Supplementary Material

Synthesis of novel imidazopyridine-oxadiazole molecular hybrids by a regioselective sulfonylation of imidazo[1,2-a]pyridines with 1,3,4-oxadiazole-2-thiols using I$_2$-FeCl$_3$ catalytic system and O$_2$/air as co-oxidant

Kartik Dutta$^{a,b}$, Nisha Kushwah$^c$, Amey P. Wadawale$^c$, and Sunil K. Ghosh$^{a,b}$

$^a$Bio-Organic Division, Bhabha Atomic Research Centre, Trombay, Mumbai 400085
$^b$Homi Bhabha National Institute, Anushaktinagar, Mumbai 400094
$^c$Chemistry Division, Bhabha Atomic Research Centre, Trombay, Mumbai-400085, India
Email: ghsunil@barc.gov.in

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1. General procedure for synthesis imidazo[1,2-a]pyridine derivatives 1a-h

Following the reported procedure,\(^1\) sodium bicarbonate (1.6 g, 20 mmol) was added to a stirred solution of 2-bromoacetophenone derivatives (10 mmol) and 2-aminopyridine derivatives (10 mmol) in 50 mL of acetonitrile and the mixture was refluxed for 2 h. After completion of reaction as monitored by TLC, the reaction mixture was diluted with water and extracted with ethyl acetate. The organic phase was then dried over anhydrous Na\(_2\)SO\(_4\), filtered, and concentrated under reduced pressure. The resulting crude product was purified by silica gel column chromatography using petroleum ether and ethyl acetate as the eluent to afford pure 1a-h. Spectroscopic data for 1a,f\(^2\); 1b-e\(^3\) and 1g,h\(^4\) were similar as reported.

2. General procedure for synthesis 2a-i

Following the reported procedure,\(^5\) a vigorously stirred solution of appropriately substituted carboxy benzohydrazide (10 mmol) in 30 mL absolute ethanol was basified with potassium hydroxide (10 mmol) until a solid precipitate came out. Carbon disulphide (15 mmol) was added to the mixture and refluxed for 6 h. After completion of the reaction as verified by TLC, ethanol was removed under vacuum. Then sticky mass was diluted with cold water and acidified with 0.5 M HCL to maintain pH = 3-4. The precipitated crude product was filtered, washed with water and air dried. Recrystallization from ethanol gave pure 2a-i in 68-75% yield. Spectroscopic data for 2a,c\(^5\) and 2e-h\(^5\) were similar as reported.

![Scheme S1 synthesis of 1,3,4-oxadiazole-2-thiols 2a-i](image)

<table>
<thead>
<tr>
<th>Ar</th>
<th>2a</th>
<th>2b</th>
<th>2c</th>
<th>2d</th>
<th>2e</th>
<th>2f</th>
<th>2g</th>
<th>2h</th>
<th>2i</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4-OMeC(_6)H(_4)</td>
<td>Ph</td>
<td>Me</td>
<td>3,4,5-OMeC(_6)H(_4)</td>
<td>4-OHC(_6)H(_4)</td>
<td>4-FC(_6)H(_4)</td>
<td>4-ClC(_6)H(_4)</td>
<td>4-BrC(_6)H(_4)</td>
<td>4-NO(_2)C(_6)H(_4)</td>
</tr>
</tbody>
</table>

3. Characterization data for 2b, 2d and 2i

5-phenyl-1,3,4-oxadiazole-2-thiol (2b) White solid (1.3 g, 75% yield); mp 202.2 – 221.9 °C; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) (ppm) 7.86 (d, \(J = 6.9\) Hz, 2 H), 7.62–7.55 (m, 3 H); \(^{13}\)C NMR (75
MHz, DMSO-\(d_6\) \(\delta\) (ppm) 177.8, 160.9, 132.7, 129.9, 126.5, 122.9; Elemental Anal. Calcd. for C\(_8\)H\(_6\)N\(_2\)O\(_2\)S C, 53.92; H, 3.39; N, 15.72; S, 17.99%. Found C, 54.25; H, 3.52; N, 15.69; S, 18.24%.

5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole-2-thiol (2d) White solid (1.9 g, 71% yield); mp 185.6-186.9 °C; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) (ppm) 7.09 (s, 2 H), 3.85 (s, 6 H), 3.73 (s, 3.09); NMR (75 MHz, DMSO-\(d_6\)) \(\delta\) (ppm) 177.7, 160.8, 153.9, 141.2, 117.9, 103.8, 60.7, 56.6; Elemental Anal. Calcd. for C\(_{11}\)H\(_{12}\)N\(_2\)O\(_4\)S C, 49.25; H, 4.51; N, 10.44; S, 11.95%. Found C, 49.25; H, 4.37; N, 10.31; S, 12.26%.

5-(4-nitrophenyl)-1,3,4-oxadiazole-2-thiol (2i) Yellow solid (1.5 g, 68% yield); mp 190.1-191.9 °C; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) (ppm) 8.37 (d \(J = 8.7\) Hz 2 H), 8.10 (d \(J = 8.7\) Hz 2 H); NMR (75 MHz, DMSO-\(d_6\)) \(\delta\) (ppm) 178.1, 159.3, 149.6, 128.5, 127.9, 125.0; Elemental Anal. Calcd. for C\(_8\)H\(_5\)N\(_3\)O\(_3\)S C, 43.05; H, 2.26; N, 18.83; S, 14.36%. Found C, 43.18; H, 2.54; N, 18.70; S, 14.67%.

3. X-ray crystallographic Characterization of compound 3c

Table S1. Crystal data and structure refinement for 3c

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<th>Property</th>
<th>Value</th>
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<td>CCDC number</td>
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<tr>
<td>Empirical formula</td>
<td>C(<em>{22})H(</em>{16})N(_4)O(_2)S</td>
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<tr>
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</tr>
<tr>
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<tr>
<td>Crystal system</td>
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</tr>
<tr>
<td>Space group (number)</td>
<td>P2(_1)2(_1)2(_1) (19)</td>
</tr>
<tr>
<td>(a) [Å]</td>
<td>8.3230(3)</td>
</tr>
<tr>
<td>(b) [Å]</td>
<td>10.8098(3)</td>
</tr>
<tr>
<td>(c) [Å]</td>
<td>20.8096(6)</td>
</tr>
<tr>
<td>(\alpha) [Å]</td>
<td>90</td>
</tr>
<tr>
<td>(\beta) [Å]</td>
<td>90</td>
</tr>
<tr>
<td>(\gamma) [Å]</td>
<td>90</td>
</tr>
<tr>
<td>Volume [Å(^3)]</td>
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</tr>
<tr>
<td>(Z)</td>
<td>4</td>
</tr>
<tr>
<td>(\rho)(_{\text{calc}}) [g/cm(^3)]</td>
<td>1.364</td>
</tr>
</tbody>
</table>
\( \mu \) [mm\(^{-1}\)] \quad 1.699

\( F(000) \) \quad 800

Crystal size [mm\(^3\)] \quad 0.150 \times 0.050 \times 0.050

Crystal colour \quad colorless

Crystal shape \quad needle

Radiation \quad Cu K\(\alpha\) (\(\lambda=1.54184\ \text{Å}\))

2\(\theta\) range [°] \quad 9.22 to 153.70
\quad (0.79 \text{ Å})

Index ranges \quad -9 \leq h \leq 10
\quad -13 \leq k \leq 13
\quad -24 \leq l \leq 26

Reflections collected \quad 29635

Independent reflections \quad 3791
\quad \( R_{\text{int}} = 0.1362 \)
\quad \( R_{\sigma} = 0.0653 \)

Completeness to \( \theta = 67.684° \) \quad 99.9 %

Data / Restraints / Parameters
\quad 3791/0/256

Goodness-of-fit on \( F^2 \) \quad 1.008

Final \( R \) indexes \quad \( R_1 = 0.0432 \)
\quad \text{[}\geq 2\sigma(\|)\text{]} \quad \text{wr}R_2 = 0.1008

Final \( R \) indexes \quad \( R_1 = 0.0629 \)
\quad \text{[all data]} \quad \text{wr}R_2 = 0.1150

Largest peak/hole \quad 0.15/-0.23
\quad [\text{eÅ}^3]

Flack X parameter \quad -0.02(3)

Extinction coefficient \quad 0.0021(5)
4. $^1$H & $^{13}$C NMR Spectra

Figure S1. $^1$H NMR spectrum of 3a

Figure S2. $^{13}$C NMR spectrum of 3a
Figure S3. $^1$H NMR spectrum of 3b

Figure S4. $^{13}$C NMR spectrum of 3b
Figure S5. $^1$H NMR spectrum of 3c

Figure S6. $^{13}$C NMR spectrum of 3c
Figure S7. $^1$H NMR spectrum of 3d

Figure S8. $^{13}$C NMR spectrum of 3d
Figure S9. $^1$H NMR spectrum of $3e$

Figure S10. $^{13}$C NMR spectrum of $3e$
Figure S11. $^1$H NMR spectrum of 3f

Figure S12. $^{13}$C NMR spectrum of 3f
Figure S13. $^1$H NMR spectrum of 3g

Figure S14. $^{13}$C NMR spectrum of 3g
Figure S15. $^1$H NMR spectrum of $3h$

Figure S16. $^{13}$C NMR spectrum of $3h$
Figure S17. $^1$H NMR spectrum of 4a

Figure S18. $^{13}$C NMR spectrum of 4a
Figure S19. $^1$H NMR spectrum of 4b

Figure S20. $^{13}$C NMR spectrum of 4b
Figure S21. $^1$H NMR spectrum of 4c

Figure S22. $^{13}$C NMR spectrum of 4c
Figure S23. $^1$H NMR spectrum of 4d

Figure S24. $^{13}$C NMR spectrum of 4d
Figure S25. $^1$H NMR spectrum of 4e

Figure S26. $^{13}$C NMR spectrum of 4e
Figure S27. $^1$H NMR spectrum of 4f

Figure S28. $^{13}$C NMR spectrum of 4f
Figure S29. $^1$H NMR spectrum of 4g

Figure S30. $^{13}$C NMR spectrum of 4g
Figure S31. $^1$H NMR spectrum of 2b

Figure S32. $^{13}$C NMR spectrum of 2b
Figure S33. $^1$H NMR spectrum of $2d$

Figure S34. $^{13}$C NMR spectrum of $2d$
Figure S35. $^1$H NMR spectrum of 2i

Figure S36. $^{13}$C NMR spectrum of 2i
5. **References**

   [https://doi.org/10.1021/acs.jchemed.6b00286](https://doi.org/10.1021/acs.jchemed.6b00286)

   [https://doi.org/10.1021/jo402134x](https://doi.org/10.1021/jo402134x)

   [https://doi.org/10.1021/acs.orglett.0c02929](https://doi.org/10.1021/acs.orglett.0c02929)

   [http://dx.doi.org/10.1098/rspa.2019.0238](http://dx.doi.org/10.1098/rspa.2019.0238)

   [https://scholar.google.co.in/scholar?cluster=7970997639781650167&hl=en&as_sdt=0,5&as_vis=1](https://scholar.google.co.in/scholar?cluster=7970997639781650167&hl=en&as_sdt=0,5&as_vis=1)