were performed in triplicate.

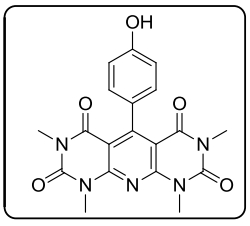
4.5.5 Spectral data

1,3,7,9-tetramethyl-5-phenylpyrido[2,3-*d*:6,5-*d*']dipyrimidine-2,4,6,8(1*H*,3*H*,7*H*,9*H*)-tetraone (5a)



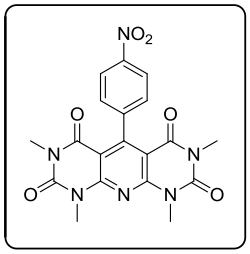
FT-IR (KBr): ν_{max}= 3420, 2944, 1681, 1546, 1420, 1361 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.49 (t, *J*= 3 Hz, 3H), 7.09 (m, 1H), 3.77 (s, 6H), 3.29 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ= 160.1, 159.2, 153.4, 151.0, 137.7, 128.1, 127.8, 125.5, 105.0, 30.5, 28.7 ppm; MS(ESI): m/z= 379 [M^+]; Anal. Calcd (%) for $C_{19}H_{17}N_5O_4$: C, 60.15; H, 4.52; N, 18.46. Found: C, 60.13; H, 4.57; N, 18.48.

5-(4-hydroxyphenyl)-1,3,7,9-tetramethylpyrido[2,3-*d*:6,5-*d*']dipyrimidine-2,4,6,8(1*H*,3*H*,7*H*,9*H*)-tetraone (5d)



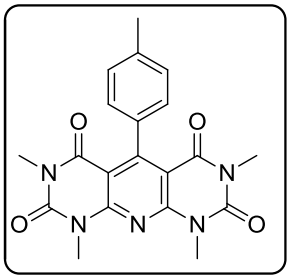
FT-IR (KBr): ν_{max}= 3413, 3301, 2944, 1718, 1666, 1561, 1420 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 6.94 (d, *J*= 8 Hz, 2H), 6.85 (d, *J*= 8 Hz, 2H), 3.77 (s, 6H), 3.31 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ= 160.6, 159.5, 155.7, 153.4, 151.0, 130.1, 129.1, 126.8, 115.5, 105.3, 30.6, 28.8 ppm, MS(ESI): m/z= 395 [M^+]; Anal. Calcd (%) for $C_{19}H_{17}N_5O_5$: C, 57.72; H, 4.33; N, 17.71. Found: C, 57.74; H, 4.32; N, 17.74.

1,3,7,9-tetramethyl-5-(4-nitrophenyl)pyrido[2,3-*d*:6,5-*d*']dipyrimidine-2,4,6,8(1*H*,3*H*,7*H*,9*H*)-tetraone (5e)



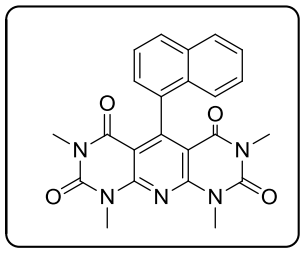
FT-IR (KBr): ν_{max}= 3435, 2929, 1681, 1568, 1420, 1346 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 8.34 (d, *J*= 8 Hz, 2H), 7.26 (d, *J*= 8 Hz, 2H), 3.78 (s, 6H), 3.28 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ= 159.2, 157.2, 153.6, 150.7, 147.3, 145.1, 126.8, 123.6, 104.6, 30.6, 28.7 ppm; MS(ESI): m/z= 424 [M^+]; Anal. Calcd (%) for $C_{19}H_{16}N_6O_6$: C, 53.77; H, 3.80; N, 19.80. Found: C, 53.78; H, 3.84; N, 19.83.

1,3,7,9-tetramethyl-5-(p-tolyl)pyrido[2,3-*d*:6,5-*d*']dipyrimidine-2,4,6,8(1*H*,3*H*,7*H*,9*H*)-tetraone (5f)



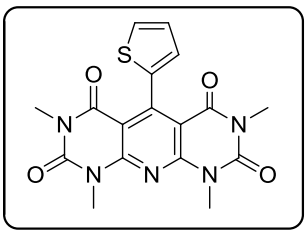
FT-IR (KBr): ν_{max}= 3546, 2929, 1658, 1554, 1428, 1361 cm^{-1}; 1H NMR (400 MHz, $CDCl_3$): δ= 7.30 (d, *J*= 8 Hz, 2H), 6.98 (d, *J*= 8 Hz, 2H), 3.76 (s, 6H), .3.29 (s, 6H), 2.4(s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ= 160.6, 159.2, 153.4, 151.0, 137.4, 134.7, 128.9, 125.4, 105.4, 105.2, 30.5, 28.7, 21.8 ppm; MS(ESI): m/z= 393[M^+]; Anal. Calcd (%) for $C_{20}H_{19}N_5O_4$: C, 61.06; H, 4.87; N, 17.80. Found: C, 61.03; H, 4.86; N, 17.82.

1,3,7,9-tetramethyl-5-(naphthalen-1-yl)pyrido[2,3-*d*:6,5-*d*']dipyrimidine-2,4,6,8(1*H*,3*H*,7*H*,9*H*)-tetraone (5h)



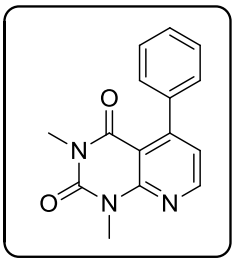
FT-IR (KBr): ν_{max}= 3435, 2937, 1681, 1539, 1405, 1361 cm^{-1}; 1H NMR (400 MHz, $CDCl_3$): δ= 7.95 (dd, *J*= 8 Hz, *J*=16 Hz, 2H), 7.56 (t, *J*= 8 Hz, 1H), 7.44 (t, *J*= 8 Hz, 1H), 7.28 (t, *J*= 8 Hz, 1H), 7.18 (d, *J*= 8 Hz, 1H), 7.09 (d, *J*= 8 Hz, 1H), 3.81(s, 6H), 3.18 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ= 159.0, 158.6, 153.6, 151.0, 135.8, 132.9, 130.99, 129.0, 128.1, 126.2, 125.4, 123.8, 122.3, 30.5, 28.7 ppm; MS(ESI): m/z= 429 [M^+]; Anal. Calcd (%) for $C_{23}H_{19}N_5O_4$: C, 64.33; H, 4.46; N, 16.31. Found: C, 64.31; H, 4.45; N, 16.34.

1,3,7,9-tetramethyl-5-(thiophen-2-yl)pyrido[2,3-*d*:6,5-*d*']dipyrimidine-2,4,6,8(1*H*,3*H*,7*H*,9*H*)-tetraone (5i)



FT-IR (KBr): ν_{max}= 3398, 2952, 1666, 1546, 1420, 1346 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ=7.555 (d, *J*= 4.8 Hz, 1H), 7.19 (dd, *J*= 3.6 Hz, *J*= 5.2 Hz, 1H), 6.81-6.82(dd, *J*= 1.2 Hz, *J*= 3.6 Hz, 1H), 3.76 (s, 6H), 3.33 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ= 158.7, 153.3, 150.9, 137.0, 127.2, 126.2, 124.9, 30.5, 28.8 ppm; MS(ESI): m/z= 385 [M^+]; Anal. Calcd (%) for $C_{23}H_{19}N_5O_4$: C, 52.98; H, 3.92; N, 18.17. Found: C, 52.95; H, 3.98; N, 18.23.

1,3-dimethyl-5-phenylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (6)



FT-IR (KBr): ν_{max}= 3406, 2944, 1710, 1658, 1546, 1465 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$): δ= 8.53 (d, *J*=4.8 Hz, 1H), 7.38(m, 3H), 7.22 (m, 2H), 6.95(d, *J*= 4.8 Hz, 1H), 3.71 (s, 3H), 3.31(s, 3H) ppm;^{13}C (100 MHz, $CDCl_3$): δ= 160.4, 154.3, 152.0, 151.7, 151.1, 138.9, 128.0, 127.7, 127.5, 121.8, 107.8, 30.0, 28.3 ppm; MS(ESI):m/z= 267 [M^+]; Anal. Calcd (%) for $C_{15}H_{13}N_3O_2$: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.43; H, 4.93; N, 15.76.

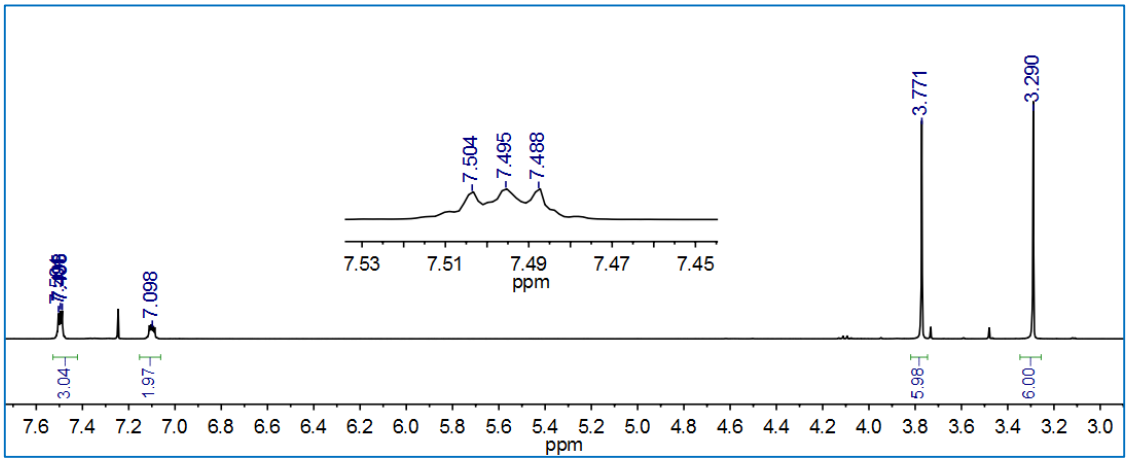


Fig. 7: ^1H NMR spectrum of **5a**

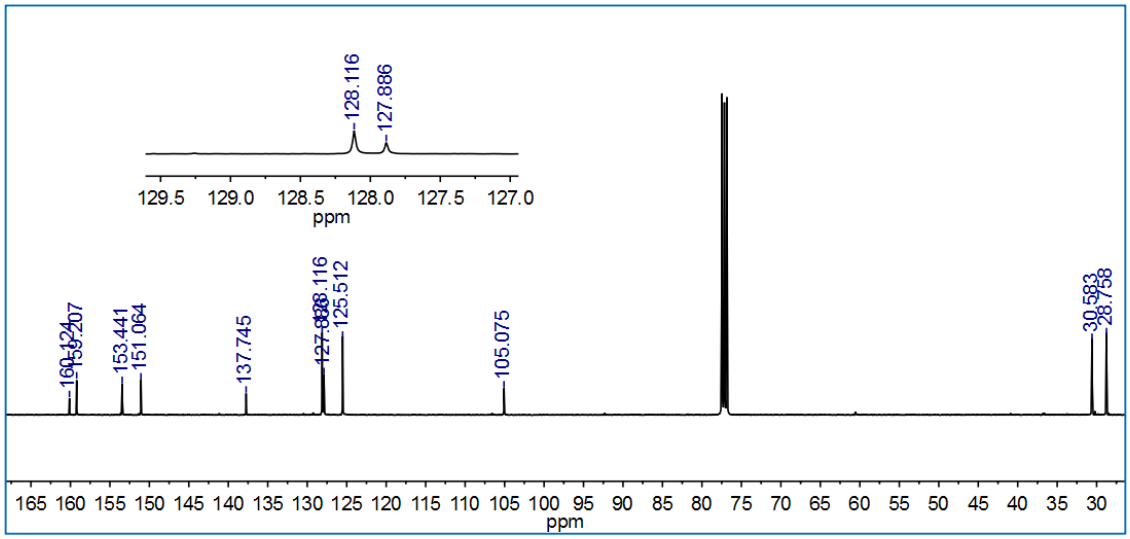


Fig. 8: ^{13}C NMR spectrum of **5a**

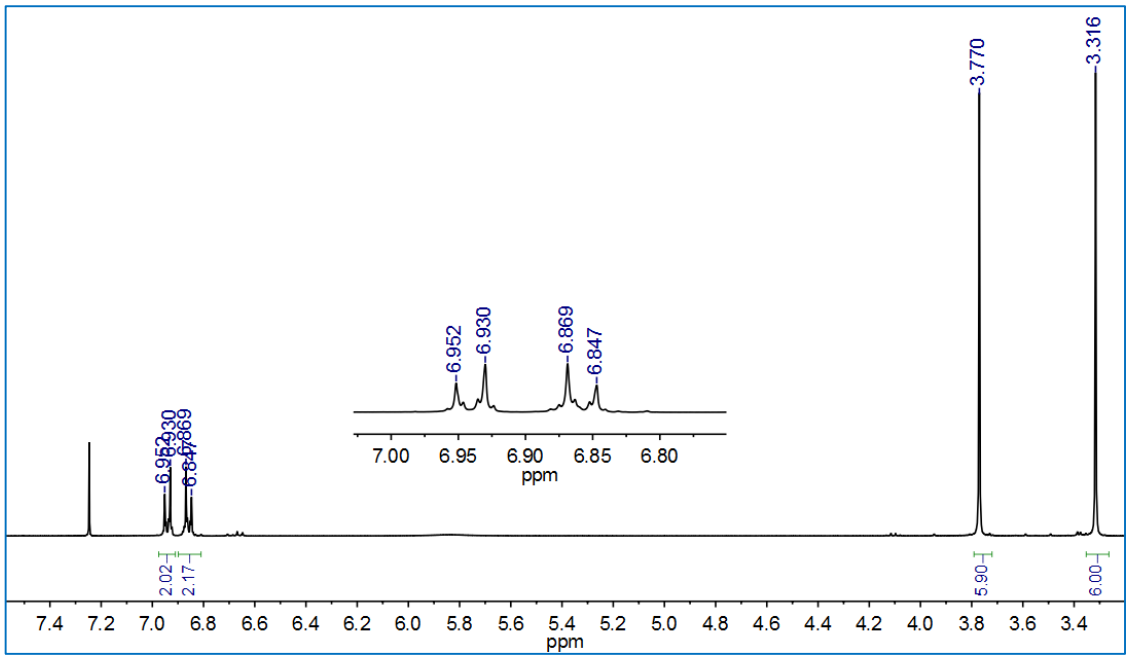


Fig. 9: ^{1}H NMR spectrum of **5d**

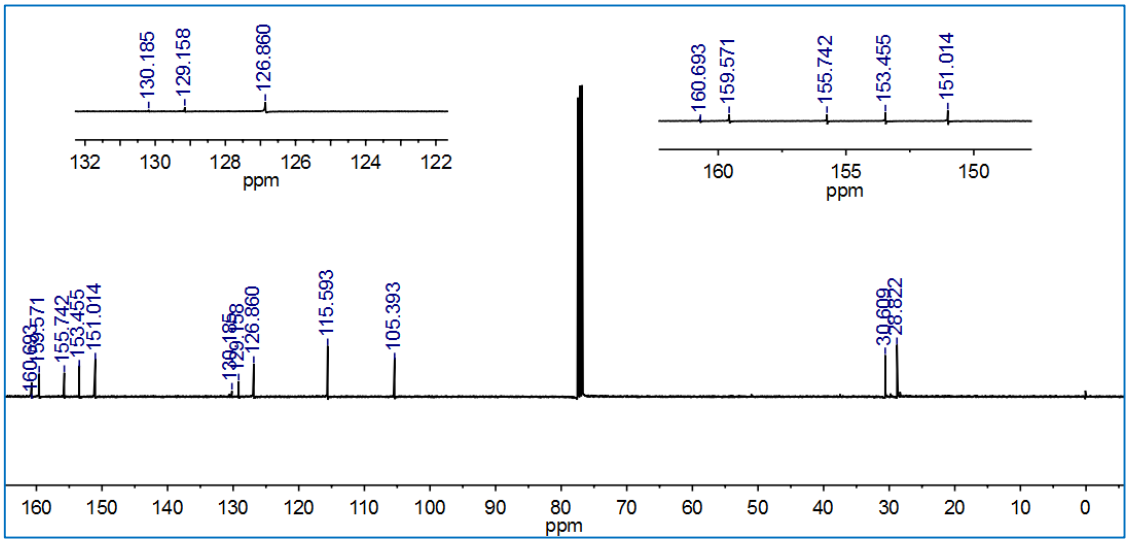


Fig. 10: ^{13}C NMR spectrum of **5d**

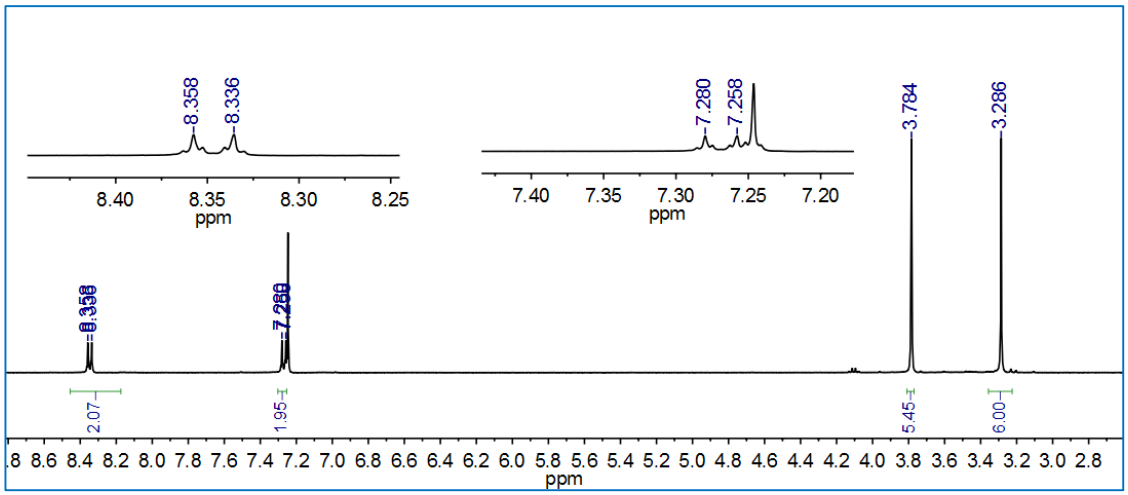


Fig. 11: ^{1}H NMR spectrum of 5e

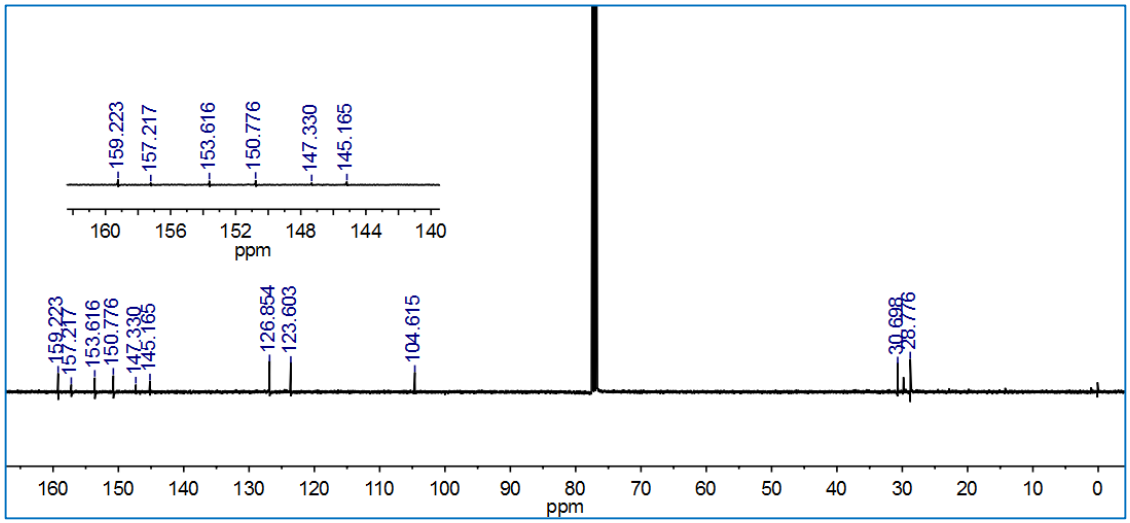


Fig. 12: ^{13}C NMR spectrum of **5e**

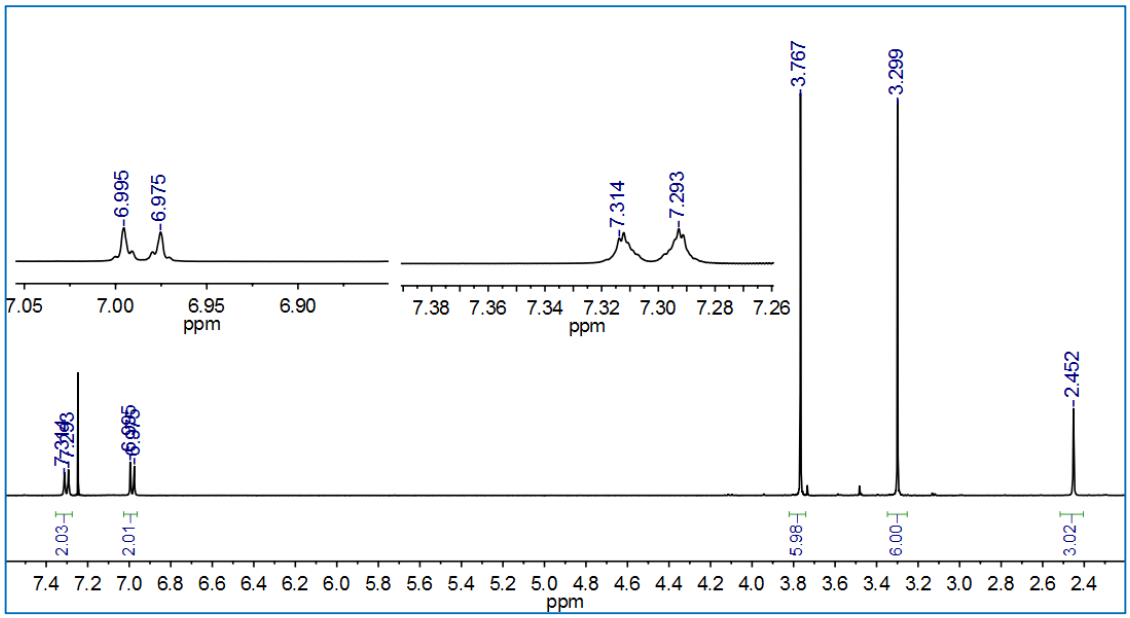


Fig. 13: ^{1}H NMR spectrum of **5f**

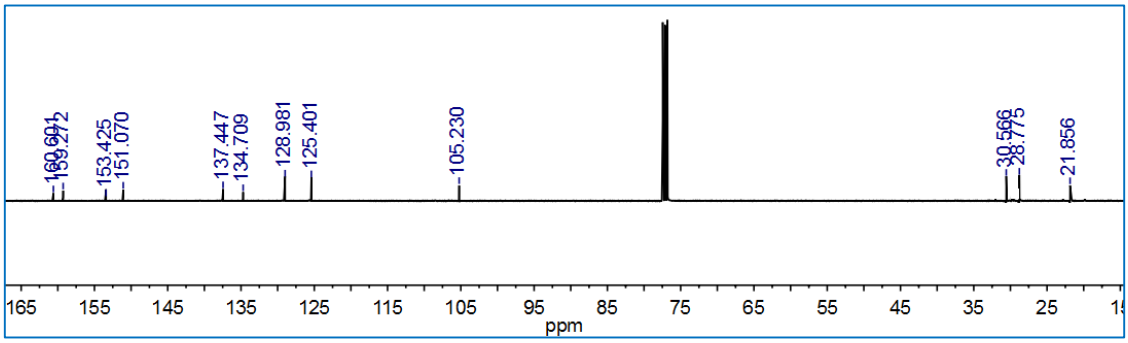


Fig. 14: ^{13}C NMR spectrum of 5f

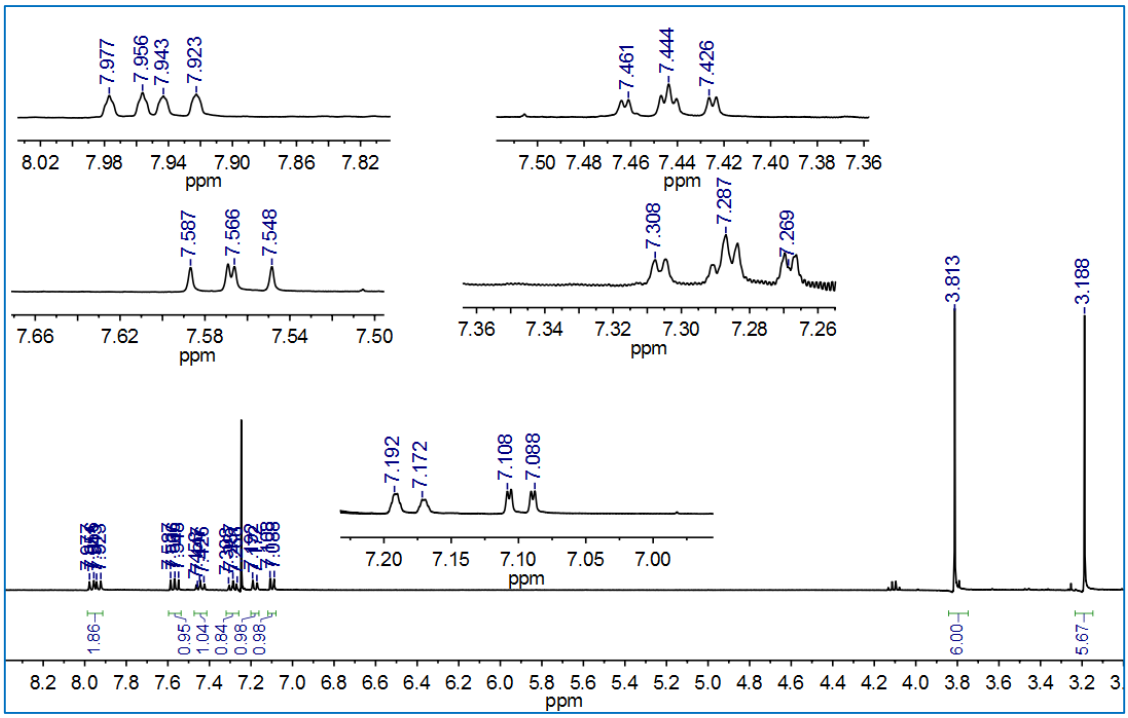


Fig. 15: ^{1}H NMR spectrum of **5h**

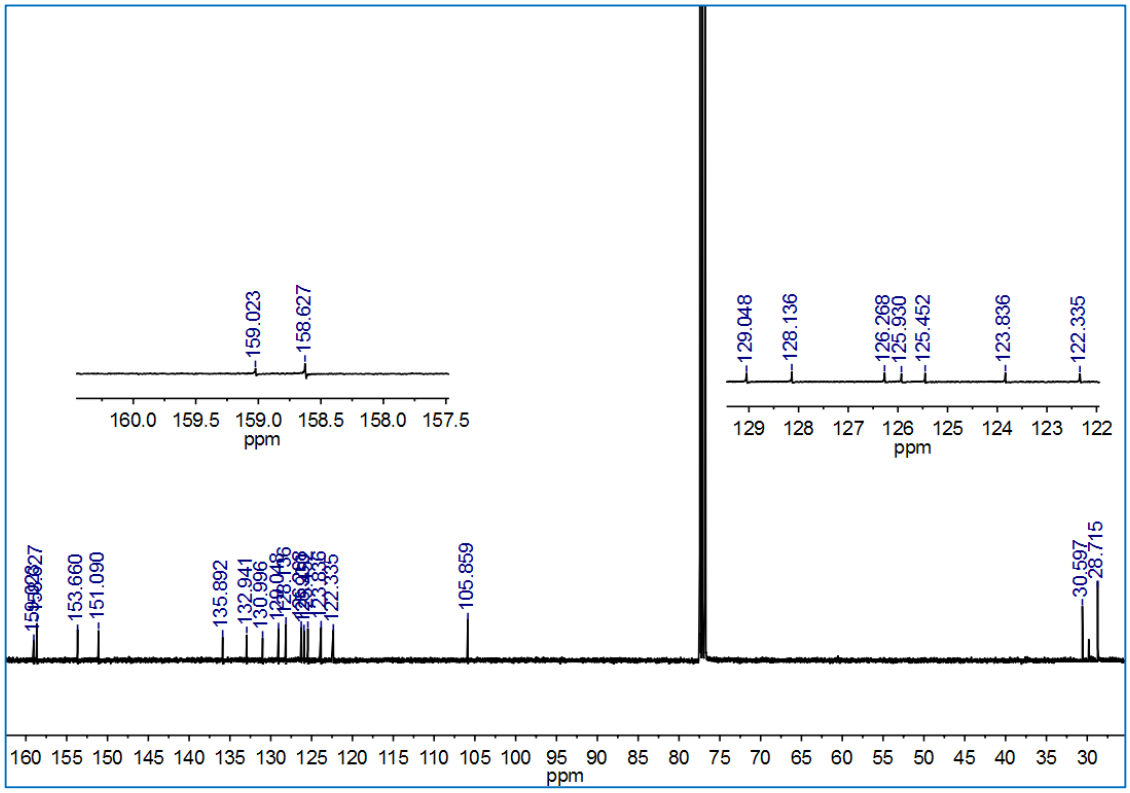


Fig. 16: ^{13}C NMR spectrum of **5h**

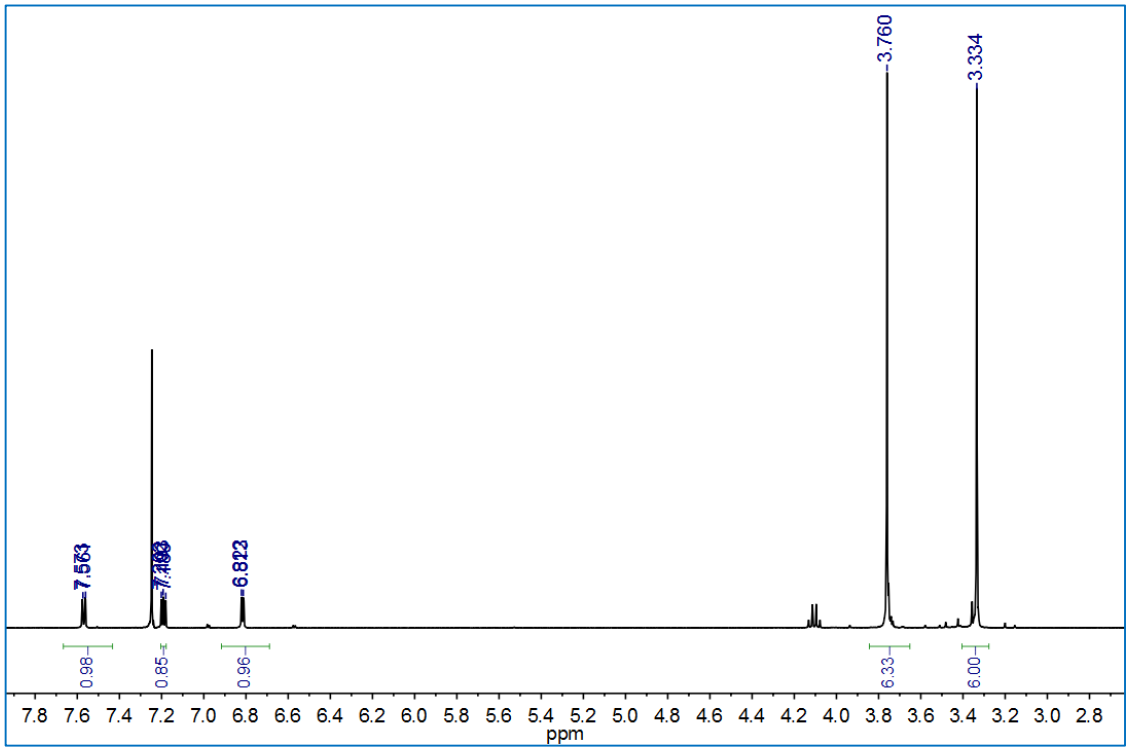


Fig. 17: ^{1}H NMR spectrum of **5i**

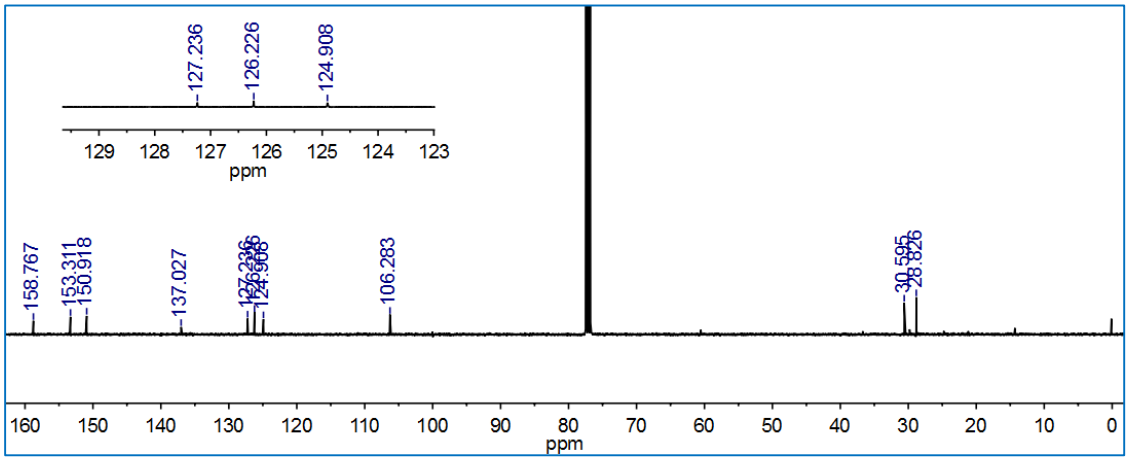


Fig. 18: ^{13}C NMR spectrum of **5i**

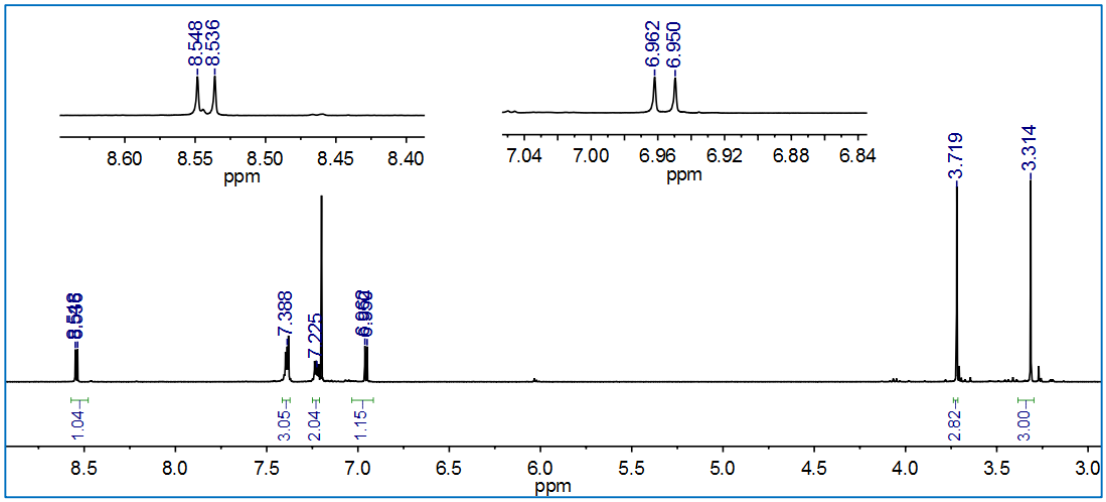


Fig. 19: ^{1}H NMR spectrum of **6**

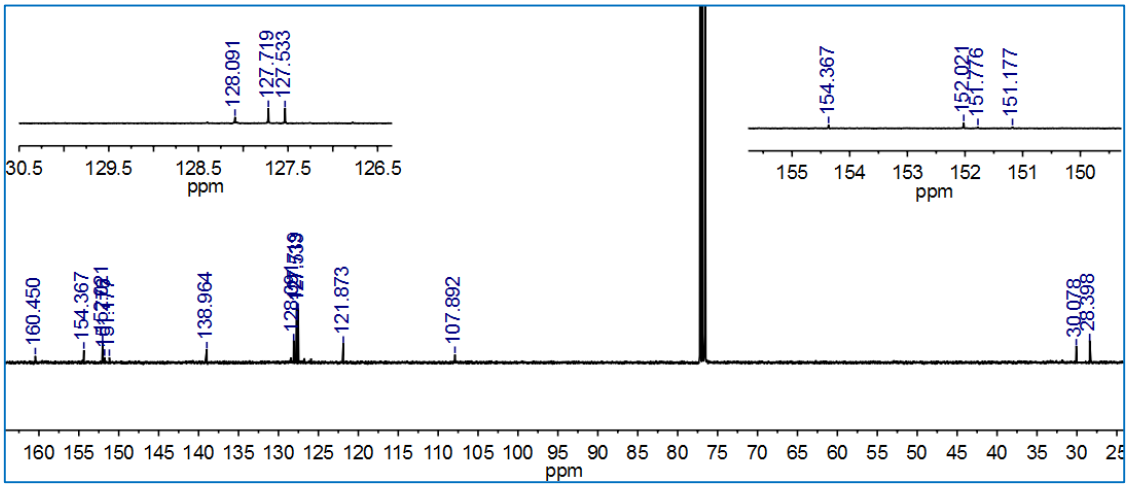


Fig. 20: ^{13}C NMR spectrum of **6**

4.6 References

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