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Tin(II)chloride catalyzed synthesis of pyranoquinolines, phenanthridinone and phenanthridine derivatives

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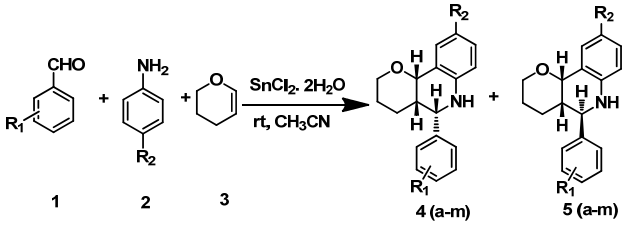
ABSTRACT

A simple, efficient and cost-effective method for the synthesis of tetrahydropyranoquinoline derivatives by a one-pot condensation of aromatic aldehyde, aromatic amine and 3,4-dihydro-2*H*-pyran respectively in the presence of tin(II)chloride ($SnCl_2.2H_2O$) has been described.

1. Introduction

Tetrahydroquinoline derivatives are important class of natural products and exhibit variety of biological activities, such as psychotropic, antiallergic, antiinflamatory and estronegic [1-4]. The pyrano tetrahydroquinolines are also found in several alkaloids [5-7] such as veprisine, flindersine and oricine. The imino Diels-Alder reaction provides a useful entry to the preparation of tetrahydroquinolines derivatives [8-10]. Imines derived from aromatic amines act as heterodienes and undergo imino Diels-Alder reaction with various dienophiles. Some improved procedures have been reported for the reaction of 3,4-dihydro-2*H*-pyran (DHP) with aniline using $BF_3.OEt_2$ [11], $GdCl_3$ [12], $InCl_3$ [13], $LiClO_4$ [14], $ZrCl_4$ [15], TMSCl [16], I_2 [17], $SbCl_3$ [18], $SbCl_3$-HPA [19], PMA [20], CF_3CO_2H [21].

Recently, $SnCl_2.2H_2O$ has emerged as catalyst in various organic transformations, including synthesis of bisindolylmethanes [22], conjugate addition of indoles to α,β-unsaturated ketones [23], the Paal-Knorr synthesis of pyrroles [24], the Fischer synthesis of indole [25], and the synthesis of β-acetamido ketones and β-acetamido ketoesters [26]. In view of its inherent properties such as environmental compatibility, reusability, greater selectivity, operational simplicity, non-corrosiveness, low cost and ease of isolation, we wish to describe our results on $SnCl_2.2H_2O$ catalyzed one-pot condensation of quinoline derivatives with aryl aldehydes, aromatic anilines, and 3,4-dihydro-2*H*-pyran at room temperature (Scheme 1).



Scheme 1

2. Experimental

2.1. Materials and methods

All the commercial reagents and solvents were used without further purification unless otherwise stated. Melting points were recorded on a Buchi 535 melting point apparatus and are uncorrected. All the reactions were monitored by thin layer chromatography performed on precoated silica gel $60F_{254}$ plates (Merck). Compounds were visualized with UV light at 254 nm and 365 nm, I_2 and heating plates after dipping in 2% phosphomolybdic acid in 15% aq. H_2SO_4 solution. IR spectra were recorded on a Perkin-Elmer 683 or a 1310 FT-IR spectrometers with KBr pellets. ^1H NMR spectra were recorded on BRUKER AMX 300 spectrometers using tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on a VG Micromass 7070H and a Finnigan Mat 1020B mass spectrometers operating at 70 eV.

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2.2. General reaction procedure for synthesis of tetrahyro-quinolines

To a suspension of $SnCl_2.2H_2O$ (46 mg, 0.2 mmol), acetonitrile (2.5 mL) and anhydrous Na_2SO_4 (150 mg) were added a solution of benzalehyde (212 mg, 2.0 mmol) in acetonitrile (2.5 mL) and a solution of aniline (205 mg, 2.2 mmol) in acetonitrile (2.5 mL) at room temperature (r.t.). The mixture was stirred for 5 min at r.t. Then 3,4-dihydro-2*H*-pyran (218 mg, 2.6 mmol) was added and the mixture stirred for the period of time as mentioned in the Table 2. Thin layer chromatography (TLC) monitored (ethyl acetate:hexane, 2:8) completion of the reaction, it was quenched with H_2O and extracted with CH_2Cl_2 (2 x 25 mL) and dried (Na_2SO_4). The solvent was evaporated and the crude residue obtained was purified by column chromatography (silica gel; ethyl acetate:hexane, 10:90) to give pure tetrahydropyrano-quinolines **4** and **5** (503 mg, 95%).

2.3. Spectral data of some of the representative compounds

2.3.1. 5-(4-Nitro-phenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (Table 2, entry d)

***Cis* isomer:** M.p.: 164-165 °C. *Rf* (20% EtOAc/*n*-hexane): 0.5. IR (KBr) (ν_{max}, cm^{-1}): 3374 (N-H), 3040, 2923, 2855, 1515, 1345, 1068, 759. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.17-1.59 (m, 4H), 2.16-2.24 (m, 1H), 3.41 (dt, *J* = 2.9 Hz, 9.5 Hz, 1H), 3.61 (dd, *J* = 3.2 Hz, 11.9 Hz, 1H), 3.81 (s, 1H), 4.68 (d, *J* = 2.2 Hz, 1H), 5.31 (d, *J* = 5.8 Hz, 1H), 6.61 (d, *J* = 8.1 Hz, 1H), 6.81 (t, *J* = 7.3 Hz, 1H), 7.07 (t, *J* = 7.3 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 2H), 8.26 (d, *J* = 8.8 Hz, 2H). MS (ESI, m/z): 311 $([M+H])^+$. Anal. Calcd. for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03; O, 15.47. Found: C, 69.64; H, 5.84; N, 9.00%.

***Trans* isomer:** M.p.: 136-137 °C. *Rf* (20% EtOAc/*n*-hexane): 0.45. IR (KBr) (ν_{max}, cm^{-1}): 3377 (N-H), 3070, 2929, 2852, 1517, 1344, 1080, 750. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.20-1.49 (m, 4H), 2.11-2.22 (m, 1H), 3.44 (dt, *J* = 2.9 Hz, 9.5 Hz, 1H), 3.77 (dd, *J* = 3.2 Hz, 1.9 Hz, 1H), 4.04 (s, 1H), 4.39 (d, *J* = 2.9 Hz, 1H), 4.85 (d, *J* = 10.2 Hz, 1H), 6.56 (d, *J* = 7.3 Hz, 1H), 6.74 (t, *J* = 7.3 Hz, 1H), 7.11 (t, *J* = 7.3 Hz, 1H), 7.23 (d, *J* = 8.8 Hz, 1H), 7.64 (d, *J* = 8.8 Hz, 2H), 8.26 (d, *J* = 8.8 Hz, 2H). MS (ESI, m/z): 311 $([M+H])^+$. Anal. Calcd. for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03; O, 15.47. Found: C, 69.66; H, 5.84; N, 9.01%.

2.3.2. 5-(2,4-Dichloro-phenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (Table 2, entry e)

***Cis* isomer:** M.p.: 132-134 °C. *Rf* (20% EtOAc/*n*-hexane): 0.5. IR (KBr) (ν_{max}, cm^{-1}): 3374 (N-H), 3040, 2923, 2855, 1515, 1345, 1068, 759. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.39-1.57 (m, 4H), 2.18-2.38 (m, 1H), 3.42 (dt, *J* = 3.0 Hz, 11.3 Hz, 1H), 3.58 (dd, *J* = 3.7 Hz, 11.3 Hz, 1H), 5.01 (d, *J* = 2.2 Hz, 1H), 5.26 (d, *J* = 5.2 Hz, 1H), 6.55 (d, *J* = 6.8 Hz, 1H), 6.77 (t, *J* = 7.5 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 1H), 7.64 (m, 2H), 7.62 (d, *J* = 8.3 Hz, 2H). MS (ESI, m/z): 334 $([M+H])^+$. Anal. Calcd. for $C_{18}H_{17}Cl_2NO$: C, 64.68; H, 5.13; Cl, 21.21; N, 4.19; O, 4.79. Found: C, 64.66; H, 5.14; N, 4.18%.

***Trans* isomer:** Thick syrup. *Rf* (20% EtOAc/*n*-hexane): 0.45. IR (KBr) (ν_{max}, cm^{-1}): 3374 (N-H), 3040, 2923, 2855, 1515, 1345, 1068, 759. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.39-1.57 (m, 4H), 2.18-2.38 (m, 1H), 3.63 (dt, *J* = 3.0 Hz, 11.3 Hz, 1H), 3.92 (dd, *J* = 3.7 Hz, 11.3 Hz, 1H), 4.37 (d, *J* = 3.7 Hz, 1H), 5.09 (d, *J* = 8.3 Hz, 1H), 6.49 (d, *J* = 6.8 Hz, 1H), 6.69 (t, *J* = 7.5 Hz, 1H), 7.05 (t, *J* = 8.3 Hz, 1H), 7.24 (m, 3H), 7.39-7.45 (m, 2H). MS (ESI, m/z): 334 $([M+H])^+$. Anal. Calcd. for $C_{18}H_{17}Cl_2NO$: C, 64.68; H, 5.13; Cl, 21.21; N, 4.19; O, 4.79. Found: C, 64.68; H, 5.12; N, 4.20.

2.3.3. 5-(3-Methoxy-phenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (Table 2, entry f)

***Cis* isomer:** Thick syrup; *Rf* (20% EtOAc/*n*-hexane): 0.5. IR (KBr) (ν_{max}, cm^{-1}): 3374 (N-H), 3040, 2923, 2855, 1515, 1345, 1068, 759. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.31-1.68 (m, 4H), 2.09-2.18 (m, 1H); 3.67 (m, 1H), 3.81 (s, 3H), 4.64 (d, *J* = 2.2 Hz, 1H), 5.27 (d, *J* = 5.2 Hz, 1H), 6.54 (d, *J* = 8.3 Hz, 1H), 6.78 (t, *J* = 11.3 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 3H), 7.24 (d, *J* = 7.5 Hz, 1H), 7.37 (d, 1H). MS (ESI, m/z): 296 $([M+H])^+$. Anal. Calcd. for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74; O, 10.83. Found: C, 77.23; H, 7.17; N, 4.75%.

***Trans* isomer:** M.p.: 99-100 °C; *Rf* (20% EtOAc/*n*-hexane): 0.48. IR (KBr) (ν_{max}, cm^{-1}): 3374 (N-H), 3040, 2923, 2855, 1515, 1345, 1068, 759. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.37-1.55 (m, 4H), 2.09-2.21 (m, 1H), 3.69 (dt, *J* = 3.0 Hz, 9.8 Hz, 1H), 3.79 (s, 3H), 4.09 (dd, *J* = 3.7 Hz, 11.3 Hz, 1H), 4.34 (d, *J* = 2.2 Hz, 1H), 4.67 (d, *J* = 10.5 Hz, 1H), 6.48 (d, *J* = 7.5 Hz, 1H), 6.65 (t, *J* = 8.3 Hz, 1H), 6.81 (dd, *J* = 3.7, 8.3 Hz, 1H), 6.94 (d, *J* = 8.3 Hz, 2H), 7.04 (dt, *J* = 1.51, 7.5 Hz, 1H), 7.16 (dd, *J* = 1.5, 7.5 Hz, 1H), 7.24 (dd, *J* = 1.5, 7.5 Hz, 1H). MS (ESI, m/z): 296 $([M+H])^+$. Anal. Calcd. for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74; O, 10.83. Found: C, 77.25; H, 7.18; N, 4.74%.

2.3.4. 9-Isopropyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (Table 2, entry i)

***Cis* isomer:** M.p.: 108-109 °C. *Rf* (20% EtOAc/*n*-hexane): 0.5. IR (KBr) (ν_{max}, cm^{-1}): 3374 (N-H), 3040, 2923, 2855, 1515, 1345, 1068, 759. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.22 (s, 3H), 1.26 (s, 3H), 1.41-1.58 (m, 4H), 2.09-2.15 (m, 1H), 2.83 (m, 1H), 3.38 (dt, *J* = 3.6 Hz, 15.2 Hz, 1H), 3.57 (dd, *J* = 3.7 Hz, 11.3 Hz, 1H), 3.71 (s, 1H), 4.65 (d, *J* = 2.2 Hz, 1H), 5.29 (d, *J* = 6.5 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 6.93 (dd, *J* = 2.2, 8.0 Hz, 1H), 7.25-7.41 (m, 6H). MS (ESI, m/z): 308 $([M+H])^+$. Anal. Calcd. for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56; O, 5.20. Found: C, 82.05; H, 8.22; N, 4.55%.

***Trans* isomer:** M.p.: 95-98 °C. *Rf* (20% EtOAc/*n*-hexane): 0.48. IR (KBr) (ν_{max}, cm^{-1}): 3374 (N-H), 3040, 2923, 2855, 1515, 1345, 1068, 759. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.22 (s, 3H); 1.27 (s, 3H), 1.41-1.58 (m, 4H), 2.09-2.15 (m, 1H), 2.83 (m, 1H), 3.38 (dt, *J* = 3.6 Hz, 15.2 Hz, 1H), 3.57 (dd, *J* = 3.7 Hz, 11.3 Hz, 1H), 3.69 (s, 1H), 4.33 (d, *J* = 2.2 Hz, 1H), 4.64 (d, *J* = 10.2 Hz, 1H), 6.55 (d, *J* = 8.3 Hz, 1H), 7.02 (dd, *J* = 2.2, 8.0 Hz, 1H), 7.31-7.44 (m, 6H). MS (ESI, m/z): 308 $([M+H])^+$. Anal. Calcd. for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56; O, 5.20. Found: C, 82.04; H, 8.19; N, 4.58%

2.3.5. 5-(4-Bromo-phenyl)-9-isopropyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-]quinoline (Table 2, entry j)

***Cis* isomer:** M.p.: 104-105 °C. *Rf* (20% EtOAc/*n*-hexane): 0.5. IR (KBr) (ν_{max}, cm^{-1}): 3368 (N-H), 2936, 2860, 1493, 1067, 818. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.21 (s, 3H), 1.25 (s, 3H), 1.42-1.59 (m, 2H), 2.02-2.13 (m, 1H), 2.74-2.88 (m, 1H), 3.32 (dt, *J* = 2.9 Hz, 10.9 Hz, 2H), 3.52 (dd, *J* = 3.6 Hz, 10.9 Hz, 2H), 4.92 (d, *J* = 2.18 Hz, 1H), 5.22 (d, *J* = 5.0 Hz, 1H), 6.45 (d, *J* = 8.0 Hz, 1H), 6.92 (dd, *J* = 2.1 Hz, 8.0 Hz, 1H), 7.22-7.30 (m, 3H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.69 (d, *J* = 8.7 Hz, 1H). MS (ESI, m/z): 386 $([M+H])^+$. Anal. Calcd. for $C_{21}H_{24}BrNO$: C, 65.29; H, 6.26; Br, 20.68; N, 3.63; O, 4.14. Found: C, 65.26; H, 6.26; N, 3.61%.

***Trans* isomer:** M.p.: 94-95 °C. *Rf* (20% EtOAc/*n*-hexane): 0.45. IR (KBr) (ν_{max}, cm^{-1}): 3368 (N-H), 2936, 2860, 1493, 1067, 818. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.94 (s, 3H), 1.23 (s, 3H), 1.39-1.54 (m, 2H), 2.02-2.13 (m, 1H), 2.72-2.82 (m, 1H), 3.62 (dt, *J* = 2.1, 11.65 Hz, 2H), 4.04 (dd, *J* = 2.1, 11.6 Hz, 2H), 4.30 (d, *J* = 2.1 Hz, 1H), 4.60 (d, *J* = 10.9 Hz, 1H), 6.45 (d, *J* = 8.0 Hz, 1H), 6.95 (dd, *J* = 2.1, 8.0 Hz, 1H), 7.01-7.02 (d, *J* = 2.18, 2H), 7.28 (d,

J = 8.01 Hz, 2H), 7.48 (d, *J* = 8.7 Hz, 1H). MS (ESI, m/z): 386 ([M+H])$^+$. Anal. Calcd. for $C_{21}H_{24}BrNO$: C, 65.29; H, 6.26; Br, 20.68; N, 3.63; O, 4.14. Found: C, 65.28; H, 6.27; N, 3.65%.

2.3.6. 9-Fluoro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (Table 2, entry k)

***Cis* isomer:** M.p.: 158-159 °C. *Rf* (20% EtOAc/*n*-hexane): 0.5. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.37-1.55 (m, 4H), 2.14 (m, 1H), 3.42 (dt, *J* = 3.02 Hz, 11.3 Hz, 1H), 3.60 (dd, *J* = 3.02 Hz, 11.3 Hz, 1H), 3.70 (br s, 1H,), 4.63 (d, *J* = 3.0 Hz, 1H), 5.23 (d, *J* = 6.0 Hz, 1H), 6.45-6.49 (d, *J* = 4.5 Hz, 1H), 6.78 (dt, *J* = 3.0 Hz, 8.3 Hz, 1H), 7.08-7.12 (dd, *J* = 3.0 Hz, 8.3 Hz, 1H), 7.24-7.39 (m, 5H). MS (ESI, m/z): 284 ([M+H])$^+$. Anal. Calcd. for $C_{18}H_{18}FNO$: C, 76.30; H, 6.40; F, 6.71; N, 4.94; O, 5.65. Found: C, 76.29; H, 6.40; N, 4.91%.

***Trans* isomer:** M.p.: 82-84 °C. *Rf* (20% EtOAc/*n*-hexane): 0.48. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.31-1.50 (m, 2H), 1.57-1.68 (m, 1H), 1.75-1.87 (m, 1H), 2.07 (m, 1H), 3.71 (dt, *J* = 2.2 Hz, 11.3 Hz, 1H), 3.91 (br s, 1H), 4.08 (dd, *J* = 3.7 Hz, 10.5 Hz, 1H), 4.31 (d, *J* = 2.2 Hz, 1H), 4.64 (d, *J* =10.5 Hz, 1H), 6.39-6.44 (2d, *J* = 4.5 Hz, 1H), 6.81(dt, *J* = 3.0 Hz, 8.3 Hz, 1H), 6.88-6.92 (dd, *J* = 3.0 Hz, 9.0 Hz, 1H), 7.24-7.39 (m, 5H). MS (ESI, m/z): 284 ([M+H])$^+$. Anal. Calcd. for $C_{18}H_{18}FNO$: C, 76.30; H, 6.40; F, 6.71; N, 4.94; O, 5.65. Found: C, 76.29; H, 6.41; N, 4.95%.

2.3.7. 2-Fluoro-6-(4-fluoro-phenyl)-5,6a,7,8,9,10a-hexahydro-6H-phenanthridin-10-one (Table 2, entry o)

***Cis* isomer:** M.p.: 120-121 °C. *Rf* (20% EtOAc/*n*-hexane): 0.5. ^{1}H NMR (300 MHz, $CDCl_3$, *δ*): 1.56-1.94 (m, 3H), 2.26-2.36 (m, 2H), 2.58-2.74 (m, 2H), 4.36-4.40 (m, 1H), 4.64 (d, *J* = 3.1 Hz, 1H), 6.40-6.46 (m, 2H), 6.72-6.81 (t, *J* = 7 .8 Hz, 1H), 7.32-7.34 (m, 4H). MS (ESI, m/z): 314 ([M+H]). Anal. Calcd. for $C_{19}H_{17}F_2NO$: C, 72.83; H, 5.47; F, 12.13; N, 4.47; O, 5.11. Found: C, 72.80; H, 5.46; N, 4.45%.

***Trans* isomer:** M.p.: 114-115 °C. *Rf* (20% EtOAc/*n*-hexane): 0.45. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.68-1.79 (m, 2H), 1.99-2.30 (m, 2H), 2.38-2.45 (m, 2H), 2.69-2.77 (m, 2H), 4.36-4.42 (m, 1H), 4.54 (d, *J* = 2.0 Hz, 1H), 6.50-6.55 (m, 2H), 6.79-6.81 (t, *J* = 8.3 Hz, 1H), 7.21-7.32 (m, 4H). MS (ESI, m/z): 314 ([M+H])$^+$. Anal. Calcd. for $C_{19}H_{17}F_2NO$: C, 72.83; H, 5.47; F, 12.13; N, 4.47; O, 5.11. Found: C, 72.85; H, 5.47; N, 4.45%.

2.3.8. 12-(2,4-Dichloro-phenyl)-2,3,4a,11,12,12a-hexahydro-1H-4-oxa-11-aza-chrysene (Table 2, entry q)

***Cis* isomer:** M.p.: 164-165 °C. *Rf* (20% EtOAc/*n*-hexane): 0.5. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.38-1.56 (m, 3H), 2.28-2.36 (m, 1H), 2.41-2.51(m, 1H), 3.20-3.32 (m, 1H), 3.47-3.53 (m, 1H), 5.04 (d, *J* = 2.2 Hz, 1H), 5.37 (d, *J* = 5.8 Hz, 1H), 7.17-7.21 (d, *J* = 8.0 Hz, 1H), 7.28-7.45 (m, 3H), 7.64-7.72 (m, 2H), 7.86-7.94 (m, 3H). MS (ESI, m/z): 384 ([M+H])$^+$. Anal. Calcd. for $C_{22}H_{19}Cl_2NO$: C, 68.76; H, 4.98; Cl, 18.45; N, 3.64; O, 4.16. Found: C, 68.76; H, 4.95; N, 3.63%.

***Trans* isomer:** Thick syrup; *Rf* (20% EtOAc/*n*-hexane) 0.45. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.25-1.51 (m, 4H), 2.23-2.26 (m, 1H); 2.37(m, 1H), 3.69-3.73 (m, 1H), 3.93-3.39 (m, 1H), 4.52 (d, *J* = 3.7 Hz, 1H), 5.24 (d, *J* = 9.0 Hz, 1H), 7.21-7.26 (m, 3H), 7.32-7.48 (m, 4H), 7.62-7.64 (d, *J* = 8.3 Hz, 1H), 7.72-7.75(d, *J* = 9.0 Hz, 1H). MS (ESI, m/z): 384 ([M+H])$^+$. Anal. Calcd. for $C_{22}H_{19}Cl_2NO$: C, 68.76; H, 4.98; Cl, 18.45; N, 3.64; O, 4.16. Found: C, 68.75; H, 4.99; N, 3.65%.

2.3.9. 12-(2-Chloro-phenyl)-2,3,4a,11,12,12a-hexahydro-1H-4-oxa-11-aza-chrysene (Table 2, entry r)

***Cis* isomer:** M.p.: 152-154 °C. *Rf* (20% EtOAc/*n*-hexane): 0.5. ^{1}H NMR (300 MHz, $CDCl_3$, *δ*): 1.21-1.59 (m, 3H), 2.48 (m, 1H), 3.29-3.36 (m, 1H), 3.52-3.61 (m, 1H), 4.29-4.30 (m, 1H), 5.18 (d, *J* = 2.6 Hz, 1H), 5.45 (d, *J* = 6.4 Hz, 1H), 7.17-7.35 (m, 2H), 7.37-7.45 (m, 5H), 7.48-7.54 (m, 2H), 7.93 (d, *J* = 2.07 Hz, 1H). MS (ESI, m/z): 350 ([M+H])$^+$. Anal. Calcd. for $C_{22}H_{20}ClNO$: C, 75.53; H, 5.76; Cl, 10.13; N, 4.00; O, 4.57. Found: C, 75.53; H, 5.74; N, 4.01%.

***Trans* isomer:** Thick syrup. *Rf* (20% EtOAc/*n*-hexane): 0.48. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 1.20-1.65 (m, 3H), 2.29 (m, 1H), 3.36-3.55 (m, 1H), 3.63-3.64 (m, 1H), 4.19-4.60 (m, 1H), 4.61 (d, *J* = 3.6 Hz, 1H), 5.31 (d, *J* = 10.9 Hz, 1H), 6.67-7.46 (m, 6H), 7.62-7.78 (m, 4H). MS (ESI, m/z): 350 ([M+H])$^+$. Anal. Calcd. for $C_{22}H_{20}ClNO$: C, 75.53; H, 5.76; Cl, 10.13; N, 4.00; O, 4.57. Found: C, 75.55; H, 5.75; N, 4.04%.

2.4. General procedure for the preparation of tetrahydropyrano[3,2-c]quinolones

A mixture of aryl amine (465 mg, 5 mmol), 3,4-dihydro-2*H*-pyran (100 mg, 12 mmol) and $SnCl_2.2H_2O$ (46 mg, 0.2 mmol) in acetonitrile (5 mL) was stirred at room temperature for the appropriate time (Table 2). TLC monitored completion of the reaction, it was quenched with H_2O and extracted with CH_2Cl_2 (2 x 25 mL) and dried (Na_2SO_4). The solvent was evaporated and the crude residue obtained was purified by column chromatography to give pure tetrahydropyrano[3,2-*c*]quinolines **12** and **13** (503 mg, 95%).

2.5. Spectral data of some of the representative compounds

2.5.1. 4-(9-Isopropyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-butan-1-ol (Table 3, entry ii)

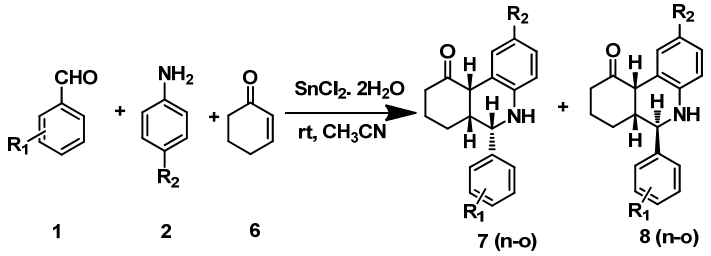
***Cis* isomer:** Thick syrup; IR (KBr) (ν_{max}, cm^{-1}): 3403 (N-H), 2923, 2853, 1506, 1458, 1265, 1089, 760. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.03 (s, 1H), 6.92 (dd, *J* = 2.2 Hz, 8.30 Hz, 1H), 6.45 (d, *J* = 8.3 Hz, 1H), 4.43 (d, *J* = 3.0 Hz, 1H), 3.95 (dd, *J* = 3.7 Hz, 15.1 Hz, 1H), 3.68-3.52 (m, 5H), 2.98 (br s, 1H), 2.83-2.74 (m, 1H), 2.01-1.95 (m, 1H), 1.77-1.41 (m, 10H), 1.23 (s, 3H), 1.21 (s, 3H). MS (ESI, m/z): 304 ([M+H])$^+$.

***Trans* isomer:** Thick syrup. IR (KBr) (ν_{max}, cm^{-1}): 3383 (N-H), 2928, 2858, 1508, 1459, 1261, 1063, 756. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.01 (s, 1H), 6.91 (m, 1H), 6.45 (d, *J* = 8.3 Hz, 1H), 5.02 (d, *J* = 5.2 Hz, 1H), 3.90 (m, 1H), 3.71-3.33 (m, 6H), 2.79-2.74 (m, 1H), 2.05-1.95 (m, 1H), 1.73-1.47 (m, 10H), 1.28-1.21 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 142.2, 137.9, 127.8, 127.0, 120.3, 114.5, 73.9, 72.5, 67.1, 62.5, 60.6, 54.2, 49.6, 36.4, 32.6, 29.6, 24.1, 22.6, 21.1. MS (ESI, m/z): 304 ([M+H])$^+$.

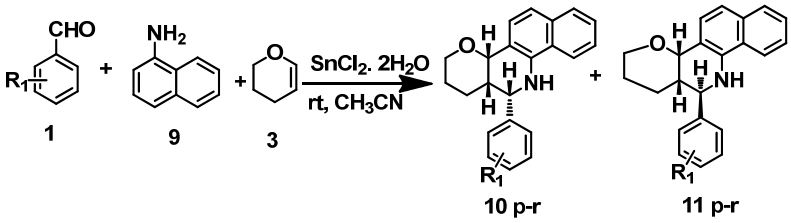
2.5.2. 4-(9-Trifluoromethoxy-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)-butan-1-ol (Table 3, entry iii)

***Cis* isomer:** Thick syrup. IR (KBr) (ν_{max}, cm^{-1}): 3428 (N-H), 2929, 2861, 1504, 1380, 1253, 1154, 616. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 6.80 (d, *J* = 2.6 Hz, 1H), 6.68 (dd, *J* = 2.6, 8.0 Hz, 1H), 6.50 (d, *J* = 8.0 Hz, 1H), 4.44 (d, *J* = 5.4 Hz, 1H), 3.92 (m, 1H), 3.68-3.48 (m, 3H), 3.48 (m, 1H), 2.00-1.96 (m, 1H), 1.70-1.32 (m, 10H); MS(ESI) m/z 346 ([M+H])$^+$.

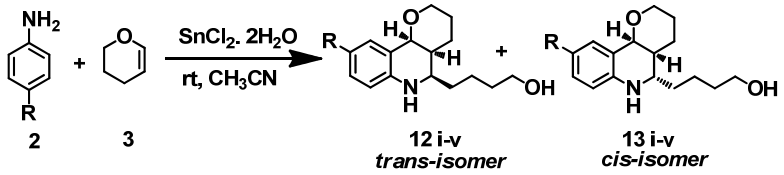
***Trans* isomer:** Thick syrup. IR (KBr) (ν_{max}, cm^{-1}): 3369 (N-H), 2935, 2859, 1502, 1349, 1251, 1159, 757. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.06 (d, *J* = 2.2 Hz, 1H), 6.86 (dd, *J* = 2.9 Hz, 8.8 Hz, 1H), 6.43 (d, *J* = 8.8 Hz, 1H), 4.97 (d, *J* = 5.1 Hz, 1H), 3.68 (m, 2H), 3.60-3.51 (m, 2H), 3.27 (m, 1H), 2.00-1.95 (m, 1H), 1.68-1.32 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 121.0, 120.4, 114.0, 78.9, 71.8, 67.0, 62.4, 60.5, 53.9, 34.8, 31.6, 30.6, 29.5, 25.3, 22.4, 19.6, 17.6. MS (ESI, m/z): 346 ([M+H])$^+$.



Scheme 2



Scheme 3



Scheme 4

3. Results and discussion

During the course of our studies directed towards the development of practical, and eco-friendly procedures [27-30], we developed the applicability of $SnCl_2.2H_2O$ for efficient, convenient and facile synthesis of quinoline derivatives by a one-pot condensation of aryl aldehydes, substituted anilines, 3,4-dihydro-2*H*-pyran and anhydrous Na_2SO_4 in acetonitrile at room temperature (Scheme 1). Initially a pilot reaction was carried out using benzaldehyde (2 mmol), aniline (2.2 mmol) and 3,4-dihydro-2*H*-pyran (2.6 mmol) in the presence of $SnCl_2.2H_2O$ (46 mg, 0.2 mmol) without any solvent. After 4 h, only 27 % of a mixture of the C-2 epimers (**4** and **5**) of a tetrahydroquinoline product was isolated as 1:1 ratio. Increasing the amount of $SnCl_2.2H_2O$ did not improve the product yield to a considerable amount. Subsequently, we investigated the effect of the different solvents on the reaction rate as well as the yields of the products. It was found that MeCN was the best solvents for our reaction. In coordinating solvents such as THF, Et_2O and DME, the reaction was very slow and resulted in lower product yields. Similar results were obtained in protic solvents such as MeOH and EtOH. After screening for different solvents, MeCN came out as the best solvent of the choice, which not only afforded the products in good yield, but also higher reaction rates (95% yield) (Table 1). It was interesting to note that the *trans* isomer **5** was always obtained as the major product (Table 2).

We first investigated the synthesis of 5-Phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinolines (**4a**) and (**5a**). Reaction of benzaldehyde **1** (212 mg, 2.0 mmol) with aromatic amine **2** (202 mg, 2.2 mmol), and 3,4-dihydro-2*H*-pyran **3** (218 mg, 2.6 mmol) in the presence of $SnCl_2.2H_2O$ (0.2 mmol), anhydrous Na_2SO_4 (150 mg) and CH_3CN (2.5 mL) at room temperature for 1.8 h gave **4a** white crystalline powder melting point 204-205 °C and **5a** as a viscous oil in 30:70 ratio (0.50 g, 95 % yield) (Scheme 1).

In order to extend the scope of this catalytic transformation, the general applicability of this method was verified by reacting with the number of substituted benzaldehydes, substituted anilines and different dienophiles. Cyclohexen-1-one (**6**) was utilized to obtain the corresponding phenanthridinone derivatives (**7n-o**) and (**8n-o**) (70:30) in 79 % yield (Scheme 2).

Table 1. Effect of solvents in the condensation of benzaldehyde, aniline and 3,4-dihydro-2*H*-pyran in the presence of $SnCl_2.2H_2O$.

Entry[a]	Solvent	Reaction time (min)	Yield (%)[b]
1	Neat	300	27
2	MeOH	240	36
3	EtOH	240	42
4	THF	180	45
5	Ether	120	44
6	DME	180	52
7	CH_2Cl_2	60	63
8	$CHCl_3$	60	64
9	CH_3CN	40	92

[a] All reactions were performed using benzaldehyde (1 mmol), aniline (1.2 mmol), 3,4-dihydro-2*H*-pyran (1.2 mmol), and $SnCl_2.2H_2O$ (0.2 mmol).
[b] Combined isolated yields.

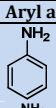
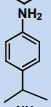
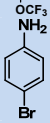
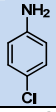
Phenanthridine skeletons [31] are present in lycorine, chelidonine and haemanthamine alkaloids. $SnCl_2.2H_2O$ also catalyzed effectively the imino Diels-Alder reaction of in situ generated *N*-benzylidene-1-napthylamine (**9**) with 3,4-dihydro-2*H*-pyran and 2,3-dihydrofuran to afford the phenanthridine derivatives (**10**) and (**11**) as a mixture of *cis* and *trans* isomers in good overall yields (59-62%) (Scheme 3). The pyran ring was *cis*-fused in the tetrahydroquinoline moiety and the stereochemistry of the products was established based on the coupling constants.

Table 2. The reaction times and isolated product yields of the selected compounds.

Entry	R1	R2	Product	Reaction Time (h)	Product ratio (%)	Yield (%)[a]	Reference
1	H	H	a	1.8	30:70	95.0	[15]
2	4-F	H	b	2.0	18:82	91.8	[15]
3	4-OMe	H	c	2.0	36:64	94.1	[15]
4	4-NO_2	H	d	2.0	22:78	82.1	-
5	2,4-Cl_2	H	e	1.8	29:71	93.2	-
6	3-OMe	H	f	2.0	33:67	87.3	-
7	4-Cl	H	g	2.0	34:66	80.7	[15]
8	4-Me	H	h	1.8	28:72	86.2	[14]
9	H	$(CH_3)_2$-CH	i	2.0	39:61	80.5	-
10	4-Br	$(CH_3)_2$-CH_4-	j	1.5	36:64	75.8	-
11	H	F	k	2.0	42:58	71.2	-
12	H	4-Cl	l	1.5	39:61	84.6	[15]
13	H	4-Br	m	1.5	44:56	82.5	[15]
14	H	H	n	1.5	30:70	79.2	[11]
15	4-F	4-F	o	1.5	28:72	76.4	-
16	H	1-Naphthyl	p	3.0	36:64	62.0	[15]
17	2,4-Cl	1-Naphthyl	q	3.0	40:60	60.8	-
18	2-Cl	1-Naphthyl	r	3.0	35:65	59.5	-

[a] Combined isolated yields.

Table 3. Reaction of anilines with dihydropyran by $SnCl_2.2H_2O$ catalyzed synthesis of tetrahydropyrano[3,2-c]quinolones.

Entry	Aryl amine	Olefin	Reaction time (h)	Yield (%)	*trans* / *cis*[a]
i			3.0	90	95:5
ii			3.5	87	93:7
iii			3.5	85	93:7
iv			3.0	88	95:5
v			3.0	89	90:10

[a] Products ratio was determined by the ^1H NMR spectrum of the crude product.

The coupling constant of C5-H ($J_{4a,5}$ = 4.6-5.5 Hz) in **4** indicated the *cis* relationship between C-**4a** and C-5, whereas in **5** ($J_{4a,5}$ = 10.2-11.10 Hz) *trans* form. The simplicity, together with the use of inexpensive, non-toxic and environmentally benign nature of $SnCl_2.2H_2O$ catalyst in MeCN solvent is a remarkable feature of the procedure.

The generality of the present protocol was then extended to *trans* (**12**), *cis* (**13**) isomers of tetrahydropyrano[3,2-*c*] quinoline. The reactions proceeded efficiently in 90% yield at ambient temperature. In most of the cases, the products were obtained as a mixture of *cis* and *trans*-isomers favoring the trans diastereomers as observed by others in most of the Povarov imino Diels-Alder reactions [32] (Scheme 4). The product ratio was determined based on previous reports [33] by ^1H NMR spectrum of the crude product and the results are summarized in Table 3.

4. Conclusion

In conclusion, we have developed a new and effective methodology for the synthesis of tetrahydropyranoquinolines, phenanthridinone, phenanthridine and pyranoquinoline (with 2 equiv. of cyclic enol ether) derivatives in one-pot synthesis using a catalytic amount of $SnCl_2.2H_2O$. The notable features of this procedure mild and neutral reaction conditions, high yields of products, the low cost and commercially availability of the catalyst, simple and easy isolation of the products the main advantages over existing procedures for the synthesis of quinoline, phenanthridinone and phenanthridine derivatives. The ambient reaction conditions, shorter reaction times, excellent product yields make this catalytic system an alternative method for the synthesis of these derivatives.

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References

[1]. Nesterova, I. N.; Alekseeva, L. M.; Andreeva, L. M.; Andreeva, N. I.; Golovira, S. M.; Granic, V. G. Khim. *Form. Zh. (Russ.)* **1995**, *29*, 31-34.
[2]. Yamada, N.; Kadowaki, S.; Takahashi, K.; Umezu, K. *Biochem. Pharmacol.* **1992**, *44*, 1211-1213.
[3]. Faber, K.; Stueckler, H.; Kappe, T. *J. Hetrocycl. Chem.* **1984**, *21*, 1177-1181.
[4]. Akhmed, Kh. S.; Bessonova, I. A. *Dokl. Akad, Nauk. Uzh., SSR* **1982**, 34-36 (Russ.); Chem. Abstr. **1983**, *98*, 83727q.
[5]. Anzino, M.; Cappelli, A.; Vomero, S.; Cagnatto, A.; Skorupska, M. *Med. Chem. Res.* **1993**, *3*, 44-46.
[6]. Quraishi, M. A.; Thakur, V. R.; Dhawan, S. N. *Indian J. Chem. Sect. B.* **1989**, *28B*, 891-893.
[7]. Ramesh, M.; Mohan, P. S.; Shanmugam, P. *Tetrahedron* **1984**, *40*, 4041-4049.
[8]. Young, K. K.; Sun, M. K.; Dae, Y. K. *J. Am. Chem. Soc.* **2010**, *132*, 1184-1149.
[9]. Vladimir, V. K. *Tetrahedron* **2009**, *65*, 2721-2750.
[10]. Paul, B.; Jonh-Carl, O.; Taeboem, O. *Tetrahedron* **2001**, *57*, 6099-6138.

[11]. Kametani, T.; Takeda, H.; Suzuki, Y.; Honda, T. *Synth. Commun*. **1985**, *15*, 499-505.
[12]. Ma, Y.; Qian, C.; Xie, M.; Sun, J. *J. Org. Chem*. **1999**, *64*, 6462-6467.
[13]. Babu, G.; Perumal, P. T. *Tetrahedron Lett.* **1998**, *39*, 3225-3228.
[14]. Yadav, J. S.; Subba Reddy, B. V.; Srinivas. R.; Madhuri, Ch.; Ramalingam, T. *Synlett*. **2001**, 0240-0242.
[15]. Mahesh, M.; Venkateswar, R. C.; Srinivas, R. K.; Raju, P. V. K.; Narayana, R. V. V. *Synth. Commun.* **2004**, *34*, 4089-4104.
[16]. Shivaji. V. M.; Sastry. M. N.; Ching-Fa, Y. *Synlett*. **2006**, 1399-1403.
[17]. Min, X.; Yue-dong, L. *Synlett*. **2005**, 2357-2361.
[18]. Gourhari, M.; Pradip, K. *Tetrahedron Lett.* **2006**, *47*, 5733-5736.
[19]. Mahajan, D.; Ganai, B. A.; Sharma, R. L.; Kapoor, K. K. *Tetrahedron Lett.* **2006**, *47*, 7919-7921.
[20]. Nagaiah, K.; Sreenu, D.; Rao, R. S.; Vashishta, G.; Yadav, J. S. *Tetrahedron Lett*. **2006**, *47*, 4409-4413.
[21]. Xing, X.; Wu, J.; Baishya, G.; Wei-Min, D. *Tetrahedron* **2006**, *62*, 11200-11206.
[22]. Gu, D. A.; Ji, S. H.; Jang, Z.Q.; Zhou, M. F.; Loh, T. P. *Synlett*. **2005**, 0959-0962.
[23]. Yadav, J. S.; Subba Reddy, B.V.; Baishya, G.; Reddy, Narsaiah, K.V. *Tetrahedron* **2005**, *61*, 9541-9544.
[24]. Wang, B. Y.; Gu, C.; Luo, T.; Yang, L.; Suo, J. *Tetrahedron Lett*. **2004**, *45*, 3417-3419.
[25]. Rebeiro, G. L.; Khadlikar, B. M. *Synthesis* **2001**, 0370-0372.
[26]. Nagarapu, L.; Venkateswarlu, P.; Gopal, P.; Srinivas, K.; Ruparani, P.; Radhika K. *J. Mol. Cat. A: Chem.* **2007**, *26*, 53-56.
[27]. Nagarapu, L.; Chary, M. V.; Satyender, A.; Srinivas, K. *Cat. Communs*. **2007**, *8*, 1173-1177.
[28]. Nagarapu, L.; Rajashaker, B.; Rakesh, P. *Appl. Catal. A: General* **2007**, *332*, 304-309.
[29]. Nagarapu, L.; Rajashaker, B.; Hari Babu, M. *J. Heterocyclic Chem.* **2009**, *48(4*), 728-731.
[30]. Nagarapu, L.; Venkata Narsimhaji, C. H.; Shukla, C. K.; Rajashaker, B. *Synthesis* **2010**, 3374-3378.
[31]. Wildman, W. C. *Alkaloids* **1960**, *6*, 289-289.
[32]. Povarov, L. S. *Russ. Chem. Rev*. **1967**, *36*, 656-657.
[33]. Yadav, J. S.; Subba Reddy, B. V.; Srinivas, R.; Kiran, K. S.; Kunwar, A. C. *Tetrahedron* **2003**, *58*, 1599-1604.