Novel Use of Selectfluor™ for the Synthesis of *cis*-Fused Pyrano- and Furanotetrahydroquinolines

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Abstract: Aryl imines formed *in situ* from aryl aldehydes and aromatic amines undergo smooth [4+2] cycloaddition reactions with cyclic enol ethers such as 3,4-dihydro-2*H*-pyran and 2,3-dihydrofuran in the presence of 10 mol % Selectfluor™ in acetonitrile at room temperature to afford pyrano- and furanotetrahydroquinoline derivatives in excellent yields with high *endo*-selectivity.

Keywords: arylimines; Selectfluor™; tetrahydroquinolines

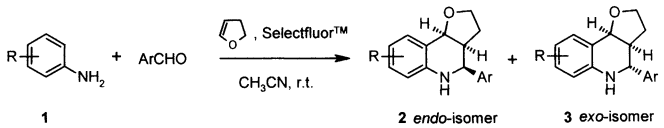
The aza-Diels–Alder reaction is becoming a mainstay for heterocycles and natural product synthesis.[1] Pyranoquinoline derivatives have been found to possess a wide spectrum of biological actions such as psychotropic, anti-allergeric, anti-inflammatory and estrogenic activities.[2] Aryl imines derived from aromatic amines can act as heterodienes and undergo imino-Diels–Alder reaction with various dienophiles in the presence of acid catalysts leading to tetrahydroquinoline derivatives.[3–5] Generally, more than stoichiometric amounts of the Lewis acids are required because the acids are trapped by nitrogen of both reactant and product.[1] However, many of these reactions cannot be carried out in a one-pot operation with a carbonyl compound, amine and enol ether because the amines and water produced during imine formation can decompose or deactivate the Lewis acids. Furthermore, most of the imines are hygroscopic, unstable at high temperatures and difficult to purify either by distillation or by column chromatography. Subsequently, one-pot procedures have been developed for this transformation using lanthanide triflates.[6] In fact, these procedures do not require the isolation of unstable imines prior to the reactions, but metal triflates are strongly acidic in nature and so the development of milder alternatives like Selectfluor™ would extend the scope of this transformation.

Recently, Selectfluor™ has been introduced commercially as a user-friendly electrophilic fluorinating agent.[7] Selectfluor™ is readily available, easy to handle and also retains its activity even in the presence of amines.[8a] More recently, Selectfluor™ has been employed as an efficient Lewis acid for the one-pot allylation reactions of imines and for the hydrolysis of acetals, dithioacetals and tetrahydropyranyl ethers.[8b] However, there are no precedents of the use of Selectfluor™ as promoter for [4+2] cycloaddition reactions.

In this report, we wish to describe the synthesis of tetrahydroquinolines in a one-pot operation using a substoichiometric amount of Selectfluor™ under mild conditions. The treatment of benzaldehyde and aniline with 2,3-dihydrofuran in the presence of 10 mol % of Selectfluor™ in acetonitrile afforded the corresponding furanoquinolines **2** and **3** in 91% yield (Scheme 1).

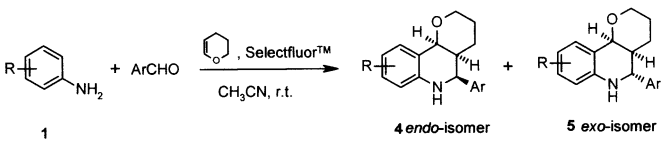
In a similar manner, various aromatic imines (formed *in situ* from aromatic aldehydes and anilines in acetonitrile) reacted smoothly with 2,3-dihydrofuran to afford the corresponding furano[3,2-*c*]quinolines in 87–94% yield. In most of the cases, the product was obtained as a mixture of **2** *endo*- and **3** *exo*-isomers favoring the *endo*-diastereomer.[5b] The diastereomers could be easily separated by column chromatography on silica gel and also characterized by NMR spectroscopy. Encouraged by the results obtained with 2,3-dihydrofuran, we turned our attention to 3,4-dihydro-2*H*-pyran and various arylimines. Interestingly, a wide range of arylimines reacted smoothly with 3,4-dihydro-2*H*-pyran under similar reaction conditions to produce pyrano[3,2-*c*]-quinolines **4** and **5** in excellent yields (Scheme 2).

Like the five-membered cyclic enol ether (DHF), the reaction of six-membered 3,4-dihydro-2*H*-pyran with



1 **2** *endo*-isomer **3** *exo*-isomer

Scheme 1.



1 **4** *endo*-isomer **5** *exo*-isomer

Scheme 2.

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Table 1. Deprotection of the *N*-Boc group from aromatic amines.[a]

Entry	R	Ar	Enol ether	Reaction time [h]	Yield [%][b]	*endo*/*exo*[c]
a	H	C_6H_5		1.5	91	95:5
b	4-Me	4-ClC_6H_4	"	2.5	87	93:7
c	3-Cl	C_6H_5	"	3.0	93	91:9
d	H	4-FC_6H_4	"	2.5	90	92:8
e	4-Me	C_6H_5	"	3.0	94	94:6
f	H	4-$MeOC_6H_4$	"	3.5	91	96:4
g	4-MeO	C_6H_5	"	2.5	89	91:9
h	H	C_6H_5		3.0	92	85:15
i	4-Cl	C_6H_5	"	3.5	90	82:18
j	H	4-FC_6H_4	"	2.5	91	88:12
k	4-F	C_6H_5	"	3.0	89	90:10
l	H	4-$NO_2C_6H_4$	"	3.5	85	80:20
m	4-Me	C_6H_5	"	4.0	93	87:13
n	H	4-ClC_6H_4	"	3.0	92	85:15
o	4-MeO	C_6H_5	"	3.5	87	80:20

[a] All products were characterized by ^{1}H NMR, IR and mass spectroscopy
[b] Isolated and unoptimized yields.
[c] *endo*/*exo*-isomers were separated by column chromatography.

arylimines also gave the products as a mixture of **4** *endo*- and **5** *exo*-isomers, favoring the *endo*-diastereomer **4**. These three-component coupling reactions proceeded efficiently at room temperature with high *endo*-selectivity. In particular, 2,3-dihydrofuran afforded higher *endo*-selectivity when compared to 3,4-dihydro-2*H*-pyran (Table 1). Among various solvents such as dichloromethane, tetrahydrofuran and acetonitrile used for this reaction, CH_3CN was found to give the highest *endo*-selectivity. However, in the absence of catalyst, the reactions did not proceed even after long reaction times (8–12 h). Arylimines show enhanced reactivity in an acetonitrile solution of Selectfluor™ thereby reducing the reaction times, and improving the yields and *endo*-selectivity significantly. As a solvent, acetonitrile appears to give the best results. This method is equally effective for both electron-rich as well as electron-deficient arylimines. The reaction conditions are mild enough to perform the reactions in the presence of either acid- or base-sensitive aldehydes. Selectfluor™ is a mild Lewis acid, retains its activity even in the presence of amines and provides a convenient procedure to perform these reactions.

In conclusion, we describe a simple and efficient method for the synthesis of *cis*-fused pyrano- and furanoquinolines through three-component one-pot coupling of aldehydes, amines and cyclic enol ethers using Selectfluor™ as a substoichiometric reagent. The method offers several advantages including mild reaction conditions, high conversions, greater *endo*-selectivity, short reaction times, cleaner reaction profiles, ease of handling and easy availability of the reagent which make it attractive and a useful addition to the existing processes for the synthesis of functionalized tetrahydroquinolines.

Experimental Section

Melting points were recorded on a Buchi R-535 apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR 240-c spectrophotometer using KBr optics. ^{1}H NMR spectra were recorded on Gemini-200 spectrometer in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV.

General Procedure

A mixture of aldehyde (1 mmol), arylamine (1 mmol), 3,4-dihydro-2*H*-pyran or 2,3-dihydrofuran (2 mmol) and Selectfluor™ (0.1 mmol) in acetonitrile (10 mL) was stirred at 27 °C for the appropriate time (Table 1). After completion of the reaction, as indicated by TLC, the reaction mixture was diluted with water and extracted with ethyl acetate (2 × 10 mL). The combined organic extracts were dried and concentrated under vacuum and the resulting product was purified by column chromatography on silica gel (Merck, 100–200 mesh, eluted with a mixture of ethyl acetate:*n*-hexane, 2:8) to afford pure tetrahydroquinoline. All products were characterized by ^{1}H, ^{13}C NMR, IR and mass spectroscopy and also by comparison with authentic compounds. The spectroscopic data of products were identical with the data reported in the literature.[4–6]

***cis*-4-Phenyl-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline**[5b] **(2a):** Solid, m.p. 93–95 °C; ^{1}H NMR ($CDCl_3$): δ = 1.55 (m, 1H), 2.25 (m, 1H), 2.75 (m, 1H), 3.80 (m, 3H), 4.70 (d, *J* = 2.8 Hz, 1H), 5.25 (d, *J* = 8.0 Hz, 1H), 6.58 (d, *J* = 8.0 Hz, 1H), 6.80 (t, *J* = 8.0 Hz, 1H), 7.05 (t, *J* = 8.0 Hz, 1H), 7.35–7.55 (m, 6H); ^{13}C NMR ($CDCl_3$): δ = 24.5, 45.8, 57.3, 66.6, 75.9, 114.9, 119.0, 122.5, 126.3, 127.6, 128.2, 128.6, 130.0, 142.3, 144.8; EIMS: *m/z* = 251 M^+, 220, 206, 174, 130, 91; IR (KBr): ν_{max} = 3348, 2975, 2855, 1615, 1480, 1039 cm^{-1}.

***cis*-4-(4-Chlorophenyl)-8-methyl-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline**[4d] **(2b):** White solid, m.p. 148–149 °C; ^{1}H NMR ($CDCl_3$): δ = 1.50 (m, 1H), 2.20 (m, 1H), 2.35 (s, 3H), 2.64 (m, 1H), 3.60 (brs, NH, 1H), 3.72 (m, 1H), 3.80 (m, 1H), 4.60 (d, *J* = 2.1 Hz, 1H), 5.20 (d, *J* = 8.0 Hz, 1H), 6.50 (d, *J* = 8.0 Hz, 1H), 6.85 (dd, *J* = 8.0 and 2.1 Hz, 1H), 7.10 (d, *J* = 2.1 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H); EIMS: *m/z* = 299 M^+, 254, 188, 160, 144, 115, 77; IR (KBr): ν_{max} = 3345, 2991, 2878, 1610, 1493, 1145, 1041 cm^{-1}.

***cis*-7-Chloro-4-phenyl-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline**[4d] **(2c):** Solid, m.p. 154–156 °C; ^{1}H NMR ($CDCl_3$): δ = 1.50 (m, 1H), 2.18 (m, 1H), 2.75 (m, 1H), 3.70–3.85 (m,

3H), 4.65 (d, $J = 2.8$ Hz, 1H), 5.20 (d, $J = 8.0$ Hz, 1H), 6.50 (d, $J = 8.2$ Hz, 1H), 7.05 (dd, $J = 8.2$, 3.1 Hz, 1H), 7.25 – 7.45 (m, 6H); EIMS: $m/z = 285$ M^+, 240, 226, 194, 91; IR (KBr): $\nu_{max} =$ 3340, 2965, 2840, 1621, 1500, 1137, 1045 cm^{-1}.

***cis*-4-(4-Fluorophenyl)-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline**[5e] **(2d)**: White solid, m.p. 173 – 175 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.50$ (m, 1H), 2.10 – 2.15 (m, 1H), 2.60 – 2.80 (m, 1H), 3.65 – 3.80 (m, 3H), 4.64 (d, $J = 2.5$ Hz, 1H), 5.20 (d, $J =$ 8.0 Hz, 1H), 6.50 (d, $J = 8.0$ Hz, 1H), 6.78 (t, $J = 8.0$ Hz, 1H), 7.05 (m, 3H), 7.30 (m, 1H), 7.40 (m, 2H); EIMS: $m/z = 269$ M^+, 240, 224, 198, 174, 130, 117, 77, 39; IR (KBr): $\nu_{max} = 3315$, 2976, 2880, 1606, 1508, 1223, 1155, 1049 cm^{-1}.

***cis*-4-Phenyl-8-methyl-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline**[4d] **(2e):** Solid, m.p. 101 – 102 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.45$ (m, 1H), 2.15 (m, 1H), 2.30 (s, 3H), 2.75 (m, 1H), 3.60 (brs, NH, 1H), 3.70 (m, 1H), 3.80 (m, 1H), 4.65 (d, $J = 2.8$ Hz, 1H), 5.30 (d, $J = 8.0$ Hz, 1H), 6.70 (t, $J = 7.8$ Hz, 1H), 7.0 (d, $J =$ 7.8 Hz, 1H), 7.25 (d, $J = 7.8$ Hz, 1H), 7.35 – 7.50 (m, 5H); EIMS: $m/z = 265$ M^+, 206, 174, 130, 91; IR (KBr): $\nu_{max} = 3348$, 2975, 2856, 1615, 1480, 1225, 1045 cm^{-1}.

***cis*-4-(4-Methoxyphenyl)-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline**[5e] **(2f):** Pale yellow solid, m.p. 155 – 156 °C, ^{1}H NMR ($CDCl_3$): $\delta = 1.58$ (m, 1H), 2.20 (m, 1H), 2.70 (m, 1H), 3.70 – 3.80 (m, 3H), 3.85 (s, 3H), 4.62 (d, $J = 2.2$ Hz, 1H), 5.22 (d, $J = 8.0$ Hz, 1H), 6.54 (d, $J = 8.0$ Hz, 1H), 6.78 (t, $J =$ 8.0 Hz, 1H), 6.90 (t, $J = 8.0$ Hz, 1H), 7.05 (d, $J = 8.0$ Hz, 2H), 7.40 (m, 3H); EIMS: $m/z = 281$ M^+, 252, 236, 224, 167, 155, 141, 121, 91, 69, 43; IR (KBr): $\nu_{max} = 3340$, 2990, 2870, 1605, 1520, 1135 cm^{-1}.

***cis*-8-Methoxy-4-phenyl-2,3,3a,4,5,9b-hexahydrofuro[3,2-*c*]quinoline**[5b] **(2g):** Pale yellow solid, m.p. 132 – 133 °C, ^{1}H NMR ($CDCl_3$): $\delta = 1.55$ (m, 1H), 2.20 (m, 1H), 2.75 (m, 1H), 3.65 – 3.85 (m, 3H), 3.78 (s, 3H), 4.62 (d, $J = 2.8$ Hz, 1H), 5.22 (d, $J = 8.0$ Hz, 1H), 6.50 (d, $J = 8.6$ Hz, 1H), 6.74 (dd, $J = 8.6$ and 2.8 Hz, 1H), 6.94 (d, $J = 2.8$ Hz, 1H), 7.25 – 7.45 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 24.3$, 45.8, 55.7, 57.9, 66.7, 76.3, 113.8, 115.9, 116.3, 123.5, 126.5, 127.4, 128.6, 139.0, 142.5, 153.0; EIMS: $m/z = 281$ M^+, 236, 206, 160, 141, 115, 91, 41; IR (KBr): $\nu_{max} = 3305$, 2985, 2875, 1611, 1518, 1229, 1049 cm^{-1}.

***cis*-5-Phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[5b] **(4h):** Solid, m.p. 129 – 130 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.25$ (m, 1H), 1.50 – 1.70 (m, 3H), 2.15 – 2.20 (m, 1H), 3.40 (dt, $J = 11.3$ and 2.4 Hz, 1H), 3.55 (dd, $J = 11.3$ and 2.4 Hz, 1H), 3.80 (brs, 1H, NH), 4.70 (d, $J = 2.7$ Hz, 1H), 5.30 (d, $J = 5.6$ Hz, 1H), 6.55 (d, $J = 8.0$ Hz, 1H), 6.78 (t, $J = 8.0$ Hz, 1H), 7.05 (t, $J = 7.8$ Hz, 1H), 7.25 – 7.45 (m, 6H); ^{13}C NMR ($CDCl_3$): $\delta =$ 18.2, 25.7, 39.0, 59.3, 60.7, 72.8, 114.4, 118.0, 120.4, 126.9, 127.5, 127.7, 128.0, 128.4, 141.2, 145.2; EIMS: $m/z = 265$ M^+, 234, 220, 194, 129, 117, 91, 77; IR (KBr): $\nu_{max} = 3340$, 2945, 2860, 1610, 1491, 1053 cm^{-1}.

***trans*-5-Phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[3a] **(5h):** Pale yellow oil; ^{1}H NMR ($CDCl_3$): $\delta =$ 1.25 – 1.60 (m, 3H), 1.80 – 1.90 (m, 1H), 2.00 – 2.10 (m, 1H), 3.75 (dt, $J = 11.5$ and 2.5 Hz, 1H), 4.00 – 4.10 (m, 2H), 4.40 (d, $J = 2.5$ Hz, 1H), 4.75 (d, $J = 10.8$ Hz, 1H), 6.50 (d, $J = 8.0$ Hz, 1H), 6.70 (t, $J = 7.5$ Hz, 1H), 7.10 (t, $J = 7.5$ Hz, 1H), 7.25 (d, $J = 8.0$ Hz, 1H), 7.40 – 7.55 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta =$ 22.3, 24.4, 39.3, 55.0, 69.2, 74.5, 114.2, 117.4, 120.5, 127.7, 127.9, 128.5, 129.4, 130.9, 142.2, 144.5; IR (KBr): $\nu_{max} = 3325$, 2941, 2864, 1607, 1487, 1048 cm^{-1}.

***cis*-9-Chloro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[5b] **(4i):** Solid, m.p. 170 – 171 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.25$ (m, 1H), 1.50 (m, 3H), 2.10 (m, 1H) 3.45 (m, 1H), 3.60 (m, 1H), 3.85 (brs, 1H), 4.65 (d, $J = 2.7$ Hz, 1H), 5.25 (d, $J = 5.7$ Hz, 1H), 6.50 (d, $J = 8.0$ Hz, 1H), 7.05 (dd, $J = 8.0$, 0.8 Hz, 1H), 7.30 – 7.40 (m, 6H); EIMS: $m/z = 301$ M^{+2},298, 240, 220, 191, 165, 131, 119, 69; IR (KBr): $\nu = 3325$, 2965, 2858, 1605, 1498, 1247, 1051 cm^{-1}.

***trans*-9-Chloro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[5b] **(5i):** Solid, m.p.124 – 126 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.30$ (m, 1H), 1.45 (m, 1H), 1.65 (m, 1H), 1.75 (m, 1H), 2.05 (m, 1H), 3.65 (dt, $J = 11.0$, 2.3 Hz, 1H), 4.05 (m, 2H), 4.35 (d, $J = 2.7$ Hz, 1H), 4.65 (d, $J = 10.8$ Hz, 1H), 6.45 (d, $J =$ 8.0 Hz ,1H), 7.05 (dd, $J = 8.0$, 2.0 Hz, 1H), 7.20 (d, $J = 2.2$ Hz, 0H), 7.25 – 7.40 (m, 5H); IR (KBr): $\nu_{max} = 3325$, 2945, 2860, 1608, 1495, 1250, 1049 cm^{-1}.

***cis*-5-(4-Fluorophenyl)-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[5e] **(4j):** White solid, m.p. 174 – 175 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.30$ (m, 1H), 1.45 – 1.60 (m, 3H), 2.12 (m, 1H), 3.40 (dt, $J = 11.5$ and 2.5 Hz, 1H), 3.56 (dd, $J = 11.5$ and 2.5 Hz, 1H), 3.75 (brs, 1H, NH), 4.65 (d, $J = 2.7$ Hz, 1H), 5.28 (d, $J = 5.7$ Hz, 1H), 6.52 (d, $J = 8.0$ Hz, 1H), 6.75 (dd, $J =$ 8.0 and 2.5 Hz, 1H), 7.05 (m, 3H), 7.40 (m, 3H); EIMS: $m/z =$ 283 M^+, 239, 225, 198, 150, 148, 91; IR (KBr): $\nu_{max} = 3325$, 2947, 2860, 1608, 1493, 1252, 1045 cm^{-1}.

***trans*-5-(4-Fluorophenyl)-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[5e] **(5j):** White solid, m.p. 143 – 144 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.30 – 1.35$ (m, 1H), 1.40 – 1.45 (m, 1H), 1.60 – 1.70 (m, 1H), 1.75 – 1.85 (m, 1H), 2.05 (m, 1H), 3.70 (dt, $J = 11.5$ and $J = 2.5$ Hz, 1H), 3.95 (brs, 1H, NH), 4.10 (d, $J =$ 2.5 Hz, 1H), 4.35 (d, $J = 2.7$ Hz, 1H), 4.70 (d, $J = 10.8$ Hz, 1H), 6.48 (d, $J = 8.0$ Hz, 1H), 6.68 (dd, $J = 8.0$ and 2.5 Hz, 1H), 7.05 (m, 3H), 7.18 (m, 1H), 7.38 (m, 2H); IR (KBr): $\nu_{max} = 3327$, 2950, 2870, 1610, 1495, 1250, 1049 cm^{-1}.

***cis*-9-Fluoro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[5e] **(4k):**; ^{1}H NMR ($CDCl_3$): $\delta = 1.28 – 1.40$ (m, 1H), 1.40 – 1.60 (m, 3H), 2.10 – 2.20 (m, 1H) 3.35 (dt, 1H, $J = 11.7$ and 2.6 Hz), 3.55 (dd, 1H, $J = 11.7$ and 2.6 Hz), 3.65 (brs, 1H, NH), 4.60 (d, $J = 2.7$ Hz, 1H), 5.20 (d, $J = 5.7$ Hz, 1H), 6.45 (dd, $J = 9.4$ and 4.3 Hz, 1H), 6.70 (dt, $J = 8.3$ and 2.0 Hz, 1H), 7.10 (dd, $J = 8.3$ and 2.0 Hz, 1H) 7.25 – 7.45 (m, 5H); EIMS: $m/z = 283$ M^+, 233, 224, 194, 129, 91, 41; IR (KBr): $\nu_{max} = 3350$, 2970, 2860, 1610, 1460, 1051 cm^{-1}.

***trans*-9-Fluoro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[5e] **(5k):** Liquid; ^{1}H NMR ($CDCl_3$): $\delta =$ 1.30 – 1.40 (m, 1H), 1.50 – 1.60 (m, 1H), 1.68 – 1.70 (m, 1H), 1.80 – 1.95 (m, 1H), 2.10 – 2.15 (m, 1H), 3.70 (dt, $J = 11.6$ and 2.6 Hz, 1H), 3.90 (brs, 1H), 4.10 (dd, $J = 11.5$ and 2.5 Hz, 1H), 4.30 (d, $J = 2.6$ Hz, 1H), 4.60 (d, $J = 10.7$ Hz, 1H), 6.40 (dd, $J =$ 9.4 and 4.3 Hz, 1H), 6.75 (dt, $J = 8.3$ and 2.0 Hz, 1H), 6.90 (dd, $J = 8.3$ and 2.0 Hz, 1H) 7.25 – 7.50 (m, 5H); IR (KBr): $\nu_{max} =$ 3350, 2950, 2875, 1608, 1478, 1049 cm^{-1}.

***cis*-5-(4-Nitrophenyl)-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[3a] **(4l):** Solid; m.p. 189 – 190 °C; ^{1}H NMR ($CDCl_3$): $\delta = 1.15 – 1.27$ (m, 1H), 1.35 – 1.60 (m, 3H), 2.10 – 2.15 (m, 1H), 3.40 (dt, $J = 11.4$ and 2.7 Hz, 1H), 3.60 (dd, $J = 11.4$ and 2.7 Hz, 1H), 3.55 (brs, 1H), 4.80 (d, $J = 2.8$ Hz, 1H), 5.30 (d, $J = 5.7$ Hz, 1H), 6.60 (d, $J = 8.0$ Hz, 1H), 6.85 (t, $J = 7.8$ Hz, 1H), 7.10 (t, $J = 7.8$ Hz, 1H), 7.40 (d, $J = 8.0$ Hz, 1H), 7.60 (d, $J = 8.2$ Hz, 2H), 8.25 (d, $J = 8.2$ Hz, 2H); EIMS: $m/z = 310$ M^+, 280, 252, 206, 189, 130, 115, 77; IR (KBr): $\nu_{max} = 3347$, 2970, 2845, 1618, 1502, 1047 cm^{-1}.

***trans*-5-(4-Nitrophenyl)-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[3a] **(5l):** Solid; m.p. 169 – 170 °C; ^{1}H NMR

($CDCl_3$): δ = 1.30 – 1.40 (m, 1H), 1.45 – 1.50 (m, 1H), 1.60 – 1.70 (m, 1H), 1.80 – 1.95 (m, 1H), 2.05 – 2.15 (m, 1H), 3.70 (t, *J* = 11.5 Hz, 1H), 4.05 – 4.15 (m, 2H), 4.40 (d, *J* = 2.5 Hz, 1H), 4.80 (d, *J* = 10.5 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 6.78 (t, *J* = 7.8 Hz, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 2H), 8.25 (d, *J* = 8.2 Hz, 2H); IR (KBr): ν_{max} = 3350, 2950, 2875, 1623, 1498, 1051 cm^{-1}.

***cis*-9-Methyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[3c] **(4m):** Solid; m.p. 129 – 130 °C; ^1H NMR ($CDCl_3$): δ = 1.15 – 1.25 (m, 1H), 1.32 – 1.60 (m, 3H), 2.05 – 2.15 (m, 4H), 3.35 (dt, *J* = 11.4 and 2.7 Hz, 1H), 3.50 (dd, *J* = 11.4 and 2.7 Hz, 1H), 3.55 (brs, 1H), 4.60 (d, *J* = 2.7 Hz, 1H), 5.25 (d, *J* = 5.6 Hz, 1H), 6.50 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 7.25 – 7.40 (m, 6H); EIMS: *m/z* = 279 M^+, 219, 158, 144, 105, 91; IR (KBr): ν_{max} = 3345, 2970, 2845, 1610, 1505, 1038 cm^{-1}.

***trans*-9-Methyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[3c] **(5m)**: Oil; ^1H NMR ($CDCl_3$): δ = 1.30 – 1.40 (m, 1H), 1.45 – 1.50 (m, 1H), 1.60 – 1.70 (m, 1H), 1.80 – 1.95 (m, 1H), 2.05 – 2.15 (m, 4H), 3.70 (dt, *J* = 11.5 and 2.4 Hz, 1H), 3.90 (brs, 1H), 4.15 (dd, *J* = 11.5 and 2.4 Hz, 1H), 4.35 (d, *J* = 2.8 Hz, 1H), 4.65(d, *J* = 10.5 Hz, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 6.95 (dd, *J* = 8.0, 1.2 Hz, 1H), 7. 0 (d, *J* = 1.2 Hz, 1H), 7.30 – 7.45 (m, 5H); IR (KBr): ν_{max} = 3350, 2957, 2865, 1611, 1499, 1041 cm^{-1}.

***cis*-5-(4-Chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[6d] **(4n):** Solid, m.p. 169 – 170 °C; ^1H NMR ($CDCl_3$): δ = 1.23 – 1.38 (m, 1H), 1.40 – 1.60 (m, 3H), 2.10 – 2.20 (m, 1H) 3.45 (dt, *J* = 11.5 and 2.5 Hz, 1H), 3.60 (dd, *J* = 11.5 and 2.5 Hz, 1H), 3.80 (brs, 1H, NH), 4.70 (d, *J* = 2.8 Hz, 1H), 5.30 (d, *J* = 5.7 Hz, 1H), 6.60 (d, *J* = 8.2 Hz, 1H), 6.80 (t, *J* = 7.8 Hz, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 7.30 – 7.45 (m, 5H); EIMS: *m/z* = 299 M^+, 268, 240, 229, 188, 156, 130, 115, 77; IR (KBr): ν_{max} = 3354, 2950, 2875, 1630, 1473, 1053 cm^{-1}.

***trans*-5-(4-Chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[6dd] **(5n):** Solid; m.p. 122 – 123 °C; ^1H NMR ($CDCl_3$): δ = 1.25 – 1.50 (m, 2H), 1.60 – 1.70 (m, 1H), 1.80 – 190 (m, 1H), 2.0 – 2.10 (m, 1H), 3.70 (dt, *J* = 11.5 and 2.5 Hz, 1H), 3.95 (brs, NH, 1H), 4.05 – 4.10 (m, 1H), 4.35 (d, *J* = 2.7 Hz, 1H), 4.70 (d, *J* = 10.8 Hz, 1H), 6.50 (d, *J* = 8.2 Hz, 1H), 6.70 (t, *J* = 8.0 Hz, 1H), 7.10 (t, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 7.30 – 7.40 (m, 4H); IR (KBr): ν_{max} = 3351, 2945, 2865, 1628, 1471, 1055 cm^{-1}.

***cis*-9-Methoxy-5-phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[5b] **(4o):** Solid; m.p. 145 – 146 °C; ^1H NMR ($CDCl_3$): δ = 1.28 – 1.40 (m, 1H), 1.40 – 1.60 (m, 3H), 2.10 – 2.20 (m, 1H) 3.45 (dt, *J* = 11.8 and 2.7 Hz, 1H), 3.60 (m, 2H), 3.80 (s, 3H), 4.65 (d, *J* = 2.7 Hz, 1H), 5.30 (d, *J* = 5.8 Hz, 1H), 6.50 (d, *J* = 8.0 Hz, 1H), 7.0 (d, *J* = 2.0 Hz, 1H), 7.18 (dd, *J* = 8.0 and 2.0 Hz, 1H), 7.25 – 7.50 (m, 5H); EIMS: *m/z* = 295 M^+, 237, 225, 160, 142, 117, 91; IR (KBr): ν_{max} = 3347, 2961, 2868, 1617, 1520, 1476, 1051 cm^{-1}.

***trans*-9-Methoxy-5-phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline**[5b] **(5o):** Solid, m.p. 99 – 100 °C (Lit. 93 – 95 °C); ^1H NMR ($CDCl_3$): δ = 1.25 – 1.50 (m, 3H), 1.60 – 1.70 (m, 1H), 1.80 – 190 (m, 1H), 2.0 – 2.10 (m, 1H), 3.45 – 3.70 (m, 3H), 3.80 (brs, 1H), 4.0 (d, *J* = 11.0 and 2.3 Hz, 1H), 4.2 (d, *J* = 2.3 Hz, 1H), 4.50 (d, *J* = 10.5 Hz, 1H), 6.30 (d, *J* = 8.0 Hz, 1H), 6.60 (dd, *J* = 8.0 and 1.8 Hz, 1H), 6.65 (d, *J* = 1.8 Hz, 1H), 7.10 – 7.45 (m, 5H); IR (KBr): ν_{max} = 3353, 2957, 2863, 1621, 1479, 1053 cm^{-1}.

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