Supporting Information

Microwave irradiation: A green approach for synthesis of functionalized N-methyl-1,4-dihydropyridines

M. Musawwer Khan†*, Saigal,† Sarfaraz Khan,† Sumbulunnisan Shareef† and Subash C. Sahoo††

†Department of Chemistry, Aligarh Muslim University, Aligarh 202002, India,
††Department of Chemistry & Center of Advanced Studies in Chemistry, Panjab University, Chandigarh-160014, India
E-mail: musawwer@gmail.com
Tel/Fax: +9105712700920

TABLE OF CONTENTS:

| TABLE OF CONTENTS                                                                 | Page No. |
|----------------------------------------------------------------------------------|----------|
| I. Single-crystal structure of compound 3n                                         | S2       |
| II. \(^1\)H and \(^{13}\)C NMR peak assignment of compound 3n                      | S3       |
| III. Materials used for green metrics calculations                                 | S3-S4    |
| IV. Summary of green metrics calculations of the synthesized compounds            | S5       |
| V. Copy of \(^1\)H and \(^{13}\)C NMR spectra                                      | S6-S21   |
| VI. Copy of HRMS spectra of compounds                                              | S22-S24  |
| VII. References                                                                   | S24      |
I. Single-crystal X-ray crystallographic structure of compound 3n:

**Table S1.** Crystal data for 3n (CCDC 1841358)

| Property                        | Value                                  |
|---------------------------------|----------------------------------------|
| Empirical formula               | C\(_{15}\)H\(_{18}\)N\(_4\)O\(_4\)S     |
| Formula weight                  | 350.40                                 |
| Wavelength                      | 0.71073 Å                              |
| Temperature                     | 293 K                                  |
| Crystal system, space group     | Triclinic, P-1                         |
| Unit cell dimension             | a = 7.3596(3) α = 104.253(4) deg.      |
|                                | b = 9.2464(6) β = 90.749(3) deg.      |
|                                | c = 14.1726(5) γ = 111.461 deg.       |
| Volume                          | 864.24(8) Å\(^3\)                     |
| Z, Calculated density           | 2, 1.3464 g/cm\(^3\)                  |
| Absorption coefficient          | 0.214 mm\(^{-1}\)                     |
| F (000)                         | 368.4235                               |
| Absorption correction           | multi-scan                             |
| Reflection collected            | 3695                                   |
| Theta range for data collection | 27.2190 to 3.5210 deg.                |
| Goodness-of-fit on F\(^2\)      | 1.0504                                 |
II. $^1$H and $^{13}$C NMR peak assignment of compound 3n

![Chemical Structure of Compound 3n](image)

Fig. S2. Characteristic $^1$H and $^{13}$C NMR peak assignment of compound 3n

III. Materials used for green metrics calculations

A. Formula used for calculations:

The following formulae were used for evaluating green chemistry metrics such as atom economy (AE), carbon efficiency (CE), reaction mass efficiency (RME), overall efficiency (OE), process mass intensity (PMI) solvent intensity (SI) and E-factor.\(^1\)\(^2\)

1. **% Atom Economy (AE)** = (Mol Wt. of desired product/ Mol Wt. of all reactants) \(\times 100\)

2. **% Carbon Efficiency (CE)** = (Amount of carbon in the product)/ Total carbon present in reactant) \(\times 100\)

3. **% Reaction Mass Efficiency (RME)** = (Mass of isolated product)/ Total mass of reactants) \(\times 100\)

4. **% Overall Efficiency (OE)** = (RME/AE) \(\times 100\)

5. **% Process Mass Intensity (PMI)** = (Total mass of input materials in a process)/ Mass of product) \(\times 100\)

6. **Solvent Intensity (SI)** = (Total mass of input solvents in a process)/ Mass of product)

7. **E-Factor** = PMI-1

B. Details of reactants and products used for metric calculations:

a) **Reactants**: NMSM, Molecular Weight = 148.18 g/mol, weight used = 0.148g;
Weight of different aromatic aldehydes: Benzaldehyde = 0.106g, 4-Chlorobenzaldehyde = 0.140g, 3-Chlorobenzaldehyde = 0.140g, 4-Nitrobenzaldehyde = 0.151g, 3-
Nitrobenzaldehyde = 0.151g, 2-Nitrobenzaldehyde = 0.151g, 4-Bromobenzaldehyde = 0.185g, 3-Bromobenzaldehyde = 0.185g, 4-Fluorobenzaldehyde = 0.124, 4-Methoxybenzaldehyde = 0.136g, 3-Methoxybenzaldehyde = 0.136g, 3,4-Dimethoxybenzaldehyde = 0.166g, 3,4,5-Trimethoxybenzaldehyde = 0.196g, 4-Methylbenzaldehyde = 0.120g, 4-Ethylbenzaldehyde = 0.134g, pyridine-3-carbaldehyde = 0.107g, Thiophene-2-carbaldehyde = 0.112g, Indole-3-carbaldehyde = 0.145, 2-naphthaldehyde = 0.156g.

b). Products:

| Compounds | 3a  | 3b  | 3c  | 3d  | 3e  | 3f  | 3g  |
|-----------|-----|-----|-----|-----|-----|-----|-----|
| Molecular Formula | C_{14}H_{16}N_4O_4S | C_{14}H_{15}N_5O_5S | C_{14}H_{15}N_5O_5S | C_{14}H_{15}ClN_4O_4S | C_{14}H_{15}ClN_4O_4S | C_{14}H_{15}BrN_4O_4S |
| Molecular Weight (g/mol) | 336.36 | 381.36 | 381.36 | 381.36 | 370.81 | 370.81 | 415.26 |
| Weight (g) | 0.317 | 0.325 | 0.329 | 0.325 | 0.323 | 0.316 | 0.358 |
| Yield (%) | 94 | 85 | 86 | 85 | 87 | 85 | 86 |

| Compounds | 3h  | 3i  | 3j  | 3k  | 3l  | 3m  | 3n  |
|-----------|-----|-----|-----|-----|-----|-----|-----|
| Molecular Formula | C_{14}H_{15}BrN_4O_4S | C_{14}H_{15}F | C_{15}H_{18}N_4O_5S | C_{15}H_{18}N_4O_5S | C_{16}H_{20}N_4O_5S | C_{17}H_{22}N_4O_5S | C_{15}H_{18}N_4O_5S |
| Molecular Weight (g/mol) | 415.26 | 354.35 | 366.39 | 366.39 | 396.41 | 426.44 | 350.39 |
| Weight (g) | 0.366 | 0.319 | 0.338 | 0.323 | 0.357 | 0.393 | 0.330 |
| %Yield | 88 | 90 | 92 | 88 | 90 | 92 | 94 |

| Compounds | 3o  | 3p  | 3q  | 3r  | 3s  |
|-----------|-----|-----|-----|-----|-----|
| Molecular Formula | C_{16}H_{20}N_4O_4S | C_{12}H_{14}N_4O_5S | C_{15}H_{18}N_4O_5S | C_{15}H_{18}N_4O_5S | C_{16}H_{20}N_4O_5S |
| Molecular Weight (g/mol) | 364.41 | 342.39 | 337.35 | 375.40 | 386.42 |
| Weight (g) | 0.336 | 0.295 | 0.270 | 0.323 | 0.341 |
| %Yield | 92 | 86 | 80 | 86 | 88 |
### IV. Green metrics calculation:

**Table S2. Summary of green metrics calculations of the synthesized compounds (3a-s)**

| Entry | %Yield<sup>a</sup> | %AE<sup>a</sup> | %CE<sup>a</sup> | %RME<sup>a</sup> | %OE<sup>a</sup> | PMI<sup>b</sup> | SI<sup>b</sup> | E-Factor<sup>b</sup> |
|-------|------------------|-----------------|-----------------|-----------------|----------------|----------------|------------|-----------------|
| 3a    | 94               | 83.59           | 93.33           | 78.78           | 94.24          | 5.00           | 3.73       | 4.00            |
| 3b    | 85               | 85.24           | 93.33           | 72.65           | 85.23          | 5.01           | 3.64       | 4.01            |
| 3c    | 86               | 85.24           | 93.33           | 73.54           | 86.27          | 4.95           | 3.59       | 3.95            |
| 3d    | 85               | 85.24           | 93.33           | 72.65           | 85.23          | 5.01           | 3.64       | 4.01            |
| 3e    | 87               | 84.97           | 93.33           | 74.02           | 87.11          | 5.01           | 3.66       | 4.01            |
| 3f    | 85               | 84.97           | 93.33           | 72.41           | 85.21          | 5.12           | 3.74       | 4.12            |
| 3g    | 86               | 86.26           | 93.33           | 74.37           | 86.21          | 4.65           | 3.30       | 3.65            |
| 3h    | 88               | 86.26           | 93.33           | 76.03           | 88.14          | 4.54           | 3.23       | 3.54            |
| 3i    | 90               | 84.29           | 93.33           | 75.88           | 90.02          | 5.02           | 3.71       | 4.02            |
| 3j    | 92               | 84.74           | 93.75           | 78.17           | 92.24          | 4.78           | 3.50       | 3.78            |
| 3k    | 88               | 84.74           | 93.75           | 74.70           | 88.15          | 5.00           | 3.66       | 4.00            |
| 3l    | 90               | 85.73           | 94.11           | 77.21           | 90.06          | 4.61           | 3.31       | 3.61            |
| 3m    | 92               | 86.61           | 94.44           | 79.82           | 92.16          | 4.26           | 3.01       | 3.26            |
| 3n    | 94               | 84.15           | 93.75           | 79.25           | 94.17          | 4.84           | 3.58       | 3.84            |
| 3o    | 92               | 84.67           | 94.11           | 78.07           | 92.20          | 4.80           | 3.52       | 3.80            |
| 3p    | 86               | 83.84           | 92.30           | 72.24           | 86.16          | 5.39           | 4.01       | 4.39            |
| 3q    | 80               | 83.63           | 92.85           | 66.93           | 80.03          | 5.87           | 4.38       | 4.87            |
| 3r    | 86               | 85.05           | 94.11           | 73.18           | 86.04          | 5.03           | 3.66       | 4.03            |
| 3s    | 88               | 85.42           | 94.73           | 75.38           | 88.24          | 4.79           | 3.47       | 3.79            |

**Considerations:**

1. *a* = values are close to 100 for these green metrics (Ideal values = 100) and *b* = values are close to 1 for these green metrics (Ideal values = 1).
2. Calculations up to the crude product in all cases.
V. Copy of $^1$H and $^{13}$C NMR spectra:
Compound 3a:
Compound 3b:
Compound 3c:
Compound 3e:
Compound 3f:
Compound 3g:
Compound 3h:
Compound 3i:
Compound 3j:
Compound 3k:
Compound 3l:
Compound 3I:
Compound 3m:
Compound 3n:
Compound 3o:
Compound 3p:
VI. Copy of HRMS spectra:

Compound 3b:

**NMR**

![HRMS spectrum of Compound 3b]

**Compound 3f:**

**NMR**

![HRMS spectrum of Compound 3f]
**Compound 3h:**

NMKG-11 #275 RT: 1.22 AV: 1 NL: 2.29E7
T: FTMS + p ESI Full mass [100.0000-1500.0000]

![Compound 3h Image]

**Compound 3k:**

NMKG-12 #264 RT: 1.18 AV: 1 NL: 9.20E7
T: FTMS + p ESI Full mass [100.0000-1500.0000]

![Compound 3k Image]
VII. References:

1. Green metrics reviews, see: (a) F. Roschangar, R. A. Sheldon and C. H. Senanayake, *Green Chem.*, 2015, **17**, 752-768; (b) J. Augé, *Green Chem.*, 2008, **10**, 225-231; (c) C. Jimenez-Gonzalez, C. S. Ponder, Q. B. Broxtermann and J. B. Manley, *Org. Process Res. Dev.*, 2011, **15**, 912-917.

2. (a) X. Zhang, G. Dhawan, A. Muthengi, S. Liu, W. Wang, M. Legris and W. Zhang, *Green Chem.*, 2017, **19**, 3851-3855. (b) P. Wadhwa, T. Kaur and A. Sharma, *RSC Adv.*, 2015, **5**, 44353-44360.