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A NOVEL SULFATED CHOLINE (IL) BASED $FeCl_4$: HETEROGENEOUS CATALYST FOR THE SYNTHESIS OF SPIRO INDOLINE-QUINAZOLINE DERIVATIVES UNDER MILD CONDITIONS

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Abstract
Sulfated choline (IL) based $FeCl_4$ (IL-$FeCl_4$) was prepared by ion exchange of catalytically active $FeCl_3$. It was characterized by FT-IR, EDX, XRD, TGA and elemental analysis. Catalytic activity of thus prepared catalyst was studies in preparation of spiro 1,2-dihydroquinoline derivatives at room temperature using ethanol as solvent. The methodology has provided cleaner conversion with shorter reaction time and high yield. The catalyst was also found to be equally effective in four successive runs for the model reaction. This catalytic system is striking in view of its ease of application and cost.

Keywords
1,2-dihydroquinazoline, Green Chemistry, Spiro indoline-quinazolinones, Heterogeneous catalyst

1. Introduction

Green chemistry has inspired organic chemists for environmentally benign reagents and conditions for synthesis of organic compounds[I]. Choline chloride is widely used as eco-friendly, environmentally benign, non-flammable and non-conventional green reaction media. This is reported to be employed as catalyst and/or solvent in organic synthesis[II-III]. The concept of green chemistry mainly depends on use of benign solvents, resources and reusable catalysts and less toxic promising reagents which are kind to the environment. A series of inexpensive and moisture-stable Lewis acidic ionic liquids have been synthesized from choline chloride and $ZnCl_2$, $FeCl_3$, $SnCl_2$, and $CuCl_2$[IV]. Choline chloride based catalysts showed significant activity in organic synthesis[V-X]. In the present study choline chloride based sulfated ionic liquid [Ch-OSO_3H][XI] was reacted with $FeCl_3$ to prepare a novel catalyst IL-$FeCl_4$.
Multicomponent reactions (MCRs) are enjoying unmatched status in modern organic synthesis and medicinal chemistry. MCRs protocols offer incredible advantages such

as high selectivity, high yields, combinatorial chemistry owing to productivity, simple procedures, convergence, facile execution and structural diversity of scaffolds[XII-XVII]. The development of quinazoline-based drugs has renewed the interest in developing new synthetic approaches. Quinazoline is present as a core entity in several naturally occurring alkaloids[XVIII-XX], microorganisms[XXI], and in several life saving drugs such as gefitinib (Iressa)[XXII-XXIII], and erlotinib[XXIV] (Tarceva). They are known to act as selective inhibitors of the DNA-gyrase, JAK2, PDE5, tyrosine kinase activity of the epidermal growth factor receptor (EGFR)[XXV] as well as CB2 receptor agonists[XXVI]. Quinazoline derivatives have also shown significant activity as antibacterial, anticancer, antitubercular, antiviral agents[XXVII-XXXII].
Several procedures have been reported for dihydroquinazoline synthesis[XXXIII-XXXIX]. These methods suffer from limitations of substrate cost, the availability of starting materials, multistep synthesis, use of expensive catalyst, ligand or additives, lower product yields, and harsh conditions.
As part of a program to develop environmentally benign protocols directed toward the synthesis of various heterocyclic compounds[XL-XLVI] we attempted to design a green protocol that allow rapid and cost-effective synthesis of spiro 1,2-dihydroquinazolines from readily available precursors. To the best of our knowledge this is the very first report on the synthesis of spiro indoline-quinazolinones derivatives catalyzed by sulfated choline based $FeCl_4$.

2. Experimental section

2.1 Materials and instrumentation

All the reactions were performed with commercially available reagents. They were used without further purification. Organic solvents were purified by standard methods[XLVII]. All the reactions were monitored by thin-layer chromatography carried out on fluorescent coated plates (aluminium plates coated with silica gel 60 F254, 0.25 mm thickness, Merck) and detection of the components was made by exposure to UV light. Melting points were measured in μThermoCal10 (Analab Scientific Pvt. Ltd., India) and the reported values are uncorrected. The synthesized compounds were identified by ^{1}H NMR spectra recorded in DMSO-d_6 on Bruker Avance 400 MHz spectrometer (Bruker Scientific Corporation Ltd., Switzerland). The chemical shifts are reported in δ ppm. IR spectra were recorded on Bruker alpha E- FTIR spectrophotometer over the range 4000-400 cm^{-1} and frequencies of only characteristic peaks are expressed. Elemental analyses were performed on Perkin Elmer 2400 series- II elemental analyzer (Perkin Elmer, USA) and all results are found within ±0.4% of the theoretical compositions. TGA data was obtained at a heating rate of 10˚C/min on a TGA/DTG TA instruments model 5000/2960 thermo gravimetric analyzer, USA. The EDX was performed using JOEL JSM-5610 scanning electron microscope (SEM). XRD instrument consists of vertical theta-theta goniometer having range of 0°-160°. 2Theta was used for the X-ray diffraction study. The radiation used in Cu K-alpha-1 and nickel metal was used as beta filter.

2.2 Catalyst preparation

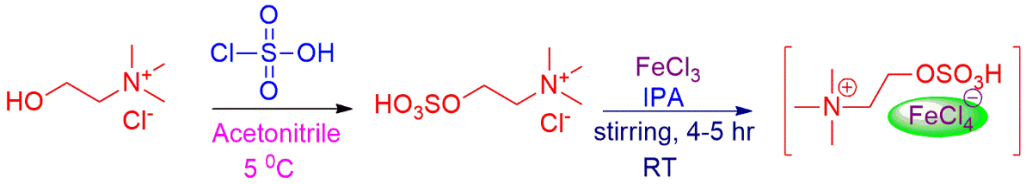
2.2.1 Synthesis of N,N,N-trimethyl-2-(sulfooxy)ethanaminium chloride (IL-SO_3H)

(IL-SO_3H), N,N,N-trimethyl-2-(sulfooxy)ethanaminium chloride was prepared according to the known process[XLVIII]. Chlorosulphonic acid (1.0 g, 8.6 mol, 1 eq.) was added drop wise to choline chloride (1.2 g, 8.6mol, 1 eq.) by maintaining the temperature below 5^{o}C over a period of 2 h **(Scheme 1)**. HCl gas, immediately liberated from the reaction vessel, was

properly trapped. After complete addition, the mixture was stirred for further 2 h at room temperature (27±1°C). The mixture was then filtered, obtained solid was washed with 30 mL of acetonitrile and dried at room temperature to afford N,N,N-trimethyl-2-(sulfooxy)ethanaminium chloride (IL).

2.2.2 General procedure for the synthesis of IL-$FeCl_4$

To the aqueous solution of N,N,N-trimethyl-2-(sulfooxy)ethanaminium chloride (1.0 g, 4.6 mol, 1 eq.), anhydrous $FeCl_3$ (1.48g, 4.6 mol, 1 eq.) was added under vigorous stirring. 4 mL isopropyl alcohol was then added drop wise and stirring was continued for 4-5 hours at room temperature. After completion of reaction, The mixture was filtered, obtained solid was washed with 30 mL of acetonitrile and dried at room temperature to afford N,N,N-trimethyl-2-(sulfooxy)ethanaminium iron(III) chloride (IL-$FeCl_4$) **(Scheme 1)**.



Scheme 1. Synthesis of the IL-$FeCL_4$ catalyst.

2.3 Experimental procedures for Spiro indolinequinazoline derivatives.

2.3.1 Synthesis of 6'-chloro-5-fluoro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one

A mixture of 5-fluoroisatine **1d** (0.1 g, 0.6 mol, 1 eq.) and 5-Chloro-2-aminobenzophenone **2a** (0.14 g, 0.6 mol, 1 eq.) was stirred at room temperature for the appropriate time and then added NH_4OAc (0.14 g, 1.8 mol, 3 eq.) in the presence of IL-$FeCl_4$ using ethanol as solvent. The progress of the reaction was monitored by TLC. After completion of the reaction, the solid product gradually formed upon cooling was poured into cold water. The product was dissolved in chloroform to filter out the catalyst which was washed thrice, with aliquots of 10 mL diethyl ether each time. Thus filtered catalyst was dried at 100 °C for 4 h and was recycled thrice for the model reaction to check the desired product was obtained as yellow solid. 6'-chloro-5-fluoro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one was purified by silica gel column chromatography (Ethyl acetate/Hexane 30:70) affording the pure product. The structures of the products were confirmed by ^{1}H NMR and elemental analysis. Thus, filtered catalyst was dried at 100°C for 4h and was recycled thrice for the model reaction to check its catalytic efficacy.

Selected spectral data of synthesized compounds

6'-chloro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one (4a)

Yield: 91%, ^{1}H-NMR (400 MHz, DMSO- d_6) δ (ppm) 6.67 (d, J= 8.8 Hz, 1H, Ar-H), 6.88-6.91(m, 2H, Ar-H), 6.97-7.01(t, 1H, Ar-H), 7.25-7.35 (m, 3H, Ar-H), 7.40 (s, 1H, Ar-NH), 7.43-7.53 (m, 5H, Ar-H), 10.35 (s, 1H, Ar-NH). Anal. calcd $C_{21}H_{14}ClN_3O$ (359.08): C, 70.10%; H, 3.92%; Cl, 9.85%; N, 11.68%; O, 4.45% Found: C, 70.23%; H, 3.45%; Cl, 9.67%; N, 11.80%; O, 4.34%.

5,6'-dichloro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one (4b)

Yield: 95%, ^{1}H-NMR (400 MHz, DMSO- d_6) δ (ppm) 6.59 (d, J=8.4 Hz, 1H, Ar-H), 6.76 (d, J= 8.4 Hz, 1H, Ar-H), 7.17-7.24 (m, 3H, Ar-H), 7.28 (s, 1H, Ar-NH), 7.38 (d, J=2 Hz, 1H, Ar-H), 7.43-7.99 (m, 5H, Ar-H) 10.52 (s, 1H, Ar-NH), Anal. calcd $C_{21}H_{13}Cl_2N_3O$ (394.26):

C, 63.98%; H, 3.32%; Cl, 17.98%; N, 10.66%; O, 4.06% Found: C, 63.43%; H, 3.42%; Cl, 17.90%; N, 10.12%; O, 4.56%.

6'-chloro-5-fluoro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one (4c)

Yield: 92%, ^{1}H-NMR (400 MHz, DMSO- d_6) δ (ppm) 6.65-6.69 (t, 1H, Ar-H), 6.94 (d, J=2.4 Hz, 1H Ar-H), 7.00-7.04 (t, 1H, Ar-H), 7.27-7.33 (m, 2H, Ar-H), 7.36-7.55 (m, 7H, Ar-NH), 10.80 (S, 1H, Ar-NH), Anal. Calcd: $C_{21}H_{13}ClFN_3O$ (377.80) C, 66.76%; H, 3.47%; Cl, 9.38%; F, 5.03%; N, 11.12%; O, 4.23%, Found: C, 66.60%; H, 3.10%; Cl, 9.98%; F, 5.89%; N, 11.10; O, 4.78%.

6',7-dichloro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one (4d)

Yield: 81%, ^{1}H-NMR (400 MHz -DMSO- d_6) δ (ppm) 6.67 (d, J=8.4 Hz, 1H, Ar-H), 6.92-7.04 (m, 2H, Ar-H), 7.27-7.31 (m, 2H, Ar-H), 7.31 (s, 1H, Ar-NH), 7.37-7.51 (m, 6H, Ar-H) 10.81 (s, 1H, Ar-NH), Anal. Calcd:$C_{21}H_{13}Cl_2N_3O$ (393.04) C, 63.98%; H, 3.32%; Cl, 17.98%; N, 10.66%; O, 4.06%, Found: C, 63.23%; H, 3.87%; Cl, 17.34%; N, 10.90%; O, 4.45%

5-bromo-6'-chloro-4'-(2-chlorophenyl)-1'H-spiro[indoline-3,2'-quinazolin]-2-one (4e)

Yield: 80%, ^{1}H-NMR (400 MHz -DMSO- d_6) δ (ppm) 6.68 (d, J=8.8 Hz, 1H, Ar-H), 6.87-6.92 (m, 1H, Ar-H), 7.12-7.17 (m, 1H, Ar-H), 7.23-7.29 (m, 2H, Ar-H), 7.43 -7.54 (m, 6H, Ar-H), 10.35 (s, 1H, Ar-NH) Anal. Calcd: $C_{21}H_{12}BrCl_2N_3O$ (470.95) C, 53.31%; H, 2.56%; Br, 16.89%; Cl, 14.98%; N, 8.88%; O, 3.38% Found: C, 53.67%; H, 2.98%; Br, 16.34%; Cl, 14.56%; N, 8.22%; O, 3.98%

5-chloro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one (4h)

Yield: 96%, ^{1}H-NMR (400 MHz -DMSO- d_6) δ (ppm) 6.60-6.65 (m, 2H, Ar-H), 6.90 (d, J=8 Hz, 1H, Ar-H), 7.00 (d, J=8 Hz, 1H, Ar-H), 7.21-7.25 (m, 3H, Ar-H), 7.29-7.50 (m, 6H, Ar-H), 10.43 (s, 1H, Ar-NH), Anal. Calcd:$C_{21}H_{14}ClN_3O$ (359.08) C, 70.10%; H, 3.92%; Cl, 9.85%; N, 11.68%; O, 4.45%, Found: C, 70.91%; H, 3.12%; Cl, 9.25%; N, 11.67%; O, 4.78%.

7-chloro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one (4k)

Yield: 83%, ^{1}H-NMR (400 MHz –DMSO- d_6) δ (ppm) 6.61-6.64 (m, 2H, Ar-H), 6.98-7.02 (m, 2H, Ar-H), 7.22-7.28 (m, 3H, Ar-H), 7.37 (d, J=8.4 Hz, 1H, Ar-H), 7,45-7.51 (m, 5H, Ar-H),10.74 (s, 1H, Ar-NH), Anal. Calcd:$C_{21}H_{14}ClN_3O$ (359.08) C, 70.10%; H, 3.92%; Cl, 9.85%; N, 11.68%; O, 4.45%, Found: C, 70.56%; H, 3.22%; Cl, 9.67%; N, 11.56%; O, 4.89%

5-fluoro-6'-nitro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one (4l)

Yield: 96%, ^{1}H-NMR (400 MHz-DMSO- d_6) δ (ppm) 6.72 (d, J=8 Hz, 1H, Ar-H), 6.94 (d, J=4.4 Hz, 1H, Ar-H), 7.20 (d, J=5.2 Hz, 1H, Ar-H), 7.26 (s, 1H, Ar-NH), 7.42-8.64 (m, 10H, Ar-H), 10.54 (s 1H Ar-NH), Anal. Calcd:$C_{21}H_{13}FN_4O_3$ (388.10) C, 64.95%; H, 3.37%; F, 4.89%; N, 14.43%; O, 12.36%, Found C, 64.95%; H, 3.37%; F, 4.89%; N, 14.43%; O, 12.36%.

6'-nitro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one (4m)

Yield: 92%, ^{1}H-NMR (400 MHz-DMSO- d_6) δ (ppm) 6.44 (d, J=6.8 Hz, 1H, Ar-H), 6.50-6.61 (m, 2H, Ar-H), 7.07- 6.72 (m, 1H, Ar-H), 7.26 (s, 1H, Ar-H) 7.33-8.63 (m, 8H, Ar-H),

10.54 (s, 1H, Ar-NH), Anal. Calcd:$C_{21}H_{14}N_4O_3$ (370.11) C, 68.10%; H, 3.81%; N, 15.13%; O, 12.96%, Found C, 68.89%; H, 3.56%; N, 15.89%; O, 12.45%.

6'-chloro-4'-phenyl-1'H,2H-spiro[acenaphthylene-1,2'-quinazolin]-2-one (4o)

Yield: 82%, ^{1}H-NMR (400 MHz-DMSO- d_6) δ (ppm) 6.66 (d, J=8.4 Hz, 1H, Ar-H), 6.86-6.88 (m, 2H, Ar-H), 6.92 (s, 1H, Ar-H),7.27-7.53 (m, 11H, Ar-H) Anal. Calcd: $C_{25}H_{15}ClN_2O$ (394.09) C, 76.05%; H, 3.83%; Cl, 8.98%; N, 7.09%; O, 4.05%, Found: C, 76.67%; H, 3.78%; Cl, 8.68%; N, 7.29%; O, 4.95%

4'-phenyl-1'H,10H-spiro[phenanthrene-9,2'-quinazolin]-10-one (4p)

Yield: 80%, ^{1}H-NMR (400 MHz-DMSO-d_6) δ (ppm) 5.70 (s, 1H, Ar-NH), 6.53-6.57 (t, 1H, Ar-H), 6.69 (d, J=7.6 Hz, 1H, Ar-H), 7.02-7.06 (t, 1H, Ar-H), 7.25-7.82 (m, 10H, Ar-H), 8.47-8.51 (m, 4H, Ar-H), Anal. Calcd:$C_{27}H_{18}N_2O$ (386.14) C, 83.92%; H, 4.69%; N, 7.25%; O, 4.14%, Found: C, 83.47%; H, 4.69%; N, 7.82%; O, 4.84%

3. Results and discussion

3.1 Characterization

The IL-$FeCl_4$ catalyst was characterized by FT-IR spectroscopy, TG analysis, EDX and XRD.

3.1.1 FT-IR analysis

FT-IR spectra of **IL-$FeCl_4$** is illustrated in **Fig. 1**. In the IR spectra, S=O stretching vibrations were detected at 1128 and 1263cm^{-1} to confirmed the presence of -SO_3H groups. IL-$FeCl_4$ also exhibited two featured bands at 1472 and 1414 cm^{-1} which can be attributed to the stretching vibration of the C-C bond and the bending vibration of the C-H bond, respectively.

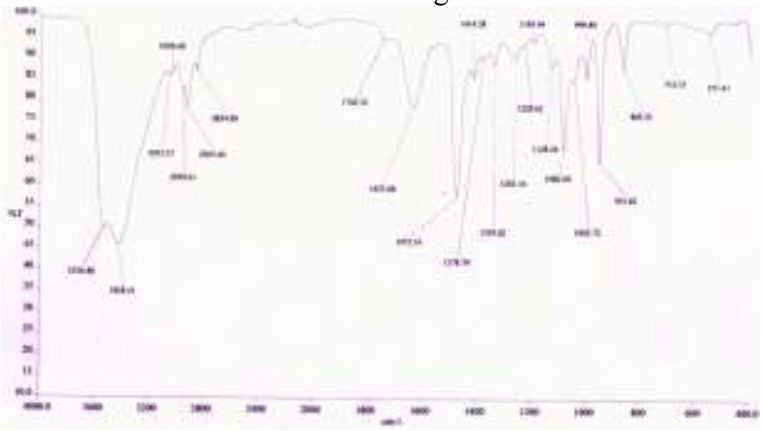


Fig. 1 FT-IR spectra of IL-$FeCl_4$.

3.1.2 TG Analysis

TGA analysis (Fig. 2) shows that the catalyst was stable up to 450 °C. 2 % weight loss at temperature below 250°C may be due to the evaporation of physically adsorbed water molecules in the catalyst. The significant decrease in the weight up to 49.8% was observed in the range of 450-550 °C.

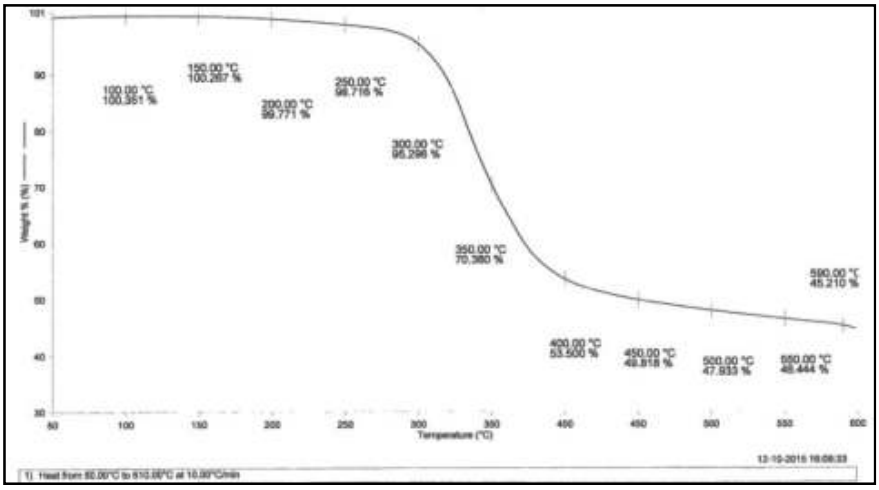
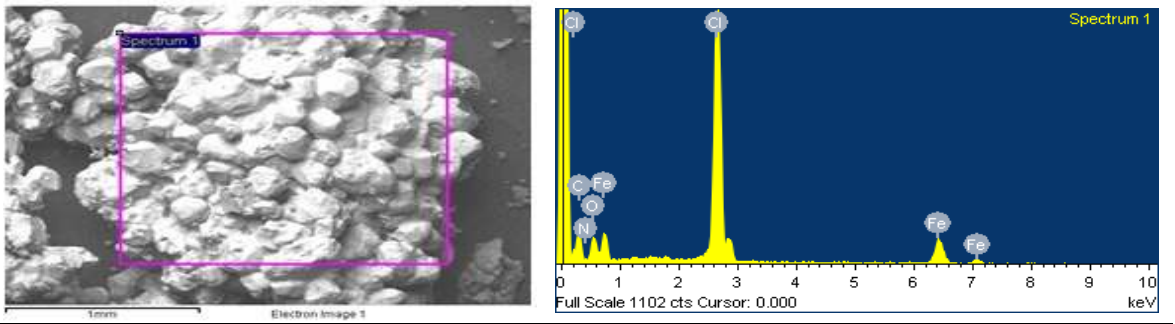


Fig. 2 TG analysis for the IL-$FeCl_4$ catalyst.

3.1.3 SEM and EDX analysis

SEM image **(Fig. 3a)** shows small white discrete particulates of sulfated choline anion with $FeCl_4$. Energy dispersive spectroscopy (EDX) analysis **(Fig. 3b)** of (IL-$FeCl_4$) recorded at random point on the surface indicated the composition of C, O, N, Cl and Fe respectively as 19.90,5.30, 4.64, 46.98, 18.50 as expected with the respectively calculated values of 19.2,5.0,4.75,46.04,18.0. Thus, the EDX and SEM combined suggested Fe, Cl, N, O elements are present in the sample.



(3a). SEM image of IL-$FeCl_4$ Catalyst (3b) EDX analysis of IL-$FeCl_4$ Catalyst

Fig. 3 SEM and EDX analysis of IL-$FeCl_4$

3.2 Optimization of reaction condition

Initially, when (1 mmol) of 2-aminobenzophenone (**1a**) was treated with (1 mmol) of 5-chloro isatin (**2b**) in the presence of 10 mol % of IL-$FeCl_4$ and (5 mmol) of Ammonium acetate without any solvent, yield was not detected (**Table1, entry 1**)

Table 1. Effect of solvents, temperature and different amount of Catalyst (IL-$FeCl_4$) on the synthesis[a] of 5-chloro-4'-phenyl-1'*H*-spiro[indoline-3,2'-quinazolin]-2-one.

Entry	Catalyst (Mol. %)	Solvent	Time (min)[b]	Temp.(°C)	Yield[c] (%)
1	10	-	240	110	n.d.
2	5	EtOH	30	RT	60
3	**10**	**EtOH**	**30**	**RT**	**98**
4	15	EtOH	30	RT	75
5	20	EtOH	30	RT	70
6	10	EtOH	180	90	78
7	10	EtOH	180	120	70
8	10	MeOH	240	110	65
9	10	Toluene	240	110	55
10	10	DMF	240	110	50
11	10	H_2O	240	110	32
12	10	DMSO	240	110	48
13	10	CCl_4	180	110	65

[a]Reaction conditions: 2-aminobenzophenone(1 mmol), 5-chloroisatine (1 mmol) NH_4OAc (5 mmol), IL-$FeCl_4$(10mol%). [b]All the reactions were run till completion as indicated by TLC. [c]Isolated yield. n.d[d]: not detected.

With various solvents **(Table 1, entry 8-13),** No better result was observed till raising the temperature up to 110°C. In case of ethanol, the reaction at temperature 90-120°C decreased the yield **(Table 1, entry 6, 7),** but at 30° C within 30 min gave 60% of isolated yield **(Table 1,Entry 2)** using 5 mol % of the catalyst. The amount of catalyst is also found to affect the reaction. Maximum yield within 30 min of reaction time was observed in ethanol at 10 mol% of IL-$FeCl_4$ **(Table 1, entry 3).** Further increase in the amount of catalyst decreased the yield **(Table 1, entry 4,5).**

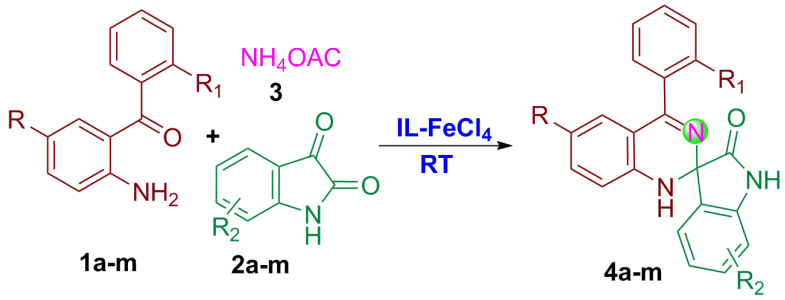
Table 2. Effect of different catalyst on the synthesis[a] of 6'-chloro-5-fluoro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one (8c)

Entry	Catalyst	Time (h)[b]	% Yield[c]
1	$ZnCl_2$	12	22
2	$NiCl_2$	15	29
3	$AgNO_3$	12	40
4	$Cu(OAc)_2$	24	54
5	Choline chloride	21	55
6	$FeCl_3.6H_2O$	24	46
7	**IL-$FeCl_4$**	**0.5**	**98**

[a]Reaction condition: 2-amino-5-chlorobenzophenone (1 mmol), 5-chloroisatin(1 mmol), ammonium acetate (5mmol), catalyst (10 mol%).[b]All reactions were run until completion as indicated by TLC. [C]Isolated yield.

The effect of different catalysts on the reaction was also studied were the reaction leading to the formation of product **4c** was considered as the model for the reason. A variety of catalysts were tried resulting **4c** in poor yield **(Table 2, entry 1-4).** The use of choline chloride and $FeCl_3.6H_2O$ alone found to be less efficient (**Table 2, entry 5,6**) the use of IL-$FeCl_4$ in 10 mol% yielded 98% of **8c** within half an hour. The generality of the novel protocol was tested by varying the substituents at R_2, R_3, and R_4position (**Table 3)**

Table-3. IL-$FeCl_4$ Synthesis of Spiro-2-dihydroquinazoline (4a-q)[a].



Scheme 2. Synthesis of 4a-q

Entry	R_2	R_3	R4	Product	Time (min)[b]	mp (°C)	Yield(%)[C]
1	Cl	H	H	**4a**	30	211-214	91
2	Cl	H	5-Cl	**4b**	35	114-116	95
3	Cl	H	5-F	**4c**	35	102-106	92
4	Cl	H	7-Cl	**4d**	35	204-206	81
5	Cl	Cl	5-Cl	**4e**	30	123-126	80
6	Cl	H	5-Cl	**4f**	30	99-103	78
7	Cl	Cl	5-F	**4g**	30	135-137	76
8	H	H	5-Cl	**4h**	35	138-140	96
9	H	H	5-Br	**4i**	35	145-148	90
10	H	H	5-F	**4j**	35	120-122	86
11	H	H	7-Cl	**4k**	30	156-158	83
12	NO_2	H	H	**4l**	30	225-226	96
13	NO_2	H	5-F	**4m**	35	195-198	92
14	H	H	Acenaphthylene-1,2-dione	**4n**	35	146-148	80
15	Cl	H	Acenaphthylene-1,2-dione	**4o**	30	156-158	82
16	H	H	Phenanthrene-9,10-dione	**4p**	30	123-125	80
17	NO_2	H	Phenanthrene-9,10-dione	**4q**	35	201-204	78

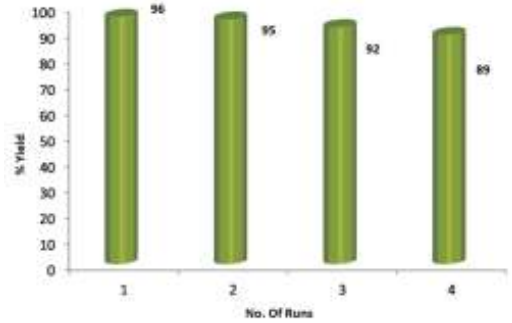
[a]2-aminobenzophenones (1 mmol), Isatin (1 mmol), ammonium acetate (5 mmol), IL –$FeCl_4$(10 mol%). [b]All reactions were run until completion as indicated by TLC. [C]Isolated yield.

We have developed a simple and efficient approach for the synthesis of spiro-2-dihydroquinazoline from 2-aminobenzophenone with this catalytic system. Various spiro-1,2-dihydroquinazoline were prepared from 2-aminobenzophenones and aldehydes/isatin of tandem reaction following sp^3 C-H functionalization in presence of metallic catalyst. Initially, we attempted the reaction of 5-chloro-2-aminobenzophenone **(1a)**, isatin **(2a)** and ammonium acetate **(3)** in the presence of catalyst IL-$FeCl_4$ (10 mol%). The reaction proceeded smoothly in ethanol affording the corresponding 6'-chloro-4'-phenyl-1'H-spiro[indoline-3,2'-quinazolin]-2-one, **4a** in 91% yield in a short reaction time **(Table 3, entry 1)**. The electronic nature of the substituents on benzene ring of 2-aminobenzophenone and isatin had no significant influence on the reactivity. Both electron-donating as well as electron-withdrawing groups found to react very well to give the product in high yields. The protocol

is almost found to be equally effective for this conversion **(Table 3, entry 2-11).** When 5-nitro-2-aminobenzophenone was treated with simple isatin the reaction product was obtained in excellent yield **(Table 3, entry 12).** The reaction with 5-fluro isatin also afforded the product in excellent yield **(Table 3, entry 13).** Sterically hindered subtracts like Acenaphthylene-1,2-dione and Phenanthrene-9,10-dione were also successfully attempted **(Table 3, entry 14-17)** to yield **4n-q** in high yield.

3.3 Recyclability

Fig. 4. Reusability study of the IL-$FeCl_4$ catalyst for the synthesis of compound (8c)[a].

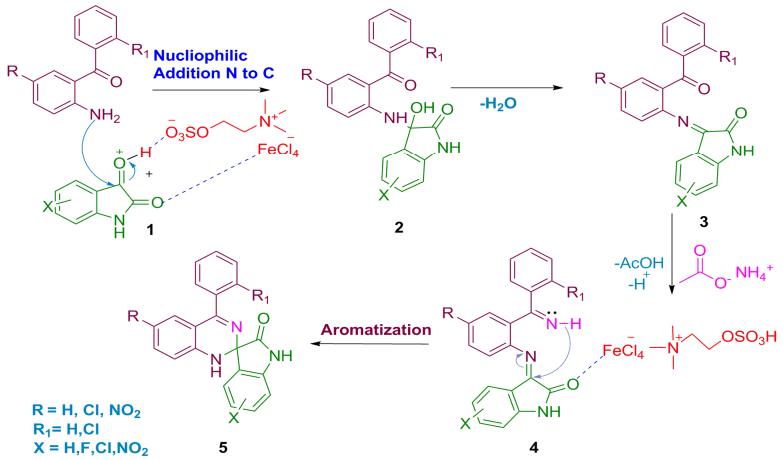


[a]Reaction conditions:2-aminobenzophenone(1 mmol), 5-Chloroisatine (1mmol) NH_4OAc (5 mmol), IL-$FeCl_4$(10mol%).

The yield of model reaction was compared by recycling of catalyst in three consecutive runs **(Table-4).** In the recycling experiment, the separated IL-$FeCl_4$ was reacted with fresh substrate for the next run under the same reaction conditions. It was noticed that the catalyst did not show any significant decrease in catalytically activity after being reused four times.

3.4 Plausible Mechanism

In initial step, nucleophilic amino nitrogen atom of 2-aminobenzophenone **1** reacts with carbonyl carbon of isatin **2** in presence of IL-$FeCl_4$. The formation of imine **4** via **3** proceeded with loss of water molecule. The oxime formation from imine **4** to yield intermediate **5** got accomplished in the presence of NH_4OAC. Finally intramolecular cyclization initiated by nucleophilic nitrogen atom of the oxime function afforded the desired spiro derivative **6 (Scheme 3).**



Scheme 3. Plausible reaction mechanism of spiro 1,2-dihydroquinazoline.

4. Conclusions

We have demonstrated green efficient procedure for the synthesis of Spiro indoline quinazoline derivatives using a novel IL-$FeCl_4$ as the catalyst. This catalyst is easy to recover and it is reusable without significant loss in its efficiency. Although the reaction was accomplished in the homogeneous model, isolation of the desired products as well as the catalyst could be achieved *via* simple filtration. In addition, this methodology offers significant improvements with regard to the product yield and reaction time.

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