Indian Journal of Advances in Chemical Science

Article

Ferric Dodecyl Sulfonate Catalyzed Facile Synthesis of Tetrahydro-β-Carboline Derivatives

K. Narasimha Reddy[1,2], S. Ramanaiah[1], N. Ananda Kumar Reddy[1,2]*

[1]Department of Chemistry, Rayalaseema University, Kurnool, Andhra Pradesh, India, [2]Department of Chemistry, Srihari Degree and PG College, Kadapa, Andhra Pradesh, India

ABSTRACT

Ferric dodecyl sulfonate (FDS) [$Fe(DS)_3$], a Lewis acid-surfactant-combined catalyst has been successfully used for the synthesis of a library of tetrahydro-β-carbolines (THBCs) through Pictet–Spengler reaction under conventional heating reaction conditions in aqueous medium. The merit of this protocol is the formation of FDS micellar spheres in water, the ability of each individual sphere to host the substrates to react easily, and efficiently to form the products in short reaction times. Hence, the reaction of tryptamine with various aldehydes has been facilitated the formation of desired THBCs in good yields. The aqueous reaction medium, dual (hydrophilic and hydrophobic) behavior of FDS catalyst, high yields of products, and short reaction times had established this as an eco-friendly and economical protocol for the synthesis of THBCs.

Key words: Pictet–Spengler reaction, Ferric dodecyl sulfonate, Aqueous medium, Micellar sphere, Tetrahydro-β-carbolines.

1. INTRODUCTION

A broad spectrum of medicinal applications of naturally occurring as well as synthesized tetrahydro-β-carboline (THBC) ring systems has been fascinating the attention of the researchers in this field [1]. This spectrum encompasses the antibacterial [2-3], antimalarial [4-6], antitumor [7-10], and anti-HIV [11-13] depending on substitutions and functionalization present on the C-1 carbon of the concerned THBCs [14]. Even though Pictet–Spengler (PS) and Bischler–Napieralski reactions are available for the traditional synthesis of THBCs, PS reaction is the most captivating method for the synthesis of THBC ring that is a part of many natural products and drug molecules [15].

Since the discovery of PS reaction in 1911, by the chemists, Ame Pictet and Theodor Spengler, different reaction protocols with various conditions have been reported. Some examples of conventional and non-conventional acid catalysts utilized for the synthesis of THBCs through PS reaction are H_2SO_4 [16], HCl [17], HCO_2H [18], AcOH [19], chloroacetic acid [20], TFA [21], Triflic acid [22], glyoxylic acid [23], benzoic acid [24], *p*-toluenesulfonic acid [25], benzenedisulfonimide [26], *D*-camphorsulfonic acid [27], and polyphosphoric acid [28]. Similarly, few Lewis acids such as titanium(IV) isopropoxide [29], trimethylsilyl chloride [30], BF_3-OEt_2 [31], $InBr_3$ [32], $ZnCl_2$ [33], $SnCl_4$ [34], $AlCl_3$ [35], [bmim]Cl-$AlCl_3$ [36], $AuCl_3$-AgOTf [37], Ytterbium(III) trifluoromethanesulfonate [$Yb(OTf)_3$] [38], $Sc(OTf)_3$ [39], $In(OTf)_3$ [40], $Sm(OTf)_3$ [41], and $Y(OTf)_3$ [42] have been reported as catalysts for the PS reaction.

Other catalysts such as deep eutectic solvent of choline chloride-urea [43], cyanuric chloride [44], AcCl [45], $SOCl_2$/MeOH [46], trifluoroacetic anhydride [47], and molecular iodine as homogeneous catalyst [48] were also used for this PS reaction. Even though these are prompt with short reaction times and good yields, they are having some disadvantages. Hence, the identification of an eco-friendly and cost-effective catalyst is of current interest for this PS reaction.

In extension of our efforts in the development of some biologically important compounds by greener methods, we report here a highly efficient procedure for the synthesis of THBCs in good yields by the condensation of tryptamine and aldehydes through ferric dodecyl sulfonate (FDS), $Fe[DS]_3$ (FDS) in catalytic amount in aqueous media under conventional heating. In the current organic chemistry research, it will be a good credential as the surfactants have identified as catalysts due to their inherent properties such as rapid dissolution, non-denaturing, chemical stability in the presence of dilute acids, bases, and salts, low aquatic toxicity, and readily biodegradable.

FDS is one of the most commonly used surfactants used as solubilizer for liquid membranes, an emulsifier, wetting agent, depressant, and complexing agent in both aqueous and non-aqueous media. In previous, it is used for the synthesis of bis(indolyl)methanes from indoles [49], bis-indolyl, tris-indolyl, di(bis-indolyl), tri(bis-indolyl), tetra(bis-indolyl) methanes, and 3-alkylated indoles [50], quinoxalines from 1,2-diketones and 1,2-diamino compounds [51], chromeno[4,3-*b*]chromene derivatives from cyclohexane-1,3-dione, 4-hydroxycoumarin, and benzaldehydes [52], and catalytic oxidation of benzene to phenol from the reaction of hydrogen peroxide [53]. To the best of our knowledge, this is the first report on the FDS catalyzed synthesis of THBCs from PS reaction.

***Corresponding author:**
E-mail: drnakreddysvdc@gmail.com

ISSN NO: 2320-0898 (p); 2320-0928 (e)
DOI: 10.22607/IJACS.2019.702003

Received: 29th March 2019;
Revised: 11th April 2019;
Accepted: 17th April 2019

2. EXPERIMENTAL

2.1. General

All the reagents and solvents were purchased from Sigma-Aldrich and were used for the purpose. Double distilled water generated in the laboratory was used as solvent in the reactions; heating reactions were performed on Remi heating stirrers. Melting points were determined in open capillaries using Guna melting point apparatus. The infrared (IR) spectra were recorded on Bruker Fourier transform IR spectrometer with single reflection sampling module and the absorptions were reported in wavenumbers (cm^{-1}). Nuclear magnetic resonance (NMR) spectra were recorded on Bruker 500 MHZ NMR spectrometer operating at 500 MHZ for ^1H NMR and 125 MHZ for ^{13}C NMR by recording in $CDCl_3$ and referenced to TMS (^1H and ^{13}C). Mass spectra were recorded on a JEOL GCMATE II GC-MS spectrophotometer at SAIF, IIT Chennai. Elemental analysis for C, H, and N elements was performed on a Thermo Finnigan Instrument. All solvents used for chromatographic, spectroscopic, and other physical studies were reagent grade and used in the study.

2.2. Synthetic Procedure for the Synthesis of THBC Derivatives (4a-j)

Tryptamine (**1,** 1mmol) and aldehydes (**2a-j,** 1mmol) with 5 mol% of FDS **(3)** in 10 mL of double distilled water were heated at 75°C in a round bottomed flask on a magnetic stirrer for a period of 1–2 h until completion of the reaction, as monitored by thin-layer chromatography. After completion of the reaction, contents were extracted into ethyl acetate and the portion was dried over anhydrous sodium sulfate, filtered and the filtrate was evaporated under reduced pressure. The crude product was collected, purified by column chromatography on silica gel as absorbent with ethyl acetate and hexane (1:2) as an eluent to get pure products (Scheme 1). Tryptamine **(1)** reacts well with aryl aldehydes **(2a-j)** having both electron-donating and electron-withdrawing substituents to furnish THBCs **(4a-j)**. FDS is proved to be effective in catalyzing the 6-endo cyclization of aldehydes such as salicylaldehyde (**2b**), 4-bromo benzaldehyde (**2h**), and 4-dimethyl amino benzaldehyde (**2j**) under conventional heating, where these are failed by Bronsted acids. This disadvantage has been overcome by FDS catalyst. Further, these synthesized compounds **(4a-j)** were characterized by spectral and elemental analysis and provided in the following sections.

2.3. Spectral and Elemental Characterization Data of THBC Derivatives (4a-j)

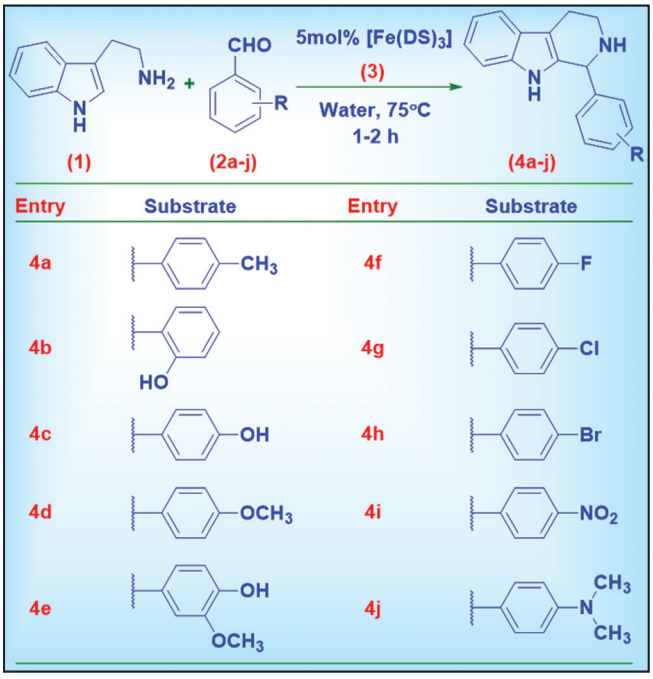
1-(p-Tolyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (4a): Yield: 93%; Pale yellow solid; m.p.: 135–137°C; IR (ZnSe): 3347 (NH), 2936 (CH) cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$): δ 12.24 (s, 1H), 7.56–7.51 (m, 2H), 7.45–7.39 (m, 3H), 7.34–7.22 (m, 3H), 5.39 (s, 1H), 3.40–3.37 (m, 2H), 3.23–3.20 (m, 2H), 2.43 (d, 2H), 2.26 (s, 1H), 1.94 (s,1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$,): δ 138.43, 137.55, 136.23, 134.14, 130.45, 129.36, 126.74, 122.85, 120.22, 116.45, 113.55, 108.41, 64.24, 51.16, 22.83, 21.53 ppm; LCMS m/z: 262 (M+); Anal. calculated for $C_{18}H_{18}N_2$ (%): C, 82.41; H, 6.92; N, 10.68; Found: C, 82.38; H, 6.89; N, 10.65.

2.4. 2-(2,3,4,9-Tetrahydro-1H-pyrido[3,4-b]indol-1-yl)phenol (4b)

Yield: 94%; Yellow solid; m.p.: 211–213°C; IR (ZnSe): 3357 (OH), 3276 (NH), 2945 (CH) cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$): δ 12.64 (s, 1H), 7.81–7.77 (m, 4H), 7.63 (s, 1H), 7.43 (s, 1H), 6.95 (s, 1H), 6.87 (s, 1H), 5.43 (s, 1H), 3.95 (s, 1H), 3.07–2.98 (m, 2H), 2.85–2.80 (m, 2H), 1.89 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$,): δ 158.46, 138.50, 134.66, 131.04, 130.44, 127.83, 126.33, 122.35, 120.25, 119.66, 118.84, 118.47, 111.55, 108.26, 56.64, 45.22, 20.82 ppm; LCMS m/z: 264 (M+); Anal. calculated for $C_{17}H_{16}N_2O$ (%): C, 77.25; H, 6.10; N, 10.06; Found: C, 77.24; H, 6.08; N, 10.05.

2.5. 4-(2,3,4,9-Tetrahydro-1H-pyrido[3,4-b]indol-1-yl)phenol (4c)

Yield: 92%; pale yellow solid; m.p.: 192–193°C; IR (ZnSe): 3382 (OH), 3317 (NH), 2927 (CH) cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$): δ 12.38 (s, 1H), 7.93 (d, 2H), 7.34 (d, 2H), 6.95–6.92 (m, 4H), 5.45 (s, 1H), 4.22 (s, 1H), 3.07–3.05 (m, 2H), 2.85–2.80 (m, 2H), 1.94 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$,): δ 153.36, 140.86, 136.54, 132.45, 130.66, 127.43, 121.34, 120.41, 118.47, 115.71, 110.29, 108.33, 60.14, 45.22, 22.09 ppm; LCMS m/z: 264 (M+); Anal. calculated for $C_{17}H_{16}N_2O$ (%): C, 77.25; H, 6.10; N, 10.60; Found: C, 77.24; H, 6.09; N, 10.56.



Scheme 1: Synthesis of ferric dodecyl sulfonate catalyzed tetrahydro-β-carboline derivatives.

2.6. 1-(4-Methoxyphenyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (4d)

Yield: 90%; pale yellow solid; m.p.: 204–205°C; IR (ZnSe): 3297 (NH), 2939 (CH) cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$): δ 12.44 (s, 1H), 8.12 (d, 2H), 7.53 (d, 2H), 6.93–7.34 (m, 4H), 5.42 (s, 1H), 3.88 (s, 3H), 3.35 (m, 1H), 3.06 (m, 1H), 2.63–2.86 (m, 2H), 1.97 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$,): δ 159.45, 136.53, 134.95, 132.29, 130.07, 127.56, 121.88, 120.52, 118.33, 113.97, 111.24, 109.17, 62.22, 55.99, 45.25, 22.09 ppm; LCMS m/z: 278 (M+); Anal. calculated for $C_{18}H_{18}N_2O$ (%): C, 77.67; H, 6.52; N, 10.06; Found: C, 77.66; H, 6.48; N, 10.05.

2.7. 2-Methoxy-4-(2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)phenol (4e)

Yield: 91%; yellow solid; m.p.: 185–187°C; IR (ZnSe): 3334 (NH), 2982 (CH) cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$): δ 12.38 (s, 1H), 7.85–7.80 (m, 3H), 7.66 (s, 1H), 7.45 (s, 1H), 7.26 (s, 1H), 7.03 (s, 1H), 5.25 (s, 1H), 4.26–4.22 (m,1H), 3.96 (s, 3H), 3.16–3.12 (m, 2H), 2.65–2.61 (m, 2H), 1.99 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$,): δ 156.43, 145.52, 138.48, 136.25, 133.33, 128.07, 121.86, 120.95, 119.16, 118.83, 117.34, 116.24, 112.38, 109.75, 62.25, 56.83, 43.42, 22.74 ppm; LCMS m/z: 294 (M+); Anal. calculated for $C_{18}H_{18}N_2O_2$ (%): C, 73.45; H, 6.16; N, 9.52; Found: C, 73.42; H, 6.15; N, 9.50.

2.8. 1-(4-Fluorophenyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (4f)

Yield: 93%; pale yellow liqid; m.p.: 138–140°C; IR (ZnSe): 3346 (NH), 2955 (CH) cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$): δ 12.43 (s, 1H), 7.49–7.42 (m, 4H), 7.25–7.20 (d, 2H), 6.83–6.81 (d, 2H), 5.85 (s, 1H), 3.41–3.38 (m, 2H), 2.85–2.83 (m, 2H), 1.77 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$,): δ 164.23, 141.31, 136.63, 134.26, 130.45, 128.22, 123.13, 121.90, 120.55, 118.88, 115.03, 114.33, 112.29, 110.09, 60.85, 45.93, 22.26 ppm; LCMS m/z: 266 (M+); Anal. calculated for $C_{17}H_{15}FN_2$ (%): C, 76.67; H, 5.68; N, 10.52; Found: C, 76.65; H, 5.67; N, 10.50.

2.9. 1-(4-Chlorophenyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (4g)

Yield: 91%; white solid; m.p.: 165–167°C; IR (ZnSe): 3297 (NH), 2973 (CH) cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$): δ 12.45 (s, 1H), 7.42–7.38 (m, 3H), 7.23–7.02 (m, 5H), 5.25 (s, 1H), 3.95–3.92 (m, 1H), 3.25–3.21 (m, 1H), 2.69–2.88 (m, 2H), 1.65 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$,): δ 139.28, 136.46, 136.28, 134.76, 129.23, 128.86, 127.55, 122.12, 121.96, 119.26, 118.94, 114.06, 111.14, 107.53, 62.03, 43.44, 26.82 ppm; LCMS m/z: 282 (M+); Anal. calculated for $C_{17}H_{15}ClN_2$ (%): C, 72.21; H, 5.35; N, 9.91; Found: C, 72.19; H, 5.34; N, 9.88.

2.10. 1-(4-Bromophenyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (4h)

Yield: 89%; yellow solid; m.p.: 227–229°C; IR (ZnSe): 3286 (NH), 2967 (CH) cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$): δ 12.35 (s, 1H), 7.55–7.50 (d, 2H), 7.48–7.36 (m, 4H), 7.24–7.19 (d, 2H), 5.54 (s, 1H), 3.25–3.20 (m, 2H), 2.88–2.85 (m, 2H), 1.73 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$,): δ 140.24, 137.03, 134.54, 132.63, 131.44, 129.83, 127.35, 126.90, 125.73, 122.85, 120.47, 119.03, 112.20, 109.81, 58.03, 46.35, 22.46 ppm; LCMS m/z: 326 (M+); Anal. calculated for $C_{17}H_{15}BrN_2$ (%): C, 62.40; H, 4.62; N, 8.56; Found: C, 62.38; H, 4.60; N, 8.55.

2.11. 1-(4-Nitrophenyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (4i)

Yield: 92%; yellow solid; m.p.: 174–175°C; IR (ZnSe): 3308 (NH), 2948 (CH) cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$): δ 12.28 (s, 1H), 8.33 (m, 2H), 7.54 (m, 2H), 7.36–7.33 (m, 4H), 5.45 (s, 1H), 3.45–3.39 (m, 2H), 2.93–2.88 (m, 2H), 1.96 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$,): δ 146.88, 145.46, 136.25, 134.16, 128.24, 123.52, 120.53, 118.92, 110.24, 109.63, 62.24, 46.43, 24.27 ppm; LCMS m/z: 293 (M+); Anal. calculated for $C_{17}H_{15}N_3O_2$ (%): C, 69.61; H, 5.15; N, 14.33; Found: C, 69.59; H, 5.13; N, 14.32.

2.12. N,N-Dimethyl-4-(2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)aniline (4j)

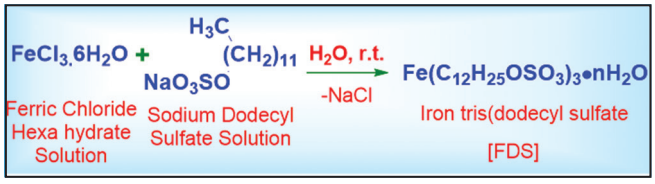
Yield: 92%; yellow solid; m.p.: 143–145°C; IR (ZnSe): 3356 (NH), 2923 (CH) cm^{-1}; ^{1}HNMR (500 MHz, $CDCl_3$): δ 12.38 (s, 1H), 7.77 (d, 2H), 7.24 (d, 2H), 6.85–6.83 (m, 4H), 5.67 (s, 1H), 3.43–3.40 (m, 2H), 3.27 (s, 6H), 2.73–2.70 (m, 2H), 2.03 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$,): δ 152.23, 138.63, 135.25, 132.05, 128.24, 127.88, 122.39, 120.41, 118.55 112.70, 111.45, 108.05, 60.23, 44.54, 40.04, 22.83 ppm; LCMS m/z: 291 (M+); Anal. calculated for $C_{19}H_{21}N_3$ (%): C, 78.32; H, 7.26; N, 14.42; Found: C, 78.29; H, 7.24; N, 14.40.

2.13. In Situ Preparation Procedure of FDS Catalyst

Effective stirring of sodium dodecyl sulfate (SDS) and ferric chloride solutions in 3:1 molar ratio at room temperature yields the desired FDS catalyst [5] (Scheme 2). This is a combined Lewis acid-surfactant catalyst (LASC) which exhibits both effects, namely, Lewis acidity of Fe^{3+} and surfactant effect of dodecyl sulfonyl group. This helps a lot to activate aldehyde molecule as a Lewis acid and increases the concentration of organic reactants to form micelles.

3. RESULTS AND DISCUSSION

The experimental parameters for the synthesis of THBCs **(4a-j)** from tryptamine **(1)** and various substituted benzaldehydes **(2a-j)** were optimized for the typical reaction of tryptamine **(1)** with 4-methyl benzaldehyde **(2a)** in terms of catalyst selection, catalyst concentration, and effective reaction temperature that are needed to accomplish the products in good yields.



Scheme 2: *In situ* preparation of ferric dodecyl sulfonate catalyst.

Table 1: Optimization of catalyst source for the synthesis of compound 4a.

Catalyst	Temperature (°C)	Reaction time (h)	Yield (%)
PBDP	90	14	82
Yb $(OTf)_3$	80	15	80
Triton X-100	85	16	84
DBSA	90	8	85
DDAB	90	9	83
PFOSA-BASC	80	5	89
FDS-LASC	75	2	93

FDS: Ferric dodecyl sulfonate, DBSA: Dodecylbenzene sulfonic acid, Yb $(OTf)_3$: Ytterbium (III) trifluoromethanesulfonate, PBDP: 10-(4-perfluorobutylsulfonaminosulfonyl phenyl) decylpolystyrene, DDAB: Didodecyl dimethyl-ammonium bromide, PFOSA-BASC: Perfluorooctanesulfonic acid-based Brønsted acid-surfactant-combined catalyst, LASC: Lewis acid-surfactant catalyst

3.1. Optimization of the Catalyst

Synthesis of **4a** has been taken as a model reaction to investigate the efficacy of some acid catalysts, surfactant catalysts, and surfactant-based catalysts and optimized the effective catalyst (Table 1). In such, we have investigated the activity of 10-(4-perfluorobutylsulfonaminosulfonyl phenyl) decylpolystyrene a polymer-supported sulfonimide which is a water-tolerant Brønsted acid catalyst, $[Yb(OTf)_3]$ a water-tolerant Lewis acid catalyst, Triton X-100 a non-ionic surfactant catalyst, dodecylbenzene sulfonic acid an anionic surfactant, didodecyl dimethyl-ammonium bromide a cationic surfactant, and perfluorooctanesulfonic acid-based Brønsted acid-surfactant-combined catalyst which is combined with SDS and FDS a combined LASC [FDS-LASC] in 10 mol%. The yields of compound **4a** obtained against selected catalysts are comparatively good, but FDS-LASC catalyst accomplished in high yield (93%). As this is a cost-effective, eco-friendly protocol with simple operating procedures, we have selected FDS-LASC as an effective catalyst for this methodology.

3.2. Optimization of Catalyst Concentration

Synthesis of **4a** loaded with various concentrations of FDS catalyst (**3**) operated at uniform reaction conditions has accomplished it in 81, 88, 93, 93, and 93% yields, respectively. It is noticed that 5 mol% of FDS catalyst is effective in producing **4a** in 93% yield and higher concentrations have not shown any effect (Table 2).

3.3. Optimization of Reaction Temperature

Synthesis of **4a** varying at different temperatures in the range of 60–90°C with 5°C variation has accomplished in 69, 80, 88, 93, 93, 93, and 93% yields (**Table 3**). From the results, we have identified the effective temperature (75°C) had produced **4a** with 93% yield and there is no increment in the yield beyond 75°C as the yield remained unaltered.

Table 2: Catalyst concentration optimization studies 4a.

Catalyst (mol%)	Time (h)	Yield (%)
1.0	5	81
2.5	4	88
5.0	2	93
7.5	2	93
10.0	2	93

Table 3: Temperature optimization studies.

Temperature (°C)	Time (h)	Yield (%)
60	4	69
65	4	80
70	4	88
75	2	93
80	3	93
85	3	93
90	4	93

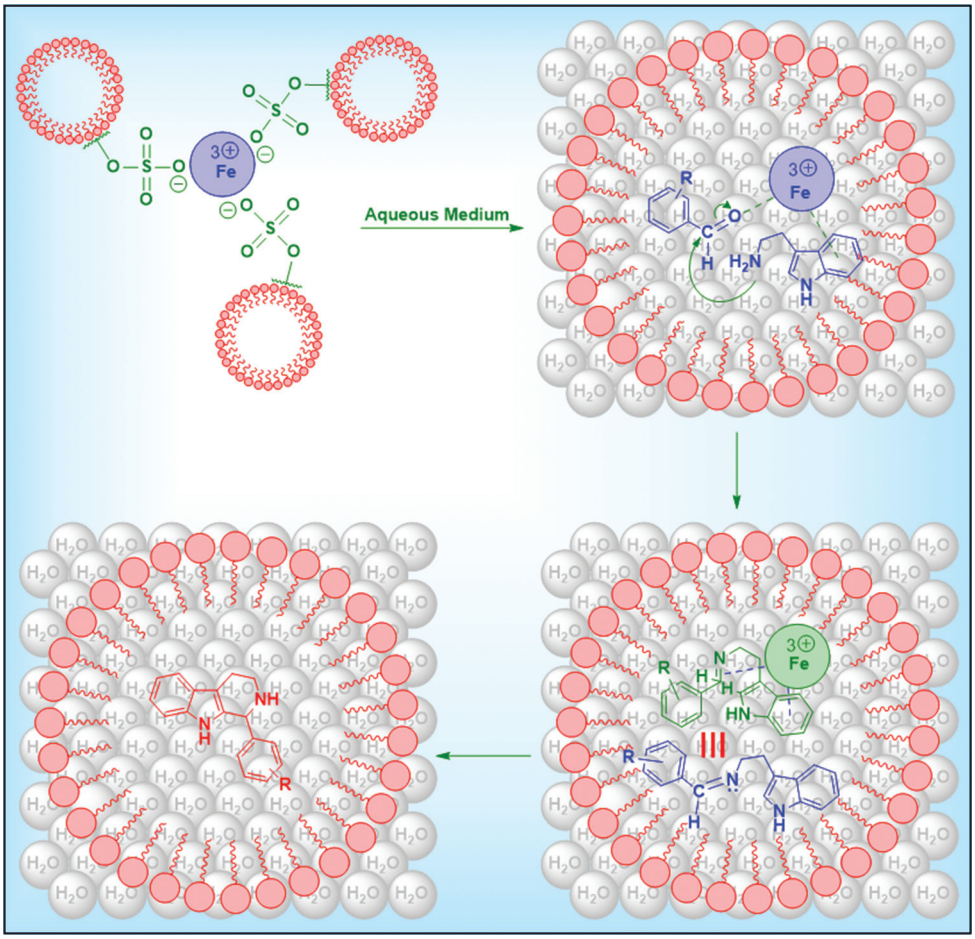


Figure 1: Mechanistic approach for ferric dodecyl sulfonate-mediated synthesis of tetrahydro-*β*-carboline derivatives.

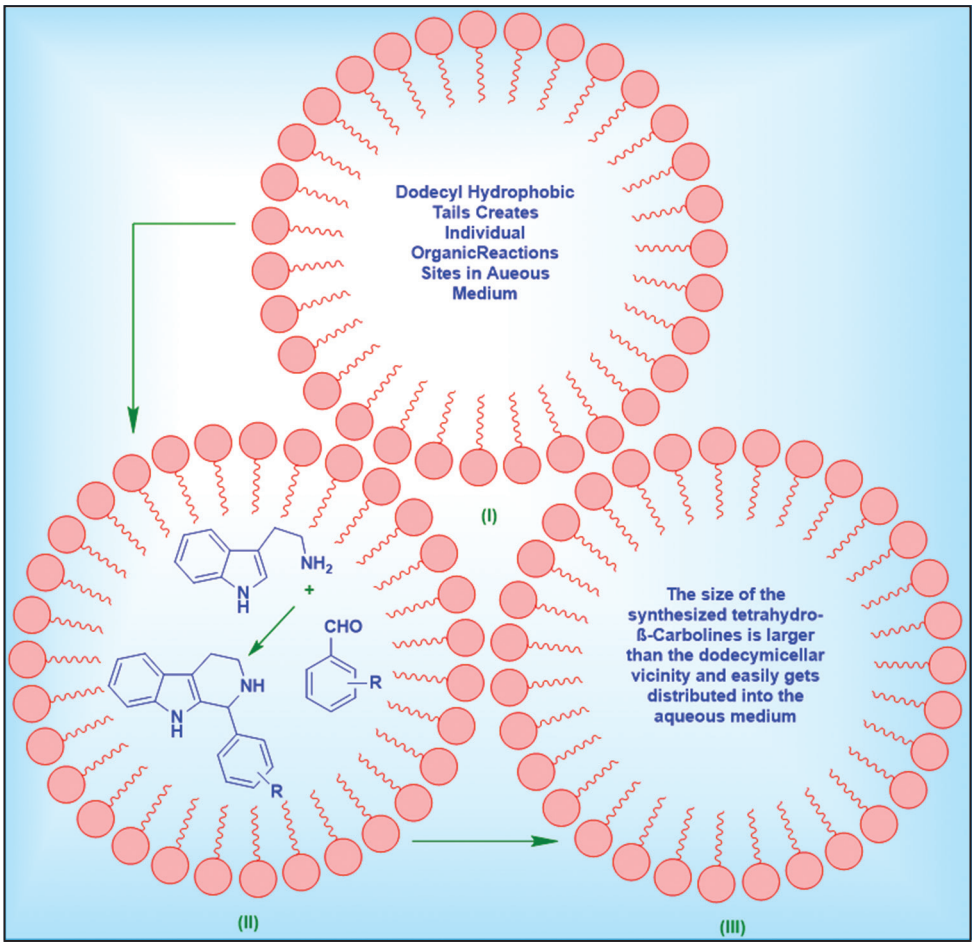


Figure 2: Surfactant and Lewis acidic strategy of ferric dodecyl sulfonate catalyst in the synthesis of tetrahydro-*β*-carbolines.

3.4. Mechanistic Action of FDS Catalyst

In PS reaction, tryptamine condenses with aldehyde to afford corresponding imine, which further on 6-*endo* cyclization by C-2 attack of imine accomplishes the THBC. Here, the Fe^{3+} ion (Lewis acidic) electronically binds with carbonyl oxygen and promotes the condensation reaction with tryptamine to form an imine. Similarly, the imine gets activated through binding with Fe^{3+} ion and promotes the 6-*endo* cyclization by donating its π-electrons and subsequent hydrogen ion migration fulfills the formation of THBC (Figure 1).

3.5. Catalytic Activity of FDS Catalyst

Here, the dual nature of FDS catalyst, namely, surfactant activity and Lewis acidity makes it to gets hydrolyzed and the ferric ions get hydrated and then binds with carbonyl oxygen (aldehyde) as well as with the electron density (tryptophan ring) and enables the system to enter into the micellar sphere next (Figure 2). Here, the substrates get reacted faster than the uncatalyzed reaction, as the micellar spheres create an independent environment to them to react and form the product by eliminating other possibilities such as backward reaction, formation of unnecessary by-products, and retaining of unreacted intermediates.

4. CONCLUSION

This is the first report on the eco-friendly synthesis of THBCs obtained by catalytic action of FDS. The merit of this protocol is the formation of FDS micellar spheres under conventional heating and to host the reactant aggregates to react and form the product, whose size is larger than the micellar size to get transferred from micellar vicinity to aqueous system after its immediate formation. Hence, this protocol with FDS-LASC catalytic activity for PS reaction has a beneficial with short reaction times, good yields and categorized as an environment benevolent one.

6. REFERENCES

1. R. N. Rao, B. Maiti, K. Chanda, (2017) Application of Pictet-Spengler reaction to indole-based alkaloids containing tetrahydro-*β*-carboline scaffold in combinatorial chemistry, ***ACS Combinatorial Science***, **19:** 199-228.
2. R. B. Volk, F. H. Furkert, (2006) Antialgal, anti-bacterial and antifungal activity of two metabolites produced and excreted by cyanobacteria during growth, ***Microbiological Research*****, 161:** 180-186.
3. H. J. Shin, H. S. Lee, D. S. Lee, (2010) The synergistic antibacterial activity of 1-acetyl-*β*-carboline and *β*-lactams against Methicillin-resistant *Staphylococcus aureus* (MRSA), ***Journal of Microbiology and Biotechnology*****, 20:** 501-505.
4. Y. Boursereau, I. Coldham, (2004) Synthesis and biological studies of 1-amino *β*-carbolines, ***Bioorganic and Medicinal Chemistry Letters*****, 14:** 5841-5844.
5. A. G. Shilabin, N. Kasanah, B. L. Tekwani, M. T. Hamann, (2008) Kinetic studies and bioactivity of potential manzamine prodrugs, ***Journal of Natural Products,*** **71(7)**: 1218-1221.
6. J. D. Winkler, A. T. Londregan, M. T. Hamann, (2006) Antimalarial activity of a new family of analogues of manzamine A, ***Organic Letters*****, 8:** 2591-2594.

7. A. Kamal, V. Srinivasulu, V. L. Nayak, M. Sathish, N. Shankaraiah, C. Bagul, N. V. S. Reddy, N. Rangaraj, N. Nagesh, (2014) Design and synthesis of C_3-pyrazole/chalcone-linked β-carboline hybrids: Antitopoisomerase I, DNA- interactive, and apoptosis-inducing anticancer agents, ***ChemMedChem*, 9:** 2084-2098.
8. M. A. Rashid, K. R. Gustafson, M. R. Boyd, (2001) New cytotoxic N-methylated β-carboline alkaloids from the marine Ascidian *Eudistoma gilboverde*, ***Journal of Natural Products*, 64:** 1454-1456.
9. M. R. Prinsep, J. W. Blunt, M. H. G. Munro, (1991) New cytotoxic β-carboline alkaloids from the marine Bryozoan, *Cribricellina cribraria*, ***Journal of Natural Products*, 54:** 1068-1076.
10. H. Guan, H. Chen, W. Peng, Y. Ma, R. Cao, X. Liu, A. Xu, (2006) Design of β-carboline derivatives as DNA-targeting antitumor agents, ***European Journal of Medicinal Chemistry*, 41:** 1167-1179.
11. X. Yu, W. Lin, J. Li, M. Yang, (2004) Synthesis and biological evaluation of novel β-carboline derivatives as Tat–TAR interaction inhibitors, ***Bioorganic and Medicinal Chemistry Letters*, 14:** 3127-3130.
12. J. G. Tang, Y. H. Wang, R. R. Wang, Z. J. Dong, L. M. Yang, Y. T. Zheng, J. K. Liu, (2008) Synthesis of analogues of flazin, in particular, flazinamide, as promising anti-HIV agents, ***Chemistry and Biodiversity*, 5:** 447-460.
13. Y. H. Wang, J. G. Tang, R. R. Wang, L. M. Yang, Z. J. Dong, L. Du, X. Shen, J. K. Liu, Y. T. Zheng, (2007) Flazinamide, a novel β-carboline compound with anti-HIV actions, ***Biochemical and Biophysical Research Communications*, 355:** 1091-1095.
14. G. C. Muscia, L. O. D. María, G. Y. Buldain, S. E. Asís, (2016) Ultrasound assisted Pictet–Spengler synthesis of tetrahydro-β-carboline derivatives, ***Journal of Heterocyclic Chemistry*, 53(2)**: 647-650.
15. P. Maity, D. Adhikari, A. K. Jana, (2019) An overview on synthetic entries to tetrahydro-β-carbolines, ***Tetrahedron*, 75:** 965-1028.
16. J. Wu, D. Talwar, S. Johnston, M. Yan, J. Xiao, (2013) Acceptorless dehydrogenation of nitrogen heterocycles with a versatile iridium catalyst, ***Angewandte Chemie International Edition*, 52:** 6983-6987.
17. R. Megyesi, A. Mándi, T. Kurtán, E. Forró, F. Fülöp, (2017) Dynamic kinetic resolution of ethyl 1,2,3,4-tetrahydro-β-carboline-1-carb-oxylate: Use of different hydrolases for stereocomplementary processes, ***European Journal of Organic Chemistry*, 2017:** 4713-4718.
18. T. L. Ho, C. Y. Su, (2001) A synthetic approach to tacamonine. Access to 3-epitacamonine and 14-epitacamonine, ***Tetrahedron*, 57:** 507-510.
19. A. Kamal, M. Sathish, A. V. G. Prasanthi, J. Chetna, Y. Tangella, V. Srinivasulu, N. Shankaraiah, A. Alarifi, (2015) An efficient one-pot decarboxylative aromatization of tetrahydro-β-carbolines by using N-chlorosuccinimide: Total synthesis of norharmane, harmane and eudistomins, ***RSC Advances*, 5:** 90121-90126.
20. S. Samundeeswari, B. Chougala, M. Holiyachi, L. Shastri, M. Kulkarni, S. Dodamani, S. Jalalpur, S. Joshi, S. Dixit, V. Sunagar, R. Hunnur, (2017) Design and synthesis of novel phenyl -1, 4-beta-carboline-hybrid molecules as potential anticancer agents, ***European Journal of Medicinal Chemistry*, 128:** 123-139.
21. K. R. Prasad, J. E. Nidhiry, (2012) Total synthesis of (+)-Eburnamonine, ***Synlett*, 23:** 1477-1480.
22. R. S. Rao, C. R. Ramanathan, (2017) Brønsted acid-mediated cyclization-dehydrosulfonylation/reduction sequences: An easy access to pyrazinoisoquinolines and pyridopyrazines, ***Beilstein Journal of Organic Chemistry*, 13:** 428-440.
23. S. M. Chang, W. Christian, M. H. Wu, T. L. Chen, Y. W. Lin, C. S. Suen, H. B. Pidugu, D. Detroja, A. Shah, M. J. Hwang, T. L. Su, T. C. Lee, (2017) Novel indolizino[8,7-b]indole hybrids as anti-small cell lung cancer agents: Regioselective modulation of topoisomerase II inhibitory and DNA crosslinking activities, ***European Journal of Medicinal Chemistry*, 127:** 235-249.
24. L. Li, P. Aibibula, Q. Jia, Y. Jia, (2017) Total syntheses of naucleamides A-C and E, geissoschizine, geissoschizol, (E)-isositsirikine, and 16-epi-(E)-isositsirikine, ***Organic Letters*, 19:** 2642-2645.
25. J. Kovvuri, B. Nagaraju, V. L. Nayak, R. Akunuri, M. P. N. Rao, A. Ajitha, N. Nagesh, A. Kamal, (2018) Design, synthesis and biological evaluation of new β-carboline-bisindole compounds as DNA binding, photocleavage agents and topoisomerase I inhibitors, ***European Journal of Medicinal Chemistry*, 143:** 1563-1577.
26. M. Barbero, S. Bazzi, S. Cadamuro, S. Dughera, (2010) o-Benzenedisulfonimide as a reusable acid catalyst for an easy, efficient, and green synthesis of tetrahydroisoquinolines and tetrahydro-β-carbolines through Pictet-Spengler reaction, ***Tetrahedron Letters*, 51:** 6356-6359.
27. O. I. Shmatova, V. N. Khrustalev, V. G. Nenajdenko, (2016) From cyclic CF_3-ketimines to a family of trifluoromethylated nazlinine and trypargine analogues, ***Organic Letters*, 18:** 4494-4497.
28. M. Amat, O. Lozano, C. Escolano, E. Molins, J. Bosch, (2007) Enantioselective synthesis of 3,3-disubstituted piperidine derivatives by enolate dialkylation of phenylglycinol-derived oxazolopiperidone lactams, ***The Journal of Organic Chemistry*, 72:** 4431-4439.
29. X. Zhang, W. Jiang, Z. Sui, (2003) Concise enantioselective syntheses of quinolactacins A and B through alternative winterfeldt oxidation, ***The Journal of Organic Chemistry*, 68:** 4523-4526.
30. R. S. Kusurkar, N. A. H. Alkobati, A. S. Gokule, V. G. Puranik, (2008) Use of the Pictet–Spengler reaction for the synthesis of 1,4-disubstituted-1,2,3,4-tetrahydro-β-carbolines and 1,4-disubstituted-β-carbolines: Formation of γ-carbolines, ***Tetrahedron*, 64:** 1654-1662.
31. S. Ahmad, L. Shukla, J. Szawkało, P. Roszkowski, J. K. Maurin, Z. Czarnocki, (2017) Synthesis of novel chiral guanidine catalyst and its application in the asymmetric Pictet-Spengler reaction, ***Catalysis Communications*, 89:** 44-47.
32. M. Agnusdei, M. Bandini, A. Melloni, A. U. Ronchi, (2003) New versatile route to the synthesis of tetrahydro-β-carbolines and tetrahydro-pyrano[3,4-b]indoles via an intramolecular Michael addition catalyzed by $InBr_3$, ***The Journal of Organic Chemistry*, 68:** 7126-7129.
33. J. Sun, L. L. Zhang, C. G. Yan, (2013) Facile construction of 1,2,6,7,12,12*b*-hexahydroindolo [2,3-*a*]quinolizines via one-pot three-component reactions of tryptamines, propiolate, and α,β-unsaturated aromatic aldehydes or ketones, ***Tetrahedron*, 69:** 5451-5459.
34. C. C. Silveira, L. A. Felix, A. L. Braga, T. S. Kaufman, (2005) 1-Substituted β-carbolines by a Pictet-Spengler cyclization with thioortho esters and carbon-carbon bond formation via *N*-sulfonyl iminium ions generated from *N*,*S*-sulfonyl acetals, ***Organic Letters*, 7:** 3701-3704.
35. H. Heaney, M. O. Taha, (2000) *N*-Acyliminium ion cyclisation versus rearrangement. The synthesis of 13,13-dimethylberberines and 3,4-dimethylisoquinolin-1-ones, ***Tetrahedron Letters*,**

41: 1993-1996.
36. A. Danda, K. Kumar, H. Waldmann, (2015) A general catalytic reaction sequence to access alkaloid-inspired indole polycycles, ***Chemical Communications*****, 51:** 7536-7539.
37. S. W. Youn, (2006) Development of the Pictet-Spengler reaction catalyzed by $AuCl_3$/AgOTf, ***The Journal of Organic Chemistry*****, 71:** 2521-2523.
38. C. Bathula, P. Dangi, S. Hati, R. Agarwal, P. Munshi, A. Singh, S. Singh, S. Sen, (2015) Diverse synthesis of natural product inspired fused and spiro-heterocyclic scaffolds via ring distortion and ring construction strategies, ***New Journal of Chemistry*****, 39:** 9281-9292.
39. C. Gremmen, B. Willemse, M. J. Wanner, G. J. Koomen, (2000) Enantiopure tetrahydro-*β*-carbolines via Pictet-Spengler reactions with *N*-sulfinyl tryptamines, ***Organic Letters*****, 2:** 1955-1958.
40. N. Devi, D. Singh, Honey, S. Mor, S. Chaudhary, R. K. Rawal, V. Kumar, A. K. Chowdhury, V. Singh, (2016) $In(OTf)_3$ catalysed an expeditious synthesis of *β*-carboline–imidazo[1,2-*a*]pyridine and imidazo[1,2-*a*]pyrazine conjugates, ***RSC Advances*****, 6:** 43881-43891.
41. N. Srinivasan, A. Ganesan, (2003) Highly efficient Lewis acid-catalysed Pictet-Spengler reactions discovered by parallel screening, ***Chemical Communications*****, 2003:** 916-917.
42. S. Wang, Z. Chai, S. Zhou, S. Wang, X. Zhu, Y. Wei, (2013) A novel Lewis acid catalyzed [3+3]-annulation strategy for the syntheses of tetrahydro-*β*-carbolines and tetrahydroiso-quinolines, ***Organic Letters,*** **15:** 2628-2631.
43. S. Handy, M. Wright, (2014) An acid-free Pictet-Spengler reaction using deep eutectic solvents (DES), ***Tetrahedron Letters,*** **55:** 3440-3442.
44. A. Sharma, M. Singh, N. N. Rai, D. Sawant, (2013) Mild and efficient cyanuric chloride catalyzed Pictet-Spengler reaction, ***Beilstein Journal of Organic Chemistry*****, 9:** 1235-1242.
45. M. S. Taylor, E. N. Jacobsen, (2004) Highly enantioselective catalytic acyl-Pictet-Spengler reactions, ***The Journal of American Chemical Society*****, 126:** 10558-10559.
46. S. Xiao, W. Lin, C. Wang, M. Yang, (2001) Synthesis and biological evaluation of DNA targeting flexible side-chain substituted *β*-carboline derivatives, ***Bioorganic and Medicinal Chemistry Letters*****, 11:** 437-441.
47. J. In, S. Hwang, C. Kim, J. H. Seo, S. Kim, (2013) Synthesis of 3,4-dihydroisoquinolin-1-ones from *N*-Boc-(*β*-arylethyl) carbamates via isocyanate intermediates, ***European Journal of Organic Chemistry,*** **2013:** 965-971.
48. R. Meesala, A. S. M. Arshad, M. N. Mordi, S. M. Mansor, (2016) Iodine-catalyzed one-pot decarboxylative aromatization of tetrahydro-*β*-carbolines, ***Tetrahedron,*** **72:** 8537-8541.
49. S. Y. Wang, S. J. Ji, (2008) Facile synthesis of bis(indolyl) methanes catalyzed by ferric dodecyl sulfonate $[Fe(DS)_3]$ in water at room temperature, ***Synthetic Communications,*** **38:** 1291-1298.
50. H. Veisi, B. Maleki, F. H. Eshbala, H. Veisi, R. Masti, S. S. Ashrafi, M. Baghayeri, (2014) *In situ* generation of iron(III) dodecyl sulfate as Lewis acid-surfactant catalyst for synthesis of bis-indolyl, tris-indolyl, Di(bis-indolyl), Tri(bis-indolyl), tetra(bis-indolyl)methanes and 3-alkylated indole compounds in water, ***RSC Advances*****, 4:** 30683-30688.
51. R. Singh, S. A. Ganaie, (2016) An efficient synthesis of quinaxoline derivatives using $Fe(DS)_3$ as a Lewis acid-surfactant-combined catalyst, ***Chemical Science Transactions*****, 5:** 603-610.
52. K. Pradhan, S. Paul, A. R. Das, (2013) $Fe(DS)_3$, an efficient Lewis acid-surfactant-combined catalyst (LASC) for the one pot synthesis of chromeno[4,3-*b*]chromene derivatives by assembling the basic building blocks, ***Tetrahedron Letters*****, 54:** 3105-3110.
53. J. Peng, F. Shi, Y. Gu, Y. Deng, (2003) Highly selective and green aqueous–ionic liquid biphasic hydroxylation of benzene to phenol with hydrogen peroxide, ***Green Chemistry*****, 5:** 224-226.

****Bibliographical Sketch***

Dr. N. Ananda Kumar Reddy is presently in-charge principal of Sri Venkateswara Degree College, Kadapa, India and has also been serving as Head, Department of Chemistry since a long-time. His research interests are Inorganic & Organic Chemistry fields, specifically use of some analytical reagents in the flotation of sulphide minerals and identification of new catalysts and development of new methodologies for the synthesis of heterocyclic compounds. To his credit he has published about 15 research papers and successfully completed two minor research projects funded by University Grants Commission (UGC), New Delhi, India. He has guided two research scholars and awarded M.Phil. and Ph.D. degrees and continuing the research supervision for currently working students. He has participated in many National Conferences and Workshops and presented his work in form of lectures and presentations.