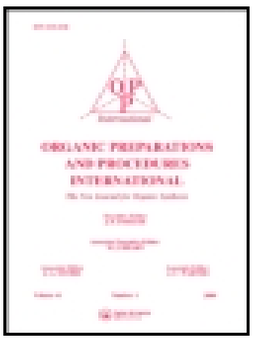


Taylor & Francis
Taylor & Francis Group

Organic Preparations and Procedures International

The New Journal for Organic Synthesis

ISSN: 0030-4948 (Print) 1945-5453 (Online) Journal homepage: https://www.tandfonline.com/loi/uopp20

A Catalyst-Free Expeditious Green Synthesis of Quinoxaline, Oxazine, Thiazine, and Dioxin Derivatives in Water under Ultrasound Irradiation

Ankush Mishra, S. Singh, M. A. Quraishi & Vandana Srivastava

To cite this article: Ankush Mishra, S. Singh, M. A. Quraishi & Vandana Srivastava (2019): A Catalyst-Free Expeditious Green Synthesis of Quinoxaline, Oxazine, Thiazine, and Dioxin Derivatives in Water under Ultrasound Irradiation, Organic Preparations and Procedures International, DOI: 10.1080/00304948.2019.1596469

To link to this article: https://doi.org/10.1080/00304948.2019.1596469

Organic Preparations and Procedures International, 0:1–12, 2019

ISSN: 0030-4948 print / 1945-5453 online
DOI: 10.1080/00304948.2019.1596469

A Catalyst-Free Expeditious Green Synthesis of Quinoxaline, Oxazine, Thiazine, and Dioxin Derivatives in Water under Ultrasound Irradiation

Ankush Mishra, S. Singh, M. A. Quraishi, and Vandana Srivastava

Department of Chemistry, Indian Institute of Technology (BHU), Varanasi- 221005, India

Quinoxaline, 1,4-oxazine, 1,4-thiazine and 1,4-dioxin derivatives are important heterocycles gaining considerable attention due to their pharmacological importance and biological activities.[1–9] These derivatives are also basic scaffolds for the synthesis of solar cells,[10] dyes,[11] pigments,[12] organic semiconductors[13] and chemical switches.[14] There are many drugs possessing these core structural units (*Figure 1*). Due to their wide range of biological activities many synthetic strategies have been reported in the literature. Conventionally, quinoxaline derivatives were synthesized by using different catalysts such as acetic acid,[15,16] molecular iodine,[17,18] *o*-iodoxybenzoic acid,[19] montmorillonite K-10,[20] polyaniline sulfate,[21] nitrilotris(methylenephosphonic acid),[22] aqueous HF,[23] sulfamic acid,[24,25] NH_4Cl-CH_3OH,[26] Amberlyst-15[27] and metal catalysts such as cerium(IV) ammonium nitrate (CAN),[28] gallium(III) triflate,[29] silica-supported antimony(III) chloride,[30] zirconium(IV) chloride,[31] $SnCl_2/SiO_2$,[32] ZnO,[33] $FeCl_3$,[34] Keplerate $\{Mo_{132}\}$ nanoballs[35] and sulfated polyborate.[36] A few methods for synthesis of quinoxalines have also been reported by microwave irradiation,[37–40] ultrasound irradiation[41,42] and use of ball mill techniques.[43–45] There are only a few reports on the synthesis of indenoxazines and indenothiazines from the reaction of ninhydrin with *o*-aminophenol and *o*-aminothiophenol respectively;[46–48] and the reaction of ninhydrin with catechol and 3-hydroxy-2-aminopyridine leading to the formation of 4b,10a-dihydroxy-4b*H*-benzo[*b*]indeno[1,2-*e*][1,4]dioxin-11(10a*H*)-one and 5a-hydroxyindeno[2,1-*b*]pyrido[2,3-*e*][1,4]oxazin-6(5a*H*)-one has not been reported up to now. A number of these reported methods for synthesis of the title heterocycles have drawbacks including harsh reaction conditions, long reaction times, expensive catalysts, toxic solvents or tedious workup. The development of facile and energy-efficient greener methods for synthesis of these heterocyclic compounds is necessary.

The use of appropriate solvents in organic synthesis is also very important from the green chemistry point of view. In this regard the use of water as solvent has attracted a great deal of interest in recent years. Indeed, water offers many advantages because it is cheap, readily available, nontoxic, nonflammable and can be more selective than organic solvents.[49,50] Catalyst-free syntheses are in full agreement with the idea of

Received June 18, 2018; in final form January 10, 2019.
Address correspondence to Vandana Srivastava, Department of Chemistry, Indian Institute of Technology (BHU), Varanasi- 221005, India. E-mail: vsrivastava.itbhu@gmail.com

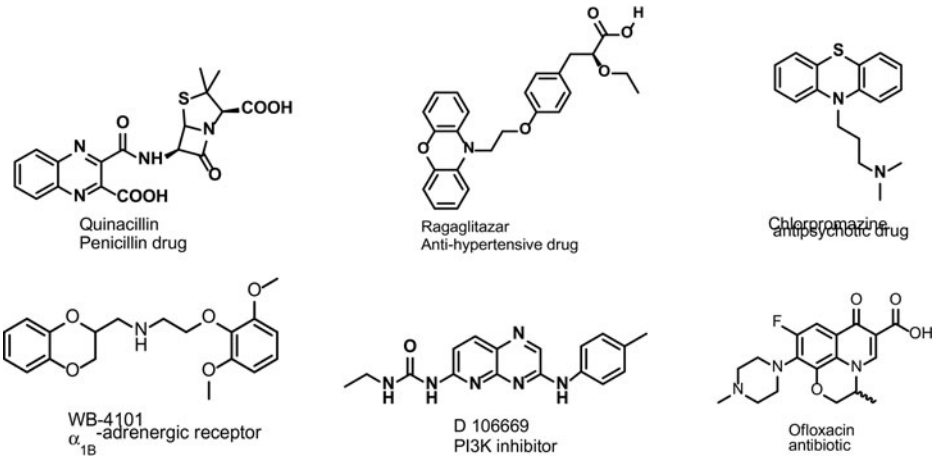


Figure 1. Structures of some pharmacologically active compounds containing quinoxaline, oxazine, thiazine, or dioxin core moieties.

green chemistry because they reduce pollutant production, use of hazardous chemicals, and cost.

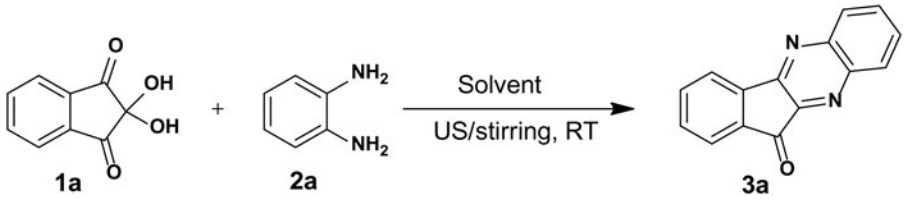
In this context, ultrasound assisted reactions have gained much attention because they offer milder reaction conditions, higher reaction rates, excellent yields and low energy consumption. Many organic transformations have been successfully achieved with the help of ultrasound irradiation. Therefore, ultrasound assisted organic synthesis, as a green synthetic approach, is considered to be a powerful technique.[51–54]

The fascinating nature of water as solvent and the beneficial effects of ultrasound have prompted us to undertake the synthesis of quinoxaline, oxazine, thiazine and dioxin derivatives. The catalyst-free reaction of ninhydrin and isatin derivatives with 1,2-difunctionalized benzene/pyridine is here reported for the first time in water under ultrasound irradiation.

In order to optimize conditions, the reaction of ninhydrin and *o*-phenylenediamine was chosen as a model for the synthesis of quinoxaline derivatives (*Scheme 1*). The reaction was carried out in various solvents under conventional and ultrasound irradiation methods. The reaction was performed at room temperature with 1.0 mmol of ninhydrin and 1.0 mmol *o*-phenylenediamine in 5.0 mL of solvent without any catalyst. The progress of the reaction was monitored by tlc (*Table 1*). It was observed that with ultrasound irradiation the reaction was completed in shorter time in excellent yield. Among the solvents tested, water was found to be the best, which gave 98% yield in 50 seconds (*Table 1*, entry 4). Pure products were separated as solids and collected by filtration. There was no requirement for further purification.

The rate of reaction was faster with ultrasound. This is attributed to the cavitation phenomena occurring during sonication. Cavitation results in formation and adiabatic collapse of micro bubbles, giving the generation of local hotspots. These hotspots generate high temperature and pressures of several thousand atmospheres which cause the reaction to occur rapidly.[53]

To examine the effect of ultrasound energy on reaction time and yield, the model reaction was carried out at different energies from 500 to 11000 J, and the results are shown in *Table 2*.



Scheme 1. Reaction of ninhydrin with o-phenylenediamine.

Table 1
Effect of Solvents on the Yield of the Product **3a** under Conventional and Ultrasound Irradiation Methods

		Conventional[a]		Ultrasonication[b]	
Entry	Solvent	Time (min)	Yield (%)[c]	Time (min)	Yield (%)[c]
1	Ethanol	15	80	10	84
2	Methanol	30	75	12	77
3	Isopropanol	35	72	15	75
4	**Water**	**10**	**85**	**50 sec**	**98**
5	Acetonitrile	60	60	40	72
6	Acetic acid	30	78	10	80
7	THF	NR	–	NR	–
8	Dioxane	NR	–	NR	–
9	Benzene	NR	–	NR	–
10	Toluene	NR	–	NR	–

Reaction conditions:
[a]Mixture of **1a** (1.0 mmol) and **2a** (1.0 mmol) in 5.0 mL of solvent was stirred at room temperature (30°C).
[b]Mixture of **1a** (1.0 mmol) and **2a** (1.0 mmol) in 5.0 mL of solvent was irradiated at 750 W, 2000 J, 20% amplitude, 30°C.
[c]Pure isolated yield.

Table 2
Effect of Ultrasound Energy on the Yield of the Product **3a**[a]

Entry	US Energy (Joule)	Time (sec.)	Yield (%)[b]
1	500	260	90
2	1000	180	92
3	1500	100	95
4	**2000**	**50**	**98**
5	5000	45	95
6	7500	35	96
7	11000	35	95

[a]Reaction condition: mixture of ninhydrin **1a** (1 mmol) and *o*-phenylenediamine **2a** (1 mmol) in 5 mL of water irradiated at 750 W, 20% amplitude, at room temperature (30°C).
[b]Pure isolated yield.

The maximum yield of the product was obtained at 2000 J ultrasound energy. An increase in the ultrasound energy above 2000 J did not show any significant improvement in terms of yield and reaction time. So, 2000 J ultrasound energy is considered as the optimum energy condition. In order to examine the effect of ultrasound amplitude on reaction rate we carried out this reaction at different ultrasound amplitudes from 20–50% at room temperature. The maximum yield (98%) of the product (**3a**) was obtained at 20% amplitude. An increase in amplitude did not improve the yield of the reaction.

To explore the applicability of the optimized reaction conditions, several derivatives of the title heterocycles were synthesized by reacting 1,2-difuncionalized benzenes and pyridines with ninhydrin and isatin derivatives. The chemical structures of the synthesized compounds were established from their spectral data. The structures of the reaction products along with their time of reaction, m.p. and yields are summarized in *Table 3*.

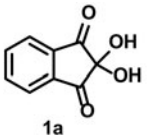
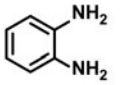
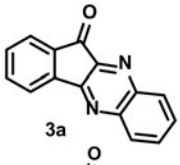
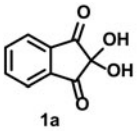
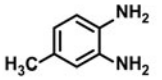
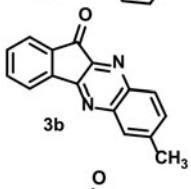
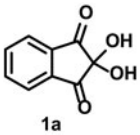
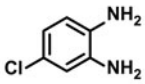
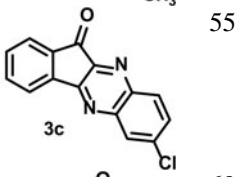
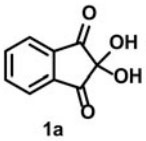
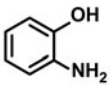
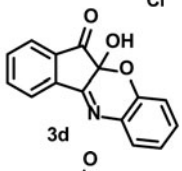
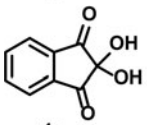
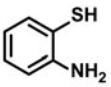
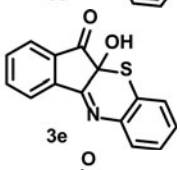
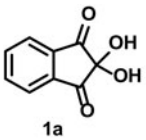
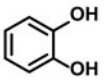
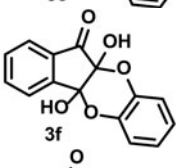
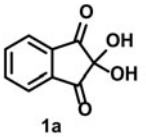
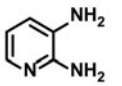
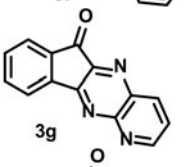
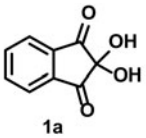
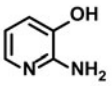
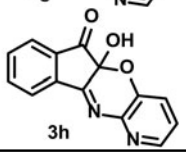
The results shown in *Table 3* reveal that the substituents on the ring do not affect the yield and reaction times. The reaction of ninhydrin with *o*-substituted amines were completed within a minute in excellent yields (>90%) while isatin derivatives required longer time. The lower reactivity of the isatin derivatives is attributed to the presence of the amidic carbonyl groups in these compounds. It is worth noting that the ultrasound irradiation facilitates nucleophilic addition-elimination reactions leading to the formation of fused quinoxaline, oxazine, thiazine, and dioxin derivatives.

In summary, we have developed an ultrasound-induced green methodology for the synthesis of quinoxaline, 1,4-oxazine, 1,4-thiazine and 1,4-dioxin derivatives in water at room temperature without using any catalyst. Pure products were separated as solids after completion of the reaction and collected by filtration. Advantages include mild reaction conditions, easy workup, isolation of products without the use of column chromatography, high yields, shorter reaction times, a green solvent, and absence of catalysts.

Experimental Section

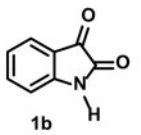
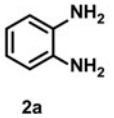
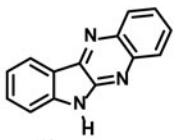
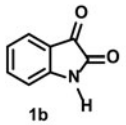
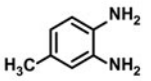
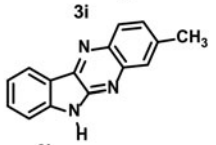
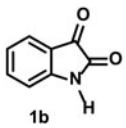
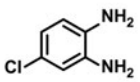
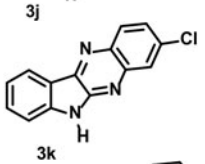
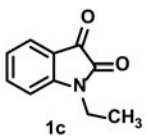
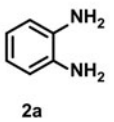
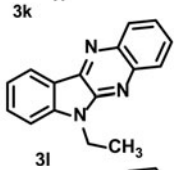
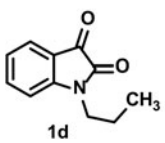
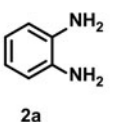
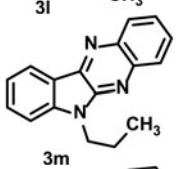
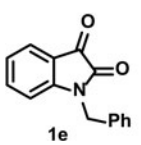
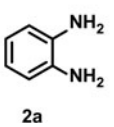
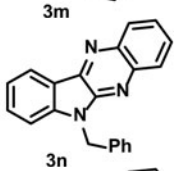
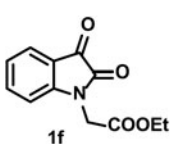
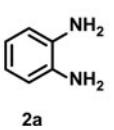
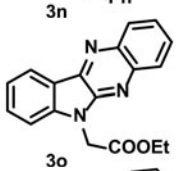
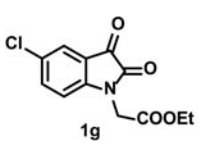
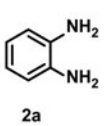
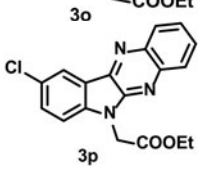
All the reactions were performed at room temperature. All reagents were purchased from Sigma-Aldrich and used without further purification. Melting points were determined in open capillary melting point apparatus and are uncorrected. Ultrasonic irradiation was performed using Sonics Vibra Cell Ultrasonic Processor Model VCX750 (Sonics & Materials, Inc.) with a fixed power of 750 W and amplitude variation from 20–80%, and a tapered micro tip was used as ultrasonic probe operating at a frequency of 20 kHz. All reactions were performed at room temperature. The reactions were monitored through analytical thin layer chromatography (TLC) precoated E. Merck 60 GF254 silica gel plates and spots were visualized using UV light or iodine vapor. Infrared spectra were recorded on Perkin–Elmer Spectrum 100 FT–IR spectrophotometer. Elemental analysis was done by Eurovector EA3000 elemental analyzer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance 500 MHz spectrometer in $CDCl_3$ and DMSO–d_6 as solvents and tetramethylsilane (TMS) as an internal standard at 298 K; chemical shifts are given in δ ppm. Routine coupling constant values for common groups were in the range of 4-8 Hz (1-2 Hz for dd); these were not separately reported. The ^{1}H NMR and ^{13}C NMR spectra of the products were compared with reported data in the literature.

Table 3
Reaction of 1, 2-diketones with 1, 2-difunctionalized Benzene/Pyridine in Water under Ultrasound Irradiation[a]

Entry	Diketone (1)	1, 2-difunctionalized benzene/ pyridine (2)	Product (3)	Time (sec)	Yield (%)[b]	Mp (°C)
1	 1a	 2a	 3a	50	98	217–18
2	 1a	 2b	 3b	35	99	175–76
3	 1a	 2c	 3c	55	96	235–36
4	 1a	 2d	 3d	60	92	255
5	 1a	 2e	 3e	55	95	225–26
6	 1a	 2f	 3f	55	86	233–34
7	 1a	 2g	 3g	55	92	>300
8	 1a	 2h	 3h	50	95	252–53

(*Continued*)

Table 3
(*Continued*)

9	 1b	 2a	 3i	230	92	295–96
10	 1b	 2b	 3j	200	95	257–58
11	 1b	 2c	 3k	250	90	275–77
12	 1c	 2a	 3l	225	87	247–48
13	 1d	 2a	 3m	220	88	218–19
14	 1e	 2a	 3n	230	91	170–71
15	 1f	 2a	 3o	210	90	185–86
16	 1g	 2a	 3p	220	92	275–76

[a]Reaction condition: mixture of 1,2-diketone (1.0 mmol) and 1,2-difunctionalized benzene/pyridine (1.0 mmol) in 5 mL of water was irradiated at 750 W, 2000 J energy, 20% ultrasound amplitude at room temperature.
[b]Isolated yield.

General procedure for synthesis of products (3a–p). Equimolar amounts of 1,2-diketone (1.0 mmol) and corresponding 1,2-difunctionalized benzene/pyridine were mixed in 5.0 ml of water. The reaction mixture was irradiated under ultrasonication at 750 W power,

2000 J, 20% amplitude at room temparature for the desired time. The progress of the reaction was monitored using thin layer chromatography (ethyl acetate: *n*-hexane, 1:4). After completion of the reaction, solid products were separated by filtration, washed with distilled water and recrystallized if necessary with appropriate solvents ethanol/toluene to obtain pure products (**3a-p**).

11H-Indeno[1,2-b]quinoxalin-11-one (3a). Yellow solid; yield 98%; m.p. 217–18°C (*lit.* m.p. 220–21°C)[46]; IR (KBr) ν (cm^{-1}): 3036, 2358, 1790, 1728, 1607, 1565, 1509, 1462, 1336, 1247, 1190, 1118, 1040, 1001, 939, 867, 825, 775, 740; ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm: 8.21–8.01 (m, 3 H), 7.92–7.82 (m, 4 H), 7.71 (t, 1 H); ^{13}C NMR (126 MHz, DMSO-d_6) δ ppm: 189.29, 156.44, 149.81, 142.12, 141.82, 140.94, 136.93, 136.62, 132.76, 132.43, 130.95, 130.35, 129.35, 124.21, 122.27.

7-Methyl-11H-indeno[1,2-b]quinoxalin-11-one (3b). Yellow solid; yield 99%; m.p. 175–76°C (lit m.p. 176°C)[55,56]; IR (KBr) ν (cm^{-1}): 3040, 2910, 1974, 1726, 1609, 1564, 1506, 1462, 1332, 1244, 1188, 1150, 1113, 1041, 1001, 965, 903, 834, 766, 731; ^{1}H NMR (500 MHz, ($CDCl_3$) δ ppm: 8.12–7.90 (m, 4 H), 7.77–7.57 (m, 3 H), 2.53 (d, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 190.24, 156.97, 143.86, 143.37, 141.73, 141.26, 136.88, 136.80, 134.81, 132.62, 132.50, 131.26, 130.75, 129.29, 129.01, 124.83, 122.54, 22.19.

7-Chloro-11H-indeno[1,2-b]quinoxalin-11-one (3c). Yellow solid; yield 96%; m.p. 245–46°C (lit m.p. 233°C)[55]; IR (KBr) ν (cm^{-1}): 3069, 2958, 2916, 2852, 2322, 1721, 1609, 1555, 1496, 1329, 1256, 1182, 1017, 946, 877, 792; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 8.05 (t, 4 H), 7.84–7.48 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 189.53, 157.53, 149.46, 143.62, 141.24, 137.06, 133.04, 132.65, 131.29, 128.92, 124.98, 122.90.

10a-Hydroxybenzo[b]indeno[1,2-e][1,4]oxazin-11(10aH)-one (3d). White solid; yield 92%; m.p. 255–56°C (lit m.p. 255°C)[46]; IR (KBr) ν (cm^{-1}): 3735, 2924, 2644, 2484, 1738, 1641, 1586, 1460, 1414, 1347, 1291, 1201, 1147, 1112, 1062, 966, 919, 855, 755, 712; ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm: 8.55 (s, 1 H, D_2O exchangeable), 8.18 (d, 1 H), 8.00 (dd, 2 H), 7.90–7.81 (m, 1 H), 7.61 (dd, 1 H), 7.37–7.13 (m, 3 H); ^{13}C NMR (126 MHz, DMSO-d_6) δ ppm: 192.22, 157.98, 144.79, 141.64, 137.55, 135.93, 134.01, 133.90, 128.94, 127.57, 124.83, 123.70, 123.38, 118.04, 85.90.

10a-Hydroxybenzo[e]indeno[2,1-b][1,4]thiazin-11(10aH)-one (3e). Green solid; yield 95%; m.p. 225–26°C (lit m.p. 228°C)[46]; IR (KBr) ν (cm^{-1}): 3738, 2949, 2701, 1728, 1635, 1636, 1585, 1458, 1398, 1340, 1251, 1165, 1114, 1074, 1005, 953, 854, 820,762, 709; ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm: 8.22 (d, 1 H), 8.08–7.97 (m, 2 H), 7.87 (t, 1 H), 7.80 (s, 1 H, D_2O exchangeable), 7.68 (dd, 1 H), 7.57 (dd, 1 H), 7.41 (m, 1 H), 7.30 (m, 1 H); ^{13}C NMR (126 MHz, DMSO-d_6) δ ppm: 195.42, 155.79, 142.95, 142.23, 137.94, 134.99, 134.22, 129.42, 128.31, 127.31, 127.23, 124.86, 124.01, 120.86, 70.94.

4b,10a-Dihydroxy-4bH-benzo[b]indeno[1,2-e][1,4]dioxin-11(10aH)-one (3f). White solid; yield 86%; m.p. 233–34°C; IR (KBr) ν (cm^{-1}): 3742, 3615, 3380, 3312, 3187, 2356, 1706, 1597, 1496, 1400, 1275, 1217, 1149, 1084, 941, 874, 762,722; ^{1}H NMR

(500 MHz, DMSO-d_6) δ ppm: 9.45 (s, 1 H, D_2O exchangeable), 8.03–7.84 (m, 4 H), 7.76–7.57 (m, 2 H), 6.94–6.79 (m, 1 H), 6.77–6.65 (m, 2 H), 6.58 (s, 1 H, D_2O exchangeable); ^{13}C NMR (126 MHz, DMSO-d_6) δ ppm: 199.38, 149.23, 144.54, 141.73, 136.58, 133.90, 130.90, 126.55, 125.20, 122.79, 121.55, 117.52, 115.43, 110.16, 82.97.

Anal. Calcd for $C_{15}H_{10}O_5$: C, 66.67; H, 3.73. Found: C, 66.59; H, 3.64.

6H-Indeno[1,2-b]pyrido[3,2-e]pyrazin-6-one (3g). Yellow solid; yield 92%; m.p. > 300°C (lit m.p. 310–11°C)[56]; IR (KBr) ν (cm^{-1}): 2912, 2350, 1914, 1714, 1555, 1490, 1375, 1331, 1233, 1152, 1094, 1027, 934, 873, 781; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 9.16 (d, 1 H), 8.60 (d, 1 H), 8.25 (d, 1 H), 7.96 (d, 1 H), 7.88–7.60 (m, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 188.86, 155.70, 140.35, 137.45, 133.56, 125.58, 125.08, 123.79.

5a-Hydroxyindeno[2,1-b]pyrido[2,3-e][1,4]oxazin-6(5aH)-one (3h). White solid; yield 95%; m.p. 252–53°C; IR (KBr) ν (cm^{-1}): 3027, 2647, 1723, 1643, 1596, 1537, 1460, 1411, 1334, 1245, 1195, 1145, 1084, 1036, 950, 868, 737; ^{1}H NMR (DMSO-d_6) δ ppm: 8.18–7.35 (m, 4 H), 6.88 (d, 2 H), 6.37 (d, 1 H), 5.41 (s, 1 H, D_2O exchangeable); ^{13}C NMR (DMSO-d_6) δ ppm: 112.37, 114.02, 118.52, 119.08, 123.43, 123.88, 136.09, 137.21, 139.26, 145.98, 150.46, 197.05.

Anal. Calcd for $C_{14}H_8N_2O_3$: C, 66.67; H, 3.20; N, 11.11. Found: C, 66.48; H, 3.25; N, 11.23.

6H-Indolo[2,3-b]quinoxaline (3i). Yellow solid; yield 92%; m.p. 295–96°C (lit m.p. 294–95)[57]; IR (KBr) ν (cm^{-1}): 3071, 3007, 2831, 2779, 2682, 1945, 1710, 1608, 1461, 1406, 1333, 1245, 1206, 1132, 1010, 924, 829, 748; ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm: 12.04 (s, 1 H), 8.35 (d, 1 H), 8.24 (d, 1 H), 8.07 (d, 1 H), 7.80 (t, 1 H), 7.71 (dd, 2 H), 7.59 (d, 1 H), 7.37 (t, 1 H); ^{13}C NMR (126 MHz, DMSO-d_6) δ ppm: 145.88, 144.04, 140.17, 139.82, 138.61, 131.38, 129.11, 129.01, 128.81, 127.55, 127.46, 126.03, 122.33, 122.24, 120.81, 120.75, 118.99, 112.04.

3-Methyl-6H-indolo[2,3-b]quinoxaline (3j). Yellow solid; yield 95%; m.p. 257–58°C; IR (KBr) ν (cm^{-1}): 3065, 2916, 2850, 2353, 1895, 1737, 1595, 1459, 1399, 1331, 1242, 1195, 1129, 1021, 816, 738; ^{1}H NMR ($CDCl_3$) δ ppm: 9.56 (s, 1 H), 8.38 (t, 2 H), 8.19–7.78 (m, 2 H), 7.67–7.25 (m, 4 H), 2.57 (d, 3 H); ^{13}C NMR ($CDCl_3$) δ ppm: 165.44, 136.67, 131.43, 131.16, 131.00, 129.88, 129.12, 128.84, 128.54, 126.97, 126.48, 122.90, 122.75, 121.46, 121.40, 111.64, 21.77.

Anal. Calcd for $C_{15}H_{11}N_3$: C, 77.23; H, 4.75; N, 18.01. Found: C, 77.13; H, 4.69; N, 17.89.

3-Chloro-6H-indolo[2,3-b]quinoxaline (3k). Yellow solid; yield 90%; m.p. 275–77°C (lit m.p. >275°C)[58] IR (KBr) ν (cm^{-1}): 3052, 2918, 2851, 2766, 1937, 1740, 1580, 1482, 1452, 1401, 1331, 1234, 1182, 1107, 1068, 1021, 939, 824, 783, 737; ^{1}H NMR (DMSO-d_6) δ ppm: 12.17 (s, 1 H), 8.35 (d, 1 H), 8.27 (d, 1 H), 8.12 (d, 1 H), 7.79–7.70 (m, 2 H), 7.60 (d, 1 H), 7.39 (t, 1 H); ^{13}C NMR (DMSO-d_6) δ ppm: 146.14, 144.15, 140.58, 137.10, 132.96, 131.67, 130.72, 126.37, 126.09, 122.36, 121.00, 118.79, 112.12.

6-Ethyl-6H-indolo[2,3-b]quinoxaline (3l). White solid; yield 87%; m.p. 247–48°C (lit m.p. 248–51°C)[59]; IR (KBr) ν (cm^{-1}): 3054, 2923, 2856, 2217, 1896, 1727, 1579, 1462, 1405, 1354, 1279, 1235, 1116, 1009, 932, 860, 808, 740; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 8.49 (d, 1 H), 8.30 (d, 1 H), 8.14 (d, 1 H), 7.72 (m, 3 H), 7.49 (d, 1 H), 7.38 (t, 1 H), 4.57 (q, 2 H), 1.53 (t, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 145.42, 144.22, 140.73, 140.33, 139.36, 131.11, 129.47, 128.88, 127.86, 126.04, 122.98, 120.94, 119.68, 109.48, 36.33, 13.79.

6-Propyl-6H-indolo[2,3-b]quinoxaline (3m). Yellow solid; yield 88%; m.p. 218–19°C (lit m.p. 218°C)[60]; IR (KBr) ν (cm^{-1}): 3056, 2922, 2856, 2359, 1729, 1579, 1461, 1405, 1363, 1276, 1203, 1116, 1071, 983, 942, 893, 743; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 8.49 (d, 1 H), 8.30 (d, 1 H), 8.14 (d, 1 H), 7.80–7.63 (m, 3 H), 7.48 (d, 1 H), 7.38 (t, 1 H), 4.46 (t, 2 H), 2.00 (dd, 2 H), 1.03 (t, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 145.87, 144.68, 140.79, 140.18, 139.36, 131.05, 129.44, 128.83, 127.92, 126.02, 122.90, 120.89, 119.58, 109.67, 43.20, 21.96, 11.74.

6-Benzyl-6H-indolo[2,3-b]quinoxaline (3n). Yellow solid; yield 91%; m.p. 170–71°C (lit m.p. 176°C)[60]; IR (KBr) ν (cm^{-1}): 2920, 2856, 1729, 1574, 1459, 1396, 1344, 1274, 1186, 1117, 1069, 982, 940, 850, 813, 736; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 8.49 (d, 1 H), 8.32 (d, 1 H), 8.14 (d, 1 H), 7.83–7.54 (m, 3 H), 7.48–7.19 (m, 7 H), 5.71 (s, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 145.94, 144.40, 140.79, 140.17, 139.65, 136.63, 131.14, 129.47, 128.96, 128.93, 128.01, 127.81, 127.32, 126.26, 122.84, 121.30, 119.79, 110.28, 45.13.

Ethyl 2-(6H-indolo[2,3-b]quinoxalin-6-yl)acetate (3o). White solid; yield 90%; m.p. 185–86°C (lit m.p. 188°C)[61]; IR (KBr) ν (cm^{-1}): 3054, 2976, 2359, 1950, 1732, 1587, 1475, 1417, 1357, 1213, 1112, 1019, 925, 866, 771, 737; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 8.49 (d, 1 H), 8.31 (d, 1 H), 8.11 (d, 1 H), 7.83–7.61 (m, 3 H), 7.49–7.30 (m, 2 H), 5.24 (s, 2 H), 4.24 (d, $J = 7.1$ Hz, 2H), 1.25 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 168.21, 145.70, 144.38, 140.55, 140.31, 139.87, 131.27, 129.50, 129.05, 127.92, 126.48, 122.99, 121.74, 119.97, 109.42, 62.00, 42.81, 14.27.

Ethyl 2-(9-chloro-6H-indolo[2,3-b]quinoxalin-6-yl)acetate (3p). White solid; yield 92%; m.p. 275–76°C (lit m.p. 248°C)[60]; IR (KBr) ν (cm^{-1}): 2921, 2854, 2346, 2213, 1733, 1577, 1460, 1362, 1275, 1209, 1120, 1019, 952, 871, 811, 739; ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 8.46 (s, 1 H), 8.29 (d, 1 H), 8.11 (d, 1 H), 7.83–7.60 (m, 3 H), 7.29 (d, 1 H), 5.22 (s, 2 H), 4.24 (q, 2 H), 1.26 (t, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 167.95, 145.78, 142.55, 140.79, 140.05, 139.15, 131.10, 129.67, 129.53, 128.00, 127.45, 126.81, 122.75, 121.19, 110.57, 62.12, 42.85, 14.27.

Acknowledgments

V. S. gratefully acknowledges IIT (BHU) for a research support grant and the Central Instrumental Facility for all the characterizations. A. M. acknowledges IIT (BHU) for a research fellowship.

References

1. H. S. A. El-Zahabi, *Archiv der Pharmazie*, **350**, 1700028 (2017).
2. D. H. Soliman, *Int. J. Org. Chem.*, **3**, 65 (2013).
3. S. Paliwal, S. Sharma, J. Dwivedi and A. Mishra, *J. Heterocyclic Chem.*, **54**, 3689 (2017).
4. U. A. Mohsen, L. Yurttas, U. Acar, Y. Ozkay, Z. Kaplacikli, H. K. Gencer and Z. Canturk, *Drug Res.*, **65**, 266 (2015).
5. G. Cheng, W. Sa, C. Cao, L. Guo, H. Hao, Z. Liu, X. Wang and Z. Yuan, *Front. Pharmacol.,* **7**, 64 (2016).
6. W. Gu, S. Wang, X. Jin, Y. Zhang, D. Hua, T. Miao, X. Tao and S. Wang, *Molecules*, **22**, 1154 (2017).
7. T. Sindhu, S. Arikkatt, G. Vincent, M. Chanran, A. Bhat and K. Krishnakumar, *Int. J. Pharma. Sci. Res.*, **4**, 134 (2013).
8. G. Vincent, B. Mathew, J. Joseph, M. Chandran, A. Bhat and K. K. Kumar, *Int. J. Pharm. Chem. Sci.*, **3**, 341 (2014).
9. A. R. Das, G. Pal, P. Bhattacharyya, A. K. Ghosh, D. Mukherjee and D. Bandyopadhyay, *Tetrahedron Lett.*, **53**, 7060 (2012).
10. C. Shen, Y. Wu, W. Zhang, H. Jiang, H. Zhang, E. Li, B. Chen, X. Duan and W.-H. Zhu, *Dyes Pigm.*, **149**, 65 (2018).
11. A. Katoh, T. Yoshida and J. Ohkanda, *Heterocycles*, **52**, 911 (2000).
12. E. Dietz and M. Urban, Process for the Preparation of Pigment Preparations Based on CI Pigment Violet 23, (June 7, 1994) U.S. Patent No. 5,318,627. Washington, DC.
13. S. Dailey, W. J. Feast, R. J. Peace, I. C. Sage, S. Till and E. L. Wood, *J. Mater. Chem.*, **11**, 2238 (2001).
14. M. J. Crossley and L. A. Johnston, *Chem. Comm.*, **2002**, 1122 (2002).
15. D. J. Brown, J. A. Ellman and E. C. Taylor, *The Chemistry of Heterocyclic Compounds, Cinnolines and Phthalazines, Supplement II*; Vol. **64**, John Wiley & Sons, 2005, passim.
16. M. R. Islami and Z. Hassani, *Arkivoc*, (**xv**), **280** (2008).
17. S. V. More, M. Sastry, C.-C. Wang and C.-F. Yao, *Tetrahedron Lett.*, **46**, 6345 (2005).
18. R. S. Bhosale, S. R. Sarda, S. S. Ardhapure, W. N. Jadhav, S. R. Bhusare and R. P. Pawar, *Tetrahedron Lett.*, **46**, 7183 (2005).
19. M. M. Heravi, K. Bakhtiari, M. H. Tehrani, N. M. Javadi and H. A. Oskooie, *Arkivoc*, (**xvi**), **16** (2006).
20. T.-k. Huang, R. Wang, L. Shi and X.-X. Lu, *Catal. Commun.*, **9**, 1143 (2008).
21. C. Srinivas, C. N. S. S. P. Kumar, V. J. Rao and S. Palaniappan, *J. Mol. Catal. A Chem.*, **265**, 227 (2007).
22. S. Fathi and A. R. Sardarian, *Phosphorus, Sulfur, Silicon Relat. Elem.*, **190**, 1471 (2015).
23. A. Chandra Shekhar, A. Ravi Kumar, G. Sathaiah, K. Raju, P. Srinivas, P. Shanthan Rao and B. Narsaiah, *J. Heterocyclic Chem.*, **51**, 1504 (2014).

24. H. R. Darabi, S. Mohandessi, K. Aghapoor and F. Mohsenzadeh, *Catal. Commun.*, **8**, 389 (2007).
25. P. G. Hegade, M. M. Mane, J. D. Patil and D. M. Pore, *Synth. Commun.*, **44**, 3384 (2014).
26. H. R. Darabi, F. Tahoori, K. Aghapoor, F. Taala and F. Mohsenzadeh, *J. Braz. Chem. Soc.*, **19**, 1646 (2008).
27. J.-Y. Liu, J. Liu, J.-D. Wang, D.-Q. Jiao and H.-W. Liu, *Synth. Commun.*, **40**, 2047 (2010).
28. S. V. More, M. Sastry and C.-F. Yao, *Green Chem.*, **8**, 91 (2006).
29. J.-J. Cai, J.-P. Zou, X.-Q. Pan and W. Zhang, *Tetrahedron Lett.*, **49**, 7386 (2008).
30. H. R. Darabi, K. Aghapoor, F. Mohsenzadeh, F.Taala, N. Asadollahnejad and A. Badiei, *Catal. Lett.*, **133**, 84 (2009).
31. K. Aghapoor, H. R. Darabi, F. Mohsenzadeh, Y. Balavar and H. Daneshyar, *Transition Met. Chem.*, **35**, 49 (2010).
32. H. R. Darabi, K. Aghapoor, F. Mohsenzadeh, M. R. Jalali, S. Talebian, L. Ebadi-Nia, E. Khatamifar and A. Aghaee, *Bull. Korean Chem. Soc.*, **32**, 213 (2011).
33. M. J. Hosseini-Sarvari, *Iran. Chem. Soc.*, **9**, 535 (2012).
34. G. R. Bardajee, F. Mizani, I. Rostami and A. Mohamadi, *Polycycl Aromat Compd*, **33**, 419 (2013).
35. A. Rezaeifard, M. Jafarpour, R. Haddad, H. Tavallaei and M. Hakimi, *J. Cluster Sci.*, **26**, 1439 (2015).
36. K. S. Indalkar, C. K. Khatri and G. U. Chaturbhuj, *J. Chem. Sci.*, **129**, 141 (2017).
37. M. Kidwai, S. Saxena and R. Mohan, *J. Korean Chem. Soc.*, **49**, 288 (2005).
38. A. Dwivedi, A. Singh and A. Mishra, *Chem. Sci. Trans.,* **3**, 465 (2014).
39. D. Bandyopadhyay, J. Cruz, L. D. Morales, H. D. Arman, E. Cuate, Y. S. Lee, B. K. Banik and D. J. Kim, *Future Med. Chem*., **5**, 1137 (2013).
40. D. Bandyopadhyay, S. Mukherjee, R. R. Rodriguez and B. K. Banik, *Molecules*, **15**, 4207 (2010).
41. W.-X. Guo, H.-L. Jin, J.-X. Chen, F. Chen, J.-C. Ding and H.-Y. Wu, *J. Braz. Chem. Soc.*, **20**, 1674 (2009).
42. K. Aghapoor, F. Mohsenzadeh, S. Talebian, M. J. Tehrani, Y. Balavar, G. Khanalizadeh and H. R. Darabi, *Monatsh. Chem.*, **142**, 619 (2011).
43. G. Kaupp and M. R. Naimi-Jamal, *Eur. J. Org. Chem.*, **2002**, 1368 (2002).
44. Z. T. Bhutia, G. Prasannakumar, A. Das, M. Biswas, A. Chatterjee and M. Banerjee, *ChemistrySelect*, **2**, 1183 (2017).
45. H. Etman, H. Metwally, M. Elkasaby, A. Khalil and M. Metwally, *American Journal of Organic Chemistry*, **1**, 10 (2011).
46. A. Schonberg, E. Singer, G. A. Hoyer and D. Rosenberg, Eur. J. *Inorg. Chem.*, **110**, 3954 (1977).
47. V. Simakov, S. Kurbatov, O. Y. Borbulevych, M. Y. Antipin and L. Olekhnovich, *Russ. Chem. Bull.*, **50**, 1064 (2001).
48. G. Kaupp, M. R. Naimi-Jamal and J. Schmeyers, *Chem. Eur. J.*, **8**, 594 (2002).

49. M. B. Gawande, V. D. Bonifácio, R. Luque, P. S. Branco and R. S. Varma, *Chem. Soc. Rev.*, **42**, 5522 (2013).

50. U. M. Lindstrom, *Organic Reactions in Water: Principles, Strategies and Applications*; John Wiley & Sons, 2008, passim.

51. J. S. Ghomi and Z. Akbarzadeh, *Ultrason. Sonochem.*, **40**, 78 (2018).

52. V. B. Nishtala, J. B. Nanubolu and S. Basavoju, *Res. Chem. Intermed.*, **43**, 1365 (2017).

53. B. Banerjee, *Ultrason. Sonochem.*, **35**, 1 (2017).

54. D. Bandyopadhyay, S. Mukherjee, L. C. Turrubiartes and B. K. Banik, *Ultrason Sonochem.*, **19**, 969 (2012).

55. H. Junek, H. Fischer-Colbrie and H. Sterk, *Chemische. Berichte.*, **110**, 2276 (1977).

56. C. Zhang, S. Li., L. Ji, S. Lui, Z. Li, S. Li and X. Meng, *Bioorg. Med. Chem. Lett.,* **25**, 4693 (2015).

57. G. Y. Sarkis and H. T. Al-Badri, *J. Heterocycl. Chem.*, **17**, 813 (1980).

58. R. S. Varma and I. A. Khan, *ChemInform*, **10** (19), (1979).

59. N. S. H. N. Moorthy, C. Karthikeyan and P.Trivedi, *J. Enzyme Inhib. Med. Chem.*, **25**, 394 (2010)

60. S. Bajpai, S. Singh and V. Srivastava, *Arab. J. Chem.*, article in press, https://doi.org/10.1016/j.arabjc.2014.11.037

61. K. Manna and Y. K. Agrawal, *Bioorg. Med. Chem. Lett.* **19**, 2688 (2009).