Supplementary Material

Trisodium citrate dihydrate catalyzed one-pot four component synthesis of spiropyran-indenoquinoxaline derivatives and their molecular docking analysis on the anti-cancer efficacies

Bubun Banerjee,1,2* Aditi Sharma,1 Pooja A. Chawla,3 Keshav Taruneshwar Jha,3 Kinkar Biswas,4 Mayukh Deb,5 Manmeet Kaur,1 Anu Priya,1 and Arvind Singh1

1Department of Chemistry, Akal University, Talwandi Sabo, Bathinda, Punjab-151302, India, Email: banerjeebubun@gmail.com. 2Visiting Researcher, Eternal University, Baru Sahib, Himachal Pradesh - 173101, India. 3Department of Pharmaceutical Chemistry, ISF College of Pharmacy, Moga, Punjab-142001, India. 4Associate Professor, Department of Chemistry, University of North Bengal, West Bengal-734014. 5Micro-Analyst, Department of Chemistry, University of North Bengal, West Bengal-734014

Email: banerjeebubun@gmail.com

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FTIR, 1H-NMR, 13C-NMR and HRMS spectra .................................................................................................................................................. S2
Characterization data of all the synthesized compounds are given below:

2-Amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydrospiro[chromene-4,11'-indenophenol][1,2-b]quinoxaline]-3-carbonitrile (5a). Orange solid; yield 92%; mp 295-297 °C, (lit. 282 °C); FTIR (cm⁻¹): 3429, 3310, 3172, 2960, 2197, 1671, 1471, 1354, 1208, 765, 705; ¹H NMR (500 MHz, DMSO-d₆): δH/ppm: 8.12 (dd, 1H, J = 8.25 Hz, aromatic H), 8.06 (d, 1H, J = 7.5 Hz, aromatic H), 8.00 (t, 1H, J = 7 Hz, aromatic H) 7.81-7.78 (m, 1H, aromatic H), 7.75-7.71 (m, 1H, aromatic H), 7.59-7.56 (m, 1H, aromatic H), 7.53-7.48 (m, 2H, aromatic H), 7.26 (s, 2H, -NH₂), 2.65 (q, 2H, J = 17.5 Hz, -CH₂-), 1.99 (q, 2H, J = 16 Hz, -CH₂-), 1.00 (s, 3H, -CH₃), 0.98 (s, 3H, -CH₃); ¹³C NMR (125 MHz, DMSO-d₆): δc/ppm: 195.49, 166.05, 165.38, 159.44, 154.67, 152.42, 142.18, 141.52, 132.85 (2C), 130.18 (2C), 129.58, 129.36 (2C), 124.99, 122.5 (2C), 118.01, 112.45, 59.21, 50.69, 47.67, 32.49, 28.14, 27.56; MS (ESI-TOF) m/z: 419.1146.
Figure S1. FTIR spectrum of 5a
Figure S2. $^1$H NMR spectrum of 5a
Figure S3. $^{13}$C NMR spectrum of 5a
Figure S4. HRMS spectrum of 5a
2-Amino-5-oxo-5,6,7,8-tetrahydrospiro[chromene-4,11'-indenophthalidin]-3-carbonitrile (5b). Orange solid; yield 88% mp 287-290 °C, (lit. 282 °C)\(^1\); FTIR (cm\(^{-1}\)): 3353, 3288, 3123, 2960, 2233, 1667, 1462, 1346, 1205, 764, 708; \(^1\)H NMR (500 MHz, DMSO\(_d_6\)): \(\delta_H/\text{ppm}: 8.12\ (d, 1H, J = 8\ Hz, \text{aromatic H}), 8.04\ (t, 2H, J = 8\ Hz, \text{aromatic H}), 7.79\ (t, 1H, J = 8\ Hz, \text{aromatic H}), 7.73\ (t, 1H, J = 7.5\ Hz, \text{aromatic H}), 7.56\ (t, 1H, J = 7.5\ Hz, \text{aromatic H}), 7.51\ (t, 2H, J = 7.5\ Hz, \text{aromatic H}), 7.25\ (s, 2H, -NH\(_2\)), 2.75\ (q, 2H, J = 11.75\ Hz, -CH\(_2\)-), 2.08\ (q, 2H, J = 10.75\ Hz, -CH\(_2\)-); \(^{13}\)C NMR (125 MHz, DMSO\(_d_6\)): \(\delta_C/\text{ppm}: 195.60, 167.21, 166.15, 159.30, 154.70, 152.59, 142.15, 141.45, 136.63, 132.82, 130.14, 129.53, 129.42, 129.34, 129.31, 125.16, 121.94, 118.04, 113.54, 59.29, 47.74, 37.12, 27.51, 20.29; MS (ESI-TOF) \(m/z\): 391.0892.
Figure S5. FTIR spectrum of 5b
Figure S6. $^1$H NMR spectrum of 5b
Figure S7. $^{13}$C NMR spectrum of 5b
Figure S8. HRMS spectrum of 5b
7'-Amino-1',3'-dimethyl-2',4'-dioxo-1',2',3',4'-tetrahydrospiro[indeno[1,2-b]quinoxaline-11,5'-pyrano[2,3-d]pyrimidine]-6'-carbonitrile (5c) Orange solid; yield 85% mp 317-318 °C; FTIR (cm⁻¹): 3548, 3161, 3023, 2879, 2226, 1556, 1343, 1202, 765, 703; ¹H NMR (500 MHz, DMSO-d₆): δH/ppm: 8.41 (d, 1H, J = 9 Hz, aromatic H), 8.14 (q, 3H, J = 8 Hz, aromatic H), 8.07 (d, 1H, J = 7 Hz, aromatic H), 7.92-7.81 (m, 4H, aromatic 2H & -NH₂), 7.71-7.67 (m, 1H, aromatic H), 2.60 (s, 3H, -CH₃), 2.33 (s, 3H, -CH₃); ¹³C NMR (125 MHz, CDCl₃): δC/ppm: 153.53 (2C), 143.42, 136.04, 135.41, 135.13, 132.82, 132.55, 131.31, 130.45, 130.31, 129.71, 127.09 (2C), 126.79 (2C), 123.20 (2C), 119.28, 113.20, 111.53, 87.87, 57.68 (2C); MS (ESI-TOF) m/z: 437.2362.
Figure S9. FTIR spectrum of 5c
Figure S10. $^1$H NMR spectrum of 5c
Figure S11. $^{13}$C NMR spectrum of 5c (Due to the low solubility of the molecule, the $^{13}$C NMR date was collected with ns = 10K in CDCl$_3$ as solvent. With DMSO-d$_6$ as solvent we couldn’t recognize all the peaks even with ns = 10K)
Figure S12. HRMS spectrum of 5c
7'-Amino-2',2'-dimethyl-4'-oxo-4'H-spiro[indeno[1,2-b]quinoxaline-11,5'-pyrano[2,3-d]1,3]dioxine]-6'-carbonitrile (5d) Orange solid; yield 87% mp 312-315 °C; FTIR (cm⁻¹): 3377, 3208, 2958, 2880, 2226, 1557, 1462, 1343, 1200, 764, 698; ¹H NMR (500 MHz, DMSO-d₆): δH/ppm: 8.17-8.12 (m, 3H, aromatic H), 8.07 (d, 1H, J = 7.5 Hz, aromatic H), 7.91-7.81 (m, 5H, aromatic 3H & -NH₂), 7.69 (t, 1H, J = 7.5 Hz, aromatic H), 2.43 (s, 6H, -CH₃); ¹³C NMR (125 MHz, CDCl₃): δc/ppm: 155.52, 143.30, 141.92, 138.63, 136.04, 135.41, 132.82, 132.55, 131.31 (2C), 130.51 (2C), 129.69 (2C), 126.79 (2C), 123.22 (2C), 111.53, 103.91, 90.21, 89.95, 29.71 (2C); MS (ESI-TOF) m/z: 424.3493.

Figure S13. FTIR spectrum of 5d
Figure S14. $^1$H NMR spectrum of 5d
Figure S15. $^{13}$C NMR spectrum of 5d (Due to the low solubility of the molecule, the $^{13}$C NMR date was collected with ns = 10K in CDCl$_3$ as solvent. With DMSO-d$_6$ as solvent we couldn’t recognize all the peaks even with ns = 10K)
Figure S16. HRMS spectrum of 5d
2'-Amino-5'-oxo-5'H-spiro[indeno[1,2-b]quinoxaline-11,4'-pyrano[3,2-c]chromene]-3'-carbonitrile (5e) Orange solid; yield 86% mp 312 °C, (lit. 299 °C)\textsuperscript{1}; FTIR (cm\textsuperscript{-1}): 3418, 3023, 2963, 2226, 1622, 1415, 1346, 1248, 764, 700; \textsuperscript{1}H NMR (500 MHz, DMSO-d\textsubscript{6}): \(\delta_H/\text{ppm}\): 8.41 (d, 1H, \(J = 6\) Hz, aromatic H), 8.18-8.07 (m, 4H, aromatic 2H & \(\text{-NH}_2\)), 8.03 (dd, 1H, \(J = 8\), 7 Hz, aromatic H), 7.88-7.82 (m, 3H, aromatic H) 7.77 (t, 3H, \(J = 9\), 7 Hz, aromatic H), 7.60-7.57 (m, 1H, aromatic H), 7.43 (d, 1H, \(J = 8\) Hz, aromatic H). \textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}): \(\delta_C/\text{ppm}\): 167.21, 153.73, 151.34, 151.03, 136.20 (2C), 136.06 (2C), 132.84 (2C), 132.57 (2C), 132.47 (2C), 131.31 (2C), 130.54 (2C), 129.93 (2C), 129.69 (2C), 123.22, 121.40, 120.88, 54.16, 50.03. MS (ESI-TOF) m/z: 441.0979.
Figure S17. FTIR spectrum of 5e
Figure S18. $^1$H NMR spectrum of 5e
Figure S19. $^{13}$C NMR spectrum of 5e (Due to the low solubility of the molecule, the $^{13}$C NMR date was collected with ns = 10K in CDCl$_3$ as solvent. With DMSO-d$_6$ as solvent we couldn’t recognize all the peaks even with ns = 10K)
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Figure S20. HRMS spectrum of 5e
2-Amino-5-oxo-5H-spiro[indeno[1,2-b]pyran-4,11'-indenophen-1,2-b]quinoline-3-carbonitrile (5f) Orange solid; yield 87% mp 315-320 °C; FTIR (cm⁻¹): 3413, 3156, 2967, 2226, 1617, 1463, 1347, 1248, 764, 700; ¹H NMR (500 MHz, DMSO): δH/ppm: 8.55 (d, 1H, J = 7.5 Hz, aromatic H), 8.22 (d, 1H, aromatic 1H), 8.14-8.09 (m, 3H, aromatic 1H & -NH₂), 7.83 (t, 1H, J = 8 Hz, aromatic H), 7.76 (q, 3H, J = 8, 7.5 Hz, aromatic H), 7.63 (t, 1H, J = 8 Hz, aromatic H), 7.25 (d, 4H, J = 3.5 Hz, aromatic H). ¹³C NMR (125 MHz, CDCl₃): δc/ppm: 187.62, 153.57, 149.69, 143.25, 141.90, 140.95, 138.90, 136.06, 135.40, 132.84 (2C), 132.57 (2C), 131.31 (2C), 130.51 (2C), 129.69 (2C), 126.79 (2C), 123.22 (2C), 113.21, 111.55, 88.80, 78.57. MS (ESI-TOF) m/z: 427.2750.
Figure S21. FTIR spectrum of 5f
Figure S22. $^1$H NMR spectrum of 5f
Figure S23. $^{13}$C NMR spectrum of 5f (Due to the low solubility of the molecule, the $^{13}$C NMR date was collected with ns = 10K in CDCl$_3$ as solvent. With DMSO-d$_6$ as solvent we couldn’t recognize all the peaks even with ns = 10K)
Figure S24. HRMS spectrum of 5f
2'-Amino-7'-methyl-5'-oxo-5'H-spiro[indenol1,2-b]quinoxaline-11,4'-pyrano[4,3-b]pyran-3'-carbonitrile (5g) Orange solid; yield 86% mp 316-317 °C; FTIR (cm⁻¹): 3483, 3017, 2957, 2226, 1614, 1557, 1344, 1200, 764, 703; ¹H NMR (500 MHz, DMSO-d₆): δH/ppm: 8.14 (q, 3H, J = 8.5, 7.5 Hz, aromatic H), 8.07 (d, 1H, J = 7 Hz, aromatic H), 7.92-7.81 (m, 6H, aromatic 4H & -NH₂), 7.69 (t, 1H, J = 7.5 Hz, aromatic H), 2.60 (s, 3H, -CH₃). ¹³C NMR (125 MHz, CDCl₃): δc/ppm: 195.54, 171.42, 155.60, 153.79, 141.98, 138.76, 136.18, 135.36, 132.80 (2C), 132.55 (2C), 131.31, 130.49, 129.69, 126.79, 123.20 (2C), 120.52, 113.13, 106.32, 83.58, 78.60, 29.71. MS (ESI-TOF) m/z: 430.2016.
Figure S25. FTIR spectrum of 5g
Figure S26. $^1$H NMR spectrum of 5g
Figure S27. $^{13}$C NMR spectrum of 5g (Due to the low solubility of the molecule, the $^{13}$C NMR date was collected with ns = 10K in CDCl$_3$ as solvent. With DMSO-d$_6$ as solvent we couldn’t recognize all the peaks even with ns = 10K)
Figure S28. HRMS spectrum of 5g
7'-Amino-4'-oxo-2'-thioxo-1',2',3',4'-tetrahydrospiro[indeno[1,2-b]quinoxaline-11,5'-pyrano[2,3-d]pyrimidine]-6'-carbonitrile (5h) Orange solid; yield 85% mp >300 °C; FTIR (cm⁻¹): 3415, 3230, 3016, 2955, 2226, 1618, 1557, 1345, 1248, 764, 702; ¹H NMR (500 MHz, DMSO-d₆): δH/ppm: 8.41 (d, 1H, J = 7.5 Hz, aromatic H), 8.14, (br s, 2H, NH), 8.75 (d, 2H, J = 6.5 Hz, aromatic 4H), 7.90-7.81 (m, 6H, 4 x aromatic H & -NH₂), 7.70-7.67 (m, 1H, aromatic H); ¹³C NMR (125 MHz, CDCl₃): δC/ppm: 212.31, 203.16, 158.63, 154.59, 142.14, 138.176, 135.03, 131.77, 131.48, 130.26 (2C), 129.44, 129.13, 128.64 (2C), 125.73 (2C), 122.26, 122.14, 115.33, 112.06, 93.21; MS (ESI-TOF) m/z: 425.2723.

Figure S29. FTIR spectrum of 5h
Figure S30. $^1$H NMR spectrum of $5h$
Figure S31. $^{13}$C NMR spectrum of 5h (Due to the low solubility of the molecule, the $^{13}$C NMR date was collected with ns = 10K in CDCl$_3$ as solvent. With DMSO-d$_6$ as solvent we couldn’t recognize all the peaks even with ns = 10K)
Figure S32. HRMS spectrum of 5h
2-Amino-5,10-dioxo-5,10-dihydrospiro[benzo[g]chromene-4,11’-indenol1,2-b]quinoxaline]-3-carbonitrile (5i) Orange solid; yield 90% mp 318-319 °C; FTIR (cm\(^{-1}\)): 3413, 3014, 2949, 2226, 1617, 1558, 1345, 1199, 764, 705; \(^1\)H NMR (500 MHz, DMSO-d\(_6\)): \(\delta_H/\text{ppm}: \)

- 8.41 (d, 1H, \(J = 8\) Hz, aromatic H),
- 8.16-8.12 (m, 3H, aromatic 1H & -NH\(_2\)),
- 8.08 (dd, 2H, \(J = 7.5\) Hz, aromatic H),
- 7.95-7.90 (m, 2H, aromatic H),
- 7.86 (t, 4H, \(J = 8\) Hz, aromatic H),
- 7.79 (t, 1H, \(J = 7.5\) Hz, aromatic H),
- 7.69 (t, 1H, \(J = 7.5\) Hz, aromatic H).

\(^{13}\)C NMR (125 MHz, DMSO-d\(_6\)): \(\delta_C/\text{ppm}: 195.79\) (2C), 158.10, 147.24, 146.77, 141.92, 141.49, 141.16, 138.13, 137.53, 137.30, 134.99, 133.72, 133.54, 133.07, 131.63, 131.26, 130.35, 129.63, 129.55, 129.24, 127.89, 126.44, 125.73, 123.55, 103.98, 103.76, 89.07; MS (ESI-TOF) m/z: 455.5160.
Figure S33. FTIR spectrum of 5i
Figure S34. $^1$H NMR spectrum of 5i
Figure S35. $^{13}$C NMR spectrum of 5i (Due to the low solubility of the molecule, the $^{13}$C NMR date was collected with ns = 10K in DMSO-d$_6$ as solvent)
Figure S36. HRMS spectrum of 5i
3-Aminospiro[benzo[f]chromene-1,11'-indenolo[1,2-b]quinoxaline]-2-carbonitrile (5j) Orange solid; yield 89% mp 303-305 °C; FTIR (cm⁻¹): 3413, 3020, 2880, 2226, 1614, 1556, 1342, 1200, 825, 764; ¹H NMR (500 MHz, DMSO-d₆): δH/ppm: 8.17-8.12 (m, 4H, aromatic 2H & -NH₂), 8.07 (d, 2H, J = 7.5 Hz, aromatic H), 7.90-7.83 (m, 8H, aromatic H), 7.69 (t, 2H, J = 7.5 Hz, aromatic H); ¹³C NMR (125 MHz, CDCl₃): δC/ppm: 143.31, 141.92, 141.57 (2C), 138.73 (2C), 136.79 (2C), 136.13 (2C), 132.82 (2C), 132.54 (2C), 131.63 (2C), 131.31 (2C), 130.49 (2C), 129.69 (2C), 126.79, 123.20, 117.486, 114.31, 113.20, 89.66; MS (ESI-TOF) m/z: 425.2837.

Figure S37. FTIR spectrum of 5j
Figure S38. $^1$H NMR spectrum of 5j
Figure S39. $^{13}$C NMR spectrum of 5j (Due to the low solubility of the molecule, the $^{13}$C NMR data was collected with ns = 10K in CDCl$_3$ as solvent. With DMSO-d$_6$ as solvent we couldn’t recognize all the peaks even with ns = 10K)
Figure S40. HRMS spectrum of 5j
2-Amino-7'-chloro-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydrospiro[chromene-4,11'-indenophthal[1,2-b]quinolizine]-3-carbonitrile (5aa) Brown solid; yield 80% mp 289 °C; FTIR (cm⁻¹): 3321, 3081, 2952, 2178, 1659, 1593, 1466, 1310, 1211, 750, 711; ¹H NMR (500 MHz, DMSO-d₆): δH/ppm: 8.19-8.02 (m, 3H, aromatic H), 7.83-7.75 (m, 1H, aromatic H), 7.59 (s, 1H, aromatic H), 7.51 (s, 2H, aromatic H), 7.30 (s, 2H, -NH₂), 2.65 (q, 2H, -CH₂), 2.00 (q, 2H, -CH₂), 0.99 (t, 6H, J = 5.5, 4.5 Hz, -CH₃); ¹³C NMR (125 MHz, DMSO-d₆): δC/ppm: 195.54, 166.60, 165.50, 159.46, 155.62, 152.65, 142.67, 134.51, 133.36, 131.11, 130.03 (2C), 129.51 (2C), 128.13 (2C), 125.08 (2C), 122.32 (2C), 117.94, 112.29, 58.89, 50.61, 47.73, 32.50, 28.13, 27.55; MS (ESI-TOF) m/z: 454.0525.
Figure S41. FTIR spectrum of 5aa

Figure S42. $^1$H NMR spectrum of 5aa
Figure S43. $^{13}$C NMR spectrum of 5aa
Figure S44. HRMS spectrum of 5aa
2-Amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydrosso[chromene-4,6'-indenof1,2-b]pyrido[3,2-e]pyrazine]-3-carbonitrile (5bb) Brown solid; yield 78% mp 277-280 °C; FTIR (cm⁻¹): 3389, 3290, 3175, 2959, 2193, 1651, 1591, 1317, 1214, 861, 783; ¹H NMR (500 MHz, DMSO-d₆): δH/ppm: 9.04 (br s, 1H, aromatic H), 8.47 (d, 1H, J = 7 Hz, aromatic H), 8.12 (d, 1H, J = 7.5 Hz, aromatic H), 7.77 (t, 1H, J = 4, 3.5 Hz, aromatic H), 7.62 (d, 1H, J = 7 Hz, aromatic H), 7.55 (q, 2H, J = 7, 7.5 Hz, aromatic H), 7.33 (s, 2H, -NH₂), 2.66 (q, 2H, -CH₂), 2.00 (q, 2H, -CH₂), 0.99 (s, 6H, -CH₃); ¹³C NMR (125 MHz, DMSO-d₆): δC/ppm: 195.58, 167.03, 165.58, 159.51, 157.64, 153.50, 153.03, 151.49, 138.42, 136.25, 133.68, 129.63, 125.12, 122.71, 122.29, 119.85, 117.92, 112.24, 111.63, 58.76, 50.58, 47.59, 32.50, 28.15, 27.54; MS (ESI-TOF) m/z: 444.1320.
Figure S45. FTIR spectrum of 5bb

Figure S46. $^1$H NMR spectrum of 5bb
Figure S47. $^{13}$C NMR spectrum of 5bb
Figure S48. HRMS spectrum of 5bb
DOCKING POSES WITH (PDB: 5JRS): BREAST CANCER

Compound 5a
Compound 5b
Compound 5c

Compound 5d

Compound 5e
**Compound 5f**

**Compound 5g**
Compound 5j

Compound 5aa
Compound 5bb
DOCKING POSES WITH (PDB: 1PMV): HEPATIC CANCER

Compound 5a

Compound 5b
Compound 5c

Compound 5d
Compound 5h

Compound 5i
Compound 5j
DOCKING POSES WITH (PDB: 3I5Z): LUNG CANCER

**Compound 5a**

**Compound 5b**

**Compound 5c**
Compound 5d

Compound 5e
Compound 5f

Compound 5g
Compound 5j

Compound 5aa

Compound 5bb
References