Triflates Promoted One-Pot Synthesis of Functionalized Unsymmetrical New Dihydro-1*h*-Indeno[1,2-B]Pyridines Through Hantzsch Reaction under Ultrasonic Irradiation

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Summary: $Yb(OTf)_3$ and $Sc(OTf)_3$ catalyzed efficient Hantzsch reaction *via* four-component coupling reactions of aldehydes, diketone, ethylacetoacetate and ammonium acetate at ambient temperature and medium was described as the preparation of pyridine derivatives. The process presented here is operationally simple, environmentally benign and has excellent yield. Furthermore, the catalyst can be recovered conveniently and reused efficiently. All the same, the condensation of aldehydes, ethyl acetoacetate and ammonium acetate result dihydroindenopyridines in 87-98% yields under ultrasound irradiation with catalyst at room temperature. Compared to conventional methods, the main advantages of the present procedure are milder conditions, shorter reaction time and higher yields.

Keywords: Indenopyridine, Multi-component Reactions, Ultrasound, Hantzsch Reaction, Triflate.

Introduction

Dihydropyridines (DHP) are of importance in biological systems as a class of useful drugs, particularly as anti-oxidants. Some of the representative compounds of this class possess acaricidal, insecticidal, bactericidal, herbicidal and inhibitor activities [1-9]. DHP drugs, namely nifedipine, nicardipine and amlodipine, are cardiovascular agents for the treatment of hypertension [10-13]. Recent studies have revealed that 1,4-DHPs exhibit several medicinal applications which include neuroprotectant and platelet anti-aggregatory activity, in addition cerebral antiischemic activity in the treatment of Alzheimer's disease and as chemo sensitizer in tumour therapy [14, 15]. In particular, indenopyridines (azafluorenes) are one of the most important privileged medicinal scaffolds, which were developed initially as antihistamines [10]. Further, indenopyridines exhibit cytotoxic, phosphodiesterase inhibitory, adenosine A2a receptor antagonistic, anti-inflammatory/ antiallergic, coronary dilating and calcium modulating activities, useful inhibitors of spermatogenesis in animals, and fungicidal activate [16, 17]. Compounds with this motif show a wide range of pharmacological activities. Hydrogenated indenopyridines have valuable therapeutic uses [18]. They also have potential antidepressant activity [19].

Classical method for the synthesis of indenopyridines is one-pot condensation of aldehydes with ethyl acetoacetate, and ammonia either in acetic acid or by refluxing in alcohol [20, 21]. However, many of these methods suffer disadvantages such as long reaction time, harsh reaction conditions, the use of a large quantity of volatile organic solvents and generally leading to low yields. Therefore, it is necessary to develop an efficient and versatile method for the preparation of indenopyridines and the progress in this field is remarkable including the recent promotion of microwave [22-25], and three-components (at 70^0C). But few of them finished the reaction at ambient temperature.

Over the past few years, much effort has gone into developing rare earth metal triflates ($RE(OTf)_3$) especially $Yb(OTf)_3$ and $Sc(OTf)_3$ catalyzed organic synthesis. As a new type of Lewis acid, they have been applied in a variety of reactions [26-30]. The most characteristic feature of these rare earth metal triflates is that they act as water-compatible strong Lewis acids in aqueous solvents. Only catalytic amount of the catalysts is enough to complete the reactions in most cases. Moreover, they can be easily recovered after reactions and reused without any loss of activity. As a part of our program aiming at developing selective and environmental friendly methodologies for the preparation of fine chemicals and in continuation of our interest in lanthanide triflates catalyzed organic reactions [31-34], we wish to highlight our finding about the $Yb(OTf)_3$ and $Sc(OTf)_3$ catalyzed four-component Hantzsch reaction using ethanol as a solvent at ambient temperature. In this study, $Yb(OTf)_3$ and

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$Sc(OTf)_3$ have been employed as a mild and efficient catalyst for Hantzsch condensation.

Organic reactions under aqueous medium and solvent free conditions have attracted much interest of chemists particularly from the viewpoints of green chemistry. Green chemistry approaches are significant due to the reduction in by-products, reduction in waste produced, and decreasing the energy costs. The possibility of performing multi-component reactions under solvent free conditions with a heterogeneous catalyst could enhance their efficiency from the economical and as well as the ecological point of view. In recent years, heterogeneous catalysis is gaining more importance due to the environmental and economical factors.

The importance of heterocycles in many fields of science (including organic, inorganic, bioorganic, agricultural, industrial, pharmaceutical, and medicinal chemistry, as well as material science) can hardly be over emphasized, and this justifies a long lasting effort to work out new synthetic protocols for their production. The use of ultrasound to promote chemical reactions is called sonochemistry. Ultrasonic chemistry has received an increasing attention in recent years [35]. Ultrasound irradiation, by virtue of cavitational collapse, is able to activate numerous organic reactions [36-38]. A large number of organic reactions can be carried out in higher yields, shorter reaction times and milder conditions under ultrasound irradiation than that of conventional methods. Moreover, these solvent-free organic syntheses have received considerable attention since they are operationally simple, often involve nontoxic materials, and proceed in excellent yields with high selectivity [39, 40]. To our best knowledge, the use of ultrasound promoted triflate catalysts one-pot Hantzsh reaction has been not reported. Herein, we wish to show a novel and simple procedure for synthesis of indenopyridines with 4-component Hantzsch reactions catalyzed by scandium(III) triflate and ytterbium(III) triflate catalysts under ultrasound irradiation at room temperature.

Results and Discussion

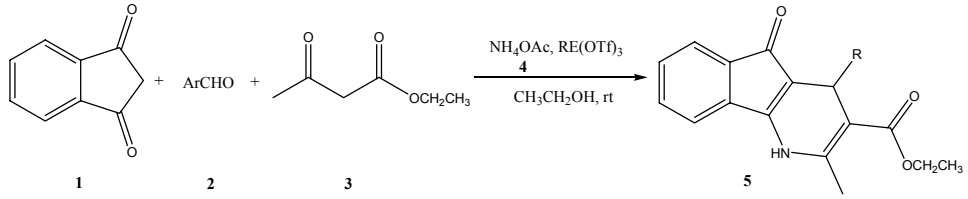
In recent years, triflates have received considerable attention as a mild Lewis acid for an array of organic transformations [41, 42] since the catalyst is quite stable in water and reusable. As part of a continuing effort in our laboratory toward the development of new methods in organic synthesis [43-46], we are interested in the possibility of developing a one-pot synthesis of polyhydroquinoline derivatives through a four component coupling Hantzsch reaction of aldehydes, 1,3-indandione, ethyl acetoacetate, and ammonium acetate in the presence of a reusable $RE(OTf)_3$ triflate catalyst at room temperature (Scheme 1).

We have examined other Lewis acids for this reaction (Table-1), $Yb(OTf)_3$ and $Sc(OTf)_3$ were found to be the most effective catalysts in terms of conversion and reaction rates. The Hantzsch condensation of 1,3-indandione, benzaldehyde, ethyl acetoacetate, and ammonium acetate in the presence of a catalytic amount of ytterbium triflate at room temperature result in the formation of Ethyl 2-methyl-5-oxo-4-phenyl-4,5-dihydro-1*H*-indeno[1,2-*b*] pyridine-3-carboxylate in 95% yield and this reaction was chosen as the model reaction (Scheme 1).

Table-1: The reaction of benzaldehyde, ethyl acetoacetate, 1,3-indandione, and ammonium acetate: effect of catalyst[a].

Entry	Catalyst	Amount of catalyst (mol%)	Time (h)	Yield (%)[b]
1	None		24	32
2	$AlCl_3$	100	24	45
3	$ZnCl_2$	100	24	41
4	$FeCl_3$	100	24	44
5	$Y(OTf)_3$	10	8	72
6	$Cu(OTf)_2$	10	12	68
7	$Nd(OTf)_3$	20	24	61
8	$Yb(OTf)_3$	0.5	6	74
9	$Yb(OTf)_3$	1	6	82
10	$Yb(OTf)_3$	2	6	85
11	$Yb(OTf)_3$	5	6	97
12	$Yb(OTf)_3$	8	6	88
13	$Yb(OTf)_3$	10	6	72
14	$Sc(OTf)_3$	1	10	75
15	$Sc(OTf)_3$	2	8	78
16	$Sc(OTf)_3$	5	6	84
17	$Sc(OTf)_3$	8	5	91
18	$Sc(OTf)_3$	10	4	98

[a] All reactions were carried out in ethanol at room temperature
[b] Isolated yields



Scheme 1: Reaction pathway to the indenopyridines by Hantzsch method.

Firstly, we have detected whether the use of ytterbium triflate was efficient or not and investigate the optimized conditions in this model reaction. The results were summarized in Table-1.

It was found that the conventional Lewis acids such as $AlCl_3$ and $FeCl_3$, as well as the condition of no catalyst showed poor effect to the yield of the product, which was probably due to their poor water tolerance. Even when large amount of catalysts was used, the results were still unsatisfactory and many side reactions could be observed (entry 1–4). When using the rare earth metal compounds (entry 5–7), the results seemed to be better.

While adding 0.5 mol% of $Yb(OTf)_3$ into the system under similar reaction conditions, the speed of reaction was obviously accelerated, but the yield was still not satisfactory (entry 8). Further studies showed that increasing the amount of $Yb(OTf)_3$ could improve the reaction significantly. Inspired by the results, we have changed the amount from 0.5 to 10 mol% (entry 8-13), finding that 5 mol% of $Yb(OTf)_3$ was good enough (entry 11). Moreover, reaction is carried out under similar conditions for different amount of $Sc(OTf)_3$ and inspired by the results, we have changed the amount from 1 to 10 mol%, finding that 10 mol% of $Sc(OTf)_3$ was good enough (entry 14-18). After the reaction was completed, the product was filtered directly and the catalyst can be extracted by water from the residue.

Lanthanide triflates are more soluble in water than that in organic solvents. The catalyst could be recovered almost quantitatively from the aqueous layer, which could subsequently be reused several times. In view of environmental friendly methodologies, the recovery and reuse of the catalyst is highly preferable.

Herein, we wish to report a novel synthesis of indenopyridines promoted by the catalytic amount of triflate under ambient conditions with excellent yields. In an initial endeavour, 1,3-indandione 1, benzaldehyde 2a, ethyl acetoacetate 3 and ammonium acetate 4 were stirred at room temperature in a few drops of ethanol. After 24 hours, only 32% of product 5a was realized after recrystallization of the crude product from ethanol (entry 1 of Table-1). To improve the product yields and to optimize the reaction conditions, triflate was used in catalytic amount (5 mol%) and a reaction was carried out under similar conditions. To our surprise, a significant improvement in the yield of the product 5a (95%) was observed (entry 11). With this optimistic result in hand, we further investigated the reaction outcome using different amounts of triflate. The increase in the quantity of triflate from 0.5 to 10 mol% not only lessens the reaction time from 24 to 6 h, but also enhanced the product yield from 32% to 95%.

We then continued to optimize the model process mentioned above by detecting the efficiency of several classic solvents chosen as the medium for comparison (Table-2).

Table-2: The reaction of benzaldehyde, ethyl acetoacetate, 1,3-indandione and ammonium acetate[a]: effects of solvent.

Entry	Solvent	Time (h)	Yield (%)[b]
1	C_2H_5OH	6	95
2	CH_3CN	6	89
3	Acetone	6	51
4	Toluene	24	27
5	CH_2Cl_2	24	38
6	Cyclohexane	24	19

[a] All reactions were carried out using $Yb(OTf)_3$ at room temperature.
[b] Isolated yields.

In each case, the substrates were mixed together with 5 mol% $Yb(OTf)_3$ agitated with 3–5 mL solvent. Obviously, the polar solvents such as ethanol and acetonitrile (entry 1, 2) were much better than non-polar solvents (entry 4–6). The results could be interpreted as a much better solubility of the catalyst and the reagents in the polar solvents. Thus, we have selected the optimized reaction conditions to examine the universality of this catalyst's application. Various aromatic and heterocyclic aldehydes were selected for undergoing the Hantzsch reaction in the presence of catalytic amount of $Yb(OTf)_3$ or $Sc(OTf)_3$ in ethanol at room temperature (Scheme 1). The results of this study are summarized in Table-3. We have re-examined the classically made tests using the same reaction conditions but under ultrasound irradiation and compared the reaction times and yields of the products with the previous results. The last values are summarized in Table-4. All the synthesized compounds have been characterized by elemental and spectral (IR, ^1H, ^{13}C NMR and mass) studies.

It can be seen from Table-4 that the condensations of various substituted aldehydes (carrying either electron donating or withdrawing substituents), ethyl acetoacetate and ammonium acetate were proceeded smoothly to afford the products in good to excellent yields (87-98%) within 30-60 min. with solvent and catalyst under ultrasound irradiation at room temperature. In these condensations, electrical effect and steric effect of substituted group affected the yields of 1,4-

dihydropyridine derivatives. In order to compare substituent effects, these reactions include different benzaldehydes, ethyl acetoacetate and ammonium acetate was carried out within 30-60 min. at room temperature under ultrasound irradiation (as shown in Table-4). The order of yields of the Hantzsch condensation under ultrasound irradiation condition is nitro- > bromo- > phenoxy- > methoxy- aldehydes. The activity of aldehydes with electron-withdrawing groups is higher than that with electron-donating groups. The position of substituents in the benzene ring of aldehyde influences this reaction.

It may be considered that the microenvironment of the reaction system with solvent is different from that in the solutions, resulting in a higher concentration of local reaction sites, and improving the global efficiency [47].

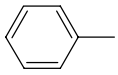
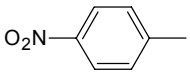
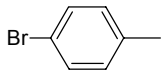
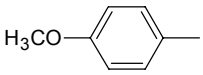
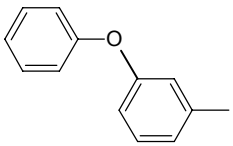
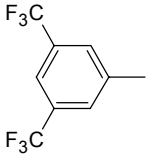
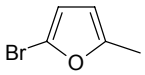
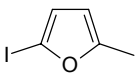
Ultrasound irradiation improved the Hantzsch reaction. The yields of dihydroindeno-pyridines under ultrasound irradiation are similar to or higher than those described in our studies.

Experimental

Materials and Methods

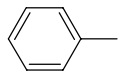
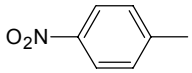
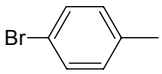
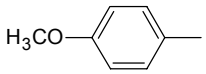
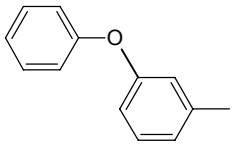
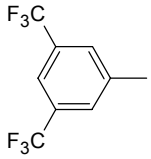
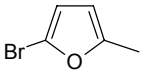
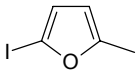
All the chemicals were obtained from Sigma-Aldrich and Merck Ltd. and used as received. Sonication was performed in Intersonik ultrasonic cleaner with a frequency of 60 kHz and a power 300 W. The reaction flasks were located in the maximum energy area in the cleaner, and the addition or removal of water controlled the temperature of the water bath. NMR spectra were recorded on Varian-INOVA at 500 MHz. The FTIR spectra were recorded on a Perkin-Elmer FT-IR spectrometer. Melting points were measured on a Gallenkamp melting-point apparatus. MS spectra were recorded on Thermo Elemental X Series ICP-MS.

Table-3: The synthesis of new indeno[1,2-b]pyridines (5a-5h) accompanied by triflate catalyst with conventional method.

Entry	Ar	Product	T (h)	Catalyst	Isolated yield[a]	Melting point (^{0}C)[b]
1		5a	6 4	$Yb(OTf)_3$ $Sc(OTf)_3$	95 96	271-272
2		5b	6 4	$Yb(OTf)_3$ $Sc(OTf)_3$	96 97	216-217
3		5c	6 4	$Yb(OTf)_3$ $Sc(OTf)_3$	94 96	175-176
4		5d	6 4	$Yb(OTf)_3$ $Sc(OTf)_3$	90 93	213-214
5		5e	6 4	$Yb(OTf)_3$ $Sc(OTf)_3$	91 92	198-199
6		5f	6 4	$Yb(OTf)_3$ $Sc(OTf)_3$	83 86	240-241
7		5g	6 4	$Yb(OTf)_3$ $Sc(OTf)_3$	89 91	207-208
8		5h	6 4	$Yb(OTf)_3$ $Sc(OTf)_3$	86 86	192-193

[a] Isolated yield based on aldehyde.
[b] Melting point are uncorrected.

Table-4: The synthesis of new indeno[1,2-b]pyridines (5a-5h) by triflate catalyst under ultrasound at room temperature.

Entry	Ar	Product	T (min)	Isolated yield[a]
1		5a	30	97
2		5b	30	98
3		5c	30	97
4		5d	45	92
5		5e	45	94
6		5f	60	87
7		5g	45	92
8		5h	45	88

[a] Isolated yield based on aldehyde.

Typical Procedure

To a mixture of benzaldehyde (1 mmol), 1,3-indandione (1 mmol), ethyl acetoacetate (1 mmol), ammonium acetate (1 mmol) in ethanol (5 mL), $Yb(OTf)_3$ (5 mol%) were added at room temperature. The reaction mixture was stirred for 6 h (TLC) at room temperature then the resulting solid product was filtered, washed with water, and dried in vacuum to afford the crude product. A pure product was obtained by further recrystallization using ethanol as a solvent. The filtrate containing the catalyst could be evaporated under reduced pressure to give a white solid. After completion of the reaction (monitored by TLC), the reaction mass was filtered in hot condition to separate the catalyst and poured on ice-water. The obtained solid condensation product was further purified by re-crystallization in ethanol. The recovered catalyst was washed with ethyl acetate, then dried at 70 ^oC and activated at 120 ^oC prior to use for next run in model reaction. And it was found that the recovered catalyst shows good yield with three successive reactions (Table-5).

Table-5: Recovery and reusability of catalyst.

Entry	Cycle	Yield (%)[a]
1	Fresh	96
2	First	94
3	Second	93
4	Third	93

[a]Yield refers to isolated product

Procedure under Ultrasound

Aldehyde (2 mmol) and ammonium acetate (2 mmol) were added to a stirred mixture of 1,3-indandione (2 mmol), ethyl acetoacetate (2 mmol) and $Yb(OTf)_3$ (5 mol%), in ethanol (5 mL) at room temperature. The reaction mixture was stirred at room temperature for 30-60 min. under ultrasound. The resulting yellow-reddish solid was filtered and recrystallized to give the pure product. The filtrate was concentrated and diluted with ethyl acetate, washed with water and the aqueous layer containing the catalyst could be evaporated under reduced pressure to give a white solid, which could be reused without losing catalytic activity.

Ethyl 2-methyl-5-oxo-4-phenyl-4,5-dihydro-1H-indeno[1,2-b]pyridine-3-carboxylate (5a)

m.p: 271-272^{0}C, yield: 97%, FTIR(neat) ν=3273, 1698, 1634 cm^{-1}; ^{1}H NMR (500 Mz, $CDCl_3$), δ=1.06 (t, J=7.32 Hz, 3H), 1.50 (s, 3H), 3.98 (q, J=7.02 Hz, 2H), 4.94 (s, 1H), 6.65 (s, NH), 6.98 (d, J=7.18 Hz, 2H), 7.04 (d, J= 7.32 Hz, 2H), 7.29 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ=13.98, 19.01, 36.02, 58.83, 104.98, 122.21, 125.83, 128.54, 129.40, 134.81, 136.51, 142.24, 156.87, 166.28, 194.48 ppm; Ms (m/z): 345; Anal. Calcd. for $C_{22}H_{19}NO_3$= C: 76.50%; H:5.54%; N:4.06%. Found: C:76.59%; H:5.57%; N:4.04%.

Ethyl 2-methyl-5-oxo-4-(4-nitrophenyl)-4,5-dihydro-1H-indeno[1,2-b]pyridine-3-carboxylate (5b)

m.p: 216-217^{0}C; yield: 98%; FTIR(neat) ν=3285, 1701, 1634 cm^{-1}; ^{1}H NMR (500 Mz, $CDCl_3$), δ=1.20 (t, J=7.03 Hz, 3H), 2.49 (s, 3H), 3.98 (q, J=7.11 Hz, 2H), 5.21 (s, 1H), 6.39 (s, NH), 7.03 (d, J=7.21 Hz,1H), 7.22 (d, J=7.26 Hz, 1H), 7.26 (m, 1H), 7.29-7.59 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ=13.18, 18.53, 36.02, 58.83, 102.75, 104.98, 121.82, 122.21, 128.54, 145.24, 151.21, 167.21, 191.55 ppm; Ms (m/z): 390; Anal. Calcd. for $C_{22}H_{18}N_2O_5$= C:67.69%; H:4.65%; N:7.18%. Found: C:67.65%; H:4.60%; N:7.17%.

Ethyl 4-(4-bromophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-indeno[1,2-b]pyridine-3-carboxylate (5c)

m.p: 175-176^{0}C; yield: 97%; FTIR(neat) ν=3281, 1700, 1635 cm^{-1}; ^{1}H NMR (500 Mz, $CDCl_3$), δ=1.18 (t, J=7.10 Hz, 3H), 2.43 (s, 3H), 3.99 (q, J=7.31 Hz, 2H), 4.90 (s, 1H) 6.70 (s, NH), 6.99 (d, J=6.34 Hz, 2H), 7.14 (d, J=7.2 Hz, 2H), 7.19-7.30 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ=13.18, 18.53, 36.02, 56.41, 105.12, 112.22, 128.54, 129.68, 131.60, 134.51, 142.41, 146.81, 166.13, 192.41 ppm; Ms(m/z): 424; Anal. Calcd. for $C_{22}H_{20}BrNO_3$= C:62.28%; H:4.28%; N:3.30%. Found: C:62.22%; H:4.27%; N:3.29%.

Ethyl 4-(4-methoxyphenyl)-2-methyl-5-oxo-4,5-dihydro-1H-indeno[1,2-b]pyridine-3-carboxylate (5d)

m.p: 213-214^{0}C; yield: 94%; FTIR(neat) ν=3266, 1698, 1635 cm^{-1}, ^{1}H NMR (500 Mz, $CDCl_3$), δ=1.08 (t, J=7.8 Hz, 3H), 2.43 (s, 3H), 3.68 (s, 3H), 3.98 (q, J=7.01Hz, 2H), 4.88 (s, 1H), 6.34 (s, NH), 6.96 (d, J=7.32 Hz, 2H), 7.13 (t, J=6.78 Hz, 2H), 7.14-7.30 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ=13.98, 16.53, 41.20, 58.83, 101.96, 121.82, 126.70, 128.54, 134.30, 135.91, 139.41, 142.24, 145.88, 149.90, 156.87, 166.28, 192.48 ppm; Ms(m/z): 375; Anal. Calcd. for $C_{23}H_{21}NO_4$= C:73.58%; H:5.64%; N:3.73%. Found: C:73.55%; H:5.60%; N:3.75%.

Ethyl 4-(3-phenoxyphenyl)-2-methyl-5-oxo-4,5-dihydro-1H-indeno[1,2-b]pyridine-3-carboxylate (5e)

m.p: 198-199^{0}C; yield: 95%; FTIR(neat) ν=3275, 1698, 1634 cm^{-1}; ^{1}H NMR (500 Mz, $CDCl_3$), δ=1.03 (t, J=7.08 Hz, 3H), 2.40 (s, 3H), 3.97 (q, J=7.00 Hz, 2H), 4.92 (s, 1H), 6.66 (s, NH) 6.86-7.31 (m, 13H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz), δ=14.26, 16.41, 45.71, 62.70, 102.98, 103.03, 127.20, 128.56, 134.50, 135.90, 142.24, 156.87 ppm; Ms(m/z): 437. Anal. Calcd. for $C_{28}H_{23}NO_4$= C:76.87%; H:5.30%; N:3.20%. Found: C:76.82%; H:5.26%; N:3.22%.

Ethyl 4-(3,5-bis(trifluoromethyl)phenyl)-5-oxo-4,5-dihydro-1H-indeno[1,2-b]pyridine-3-carb-oxylate (5f)

m.p: 240-241^{0}C; yield: 87%; FTIR(neat) ν=3274, 1697, 1633 cm^{-1}; ^{1}H NMR (500 Mz, DMSO-d_6), δ=1.09 (t, J=7.01 Hz, 3H), 2.47 (s, 3H), 3.92 (q, J=7.01Hz, 2H), 5.01 (s, 1H), 6.41 (s, NH), 7.24 (d, J=6.83 Hz, 1H), 7.34 (t, J=7.32 Hz, 1H), 7.45 (t, J=7.60 Hz, 1H), 7.62 (d, J=7.32 Hz, 1H), 7.82 (s, 2H), 7.88 (s, 1H) ppm; ^{13}C NMR (DMSO, 100 MHz), δ=14.24, 19.38, 40.85, 60.16, 105.35, 107.55, 120.79, 121.34, 127.29, 130.86, 133.81, 136.41, 147.58, 150,37, 166.79, 191.40 ppm; Ms(m/z): 481; Anal. Calcd. for $C_{24}H_{17}F_6NO_3$= C:59.88%; H:3.56%; N:2.91%. Found: C: 59.91%; H:3.58%; N:2.90.

Ethyl 4-(5-bromo-2-furyl)-2-methyl-5-oxo-4,5-dihydro-1H-indeno[1,2-b]pyridine-3-carboxy-late (5g)

m.p: 207-208^{0}C, yield: 92%, FTIR(neat) ν=3275, 1689, 1634 cm^{-1}, ^{1}H NMR (500 Mz, DMSO-d_6), δ=1.14 (t, J=7.27 Hz, 3H), 2.48 (s, 3H), 4.07 (q, J=7.2 Hz, 2H), 4.88 (s, 1H), 6.04 (s, NH), 6.36 (d, J=7.44 Hz, 2H), 7.28-7.59 (m, 4H, 4H) ppm. ^{13}C NMR (DMSO, 100 MHz), δ=14.71, 19.23, 31.59, 60.24, 104.15, 108.86, 113.13, 119.55, 130.98, 132.49, 136.60, 146.32, 155,31, 160.68, 191.24 ppm; Ms(m/z): 414; Anal. Calcd. for $C_{20}H_{16}BrNO_4$= C: 57.99% ; H:3.89% ; N:3.38%. Found: C: 57.96% ; H:3.90% ; N:3.38%.

Ethyl 4-(5-iodo-2-furyl)-2-methyl-5-oxo-4,5-dihydro-1H-indeno[1,2-b]pyridine-3-carboxylate (5h)

m.p: 192-193^{0}C, yield: 88%, FTIR(neat) ν=3273, 1694, 1634 cm^{-1}, ^{1}H NMR (500 Mz, DMSO-d_6), δ=1.11 (t, J=7.68 Hz, 3H), 2.47 (s, 3H), 4.01 (q, J=6.78 Hz, 2H), 4.89 (s, 1H), 6.25 (s, NH), 6.35 (d, J=7.26 Hz, 1H), 6.05 (d, 1H), 7.31-7.76 (m, 4H) ppm. ^{13}C NMR (DMSO, 100 MHz), δ=14.21, 19.41, 31.01, 61.71, 102.79, 109.11, 111.81, 117.91, 128.51, 135.12, 147.81, 161.70, 191.41 ppm; Ms(m/z): 414; Anal. Calcd. for $C_{20}H_{16}INO_4$= C: 52.08%; H:3.50%; N:3.04%. Found: C:52.05%; H:3.48%; N:3.02%.

Conclusion

In conclusion, we have successfully developed an easy and efficient method to prepare a variety of 1*H*-indeno[1,2-*b*] pyridines from the reaction of different aryl aldehydes, 1,3-indandione, ethyl acetoacetate and ammonium acetate in the presence of catalytic amount of triflate under ultrasonic irradiation at room temperature. The catalytic activity of triflate is remarkable compared to the use of many low cost other agents. Commercially available triflate as catalyst for the synthesis of substituted dihydro-1*H*-indeno[1,2-*b*] pyridines in excellent yields is also significant under the aspect of environmentally benign processes. The advantages can be highlighted as shorter reaction times, milder conditions, simplicity of the reaction, excellent product yields, the use of relatively non-toxic reagents and solvents, reusability of the catalyst and commercially available triflate as a power catalyst for the synthesis of substituted dihydro-1*H*-indeno[1,2-*b*] pyridines.

The present procedure of the synthesis of these compounds under ultrasound irradiation with

solvent and catalyst at room temperature improved the Hantzsch reaction, which has many obvious advantages including mild conditions, higher yields, short reaction times, easy work-up and being less toxic. We feel the method will find important applications for the synthesis of indenopyridines [48-50].

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