InCl$_3$ as an efficient catalyst for intramolecular imino Diels–Alder reactions: synthesis of tetrahydrochromanoquinolines

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Dedicated to Professor S. Swaminathan on his 80$^{th}$ anniversary
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Abstract
InCl$_3$ is found to be an efficient catalyst for the Intramolecular Imino Diels–Alder (IMIDA) reaction of aldimines derived from aromatic amines and $O$-allyl derivatives of salicylaldehydes to afford the corresponding tetrahydrochromano[4,3-$b$]quinolines in excellent yields under mild conditions and short reaction times.

Keywords: InCl$_3$, intramolecular imino Diels–Alder reaction, tetrahydrochromano-quinolines

Introduction
The [4+2] Diels–Alder reaction between $N$-arylimines and electron-rich dienophiles is a powerful synthetic tool for constructing $N$-containing six-membered heterocyclic compounds as well as in the synthesis of natural products$^1$ including tetrahydroquinoline derivatives.$^2$ Tetrahydroquinoline derivatives are found to exhibit a wide range of biological activities,$^3$ including psychotropic, anti-allergic, anti-inflammatory and estrogenic behaviour. In addition, intramolecular imino Diels–Alder reactions provide multiple opportunities for the stereoselective construction of tetrahydroquinolines. The inter- and intramolecular imino Diels–Alder reaction of imines with electron rich dienophiles has been catalyzed by Lewis acids such as BF$_3$·Et$_2$O,$^{3b,4}$ transition metal carbonyls,$^5$ lanthanide triflate$^6$ as well as Brønsted acids such as TFA$^7$ and $p$-TsOH.$^8$ It has previously been reported that for the intramolecular imino Diels–Alder reaction of aldimes derived from aromatic amines and $O$-allyl derivatives of salicylaldehyde, Yb(OTf)$_3$, TFA,$^9$ BiCl$_3$,$^{10}$ LiClO$_4$,$^{11}$ are effective catalysts. Recently, we have reported from our laboratory triphenylphosphonium perchlorate$^{12}$ as an efficient catalyst for this useful transformation. However, some of these reagents suffer from one or other disadvantages such as strongly acidic nature, nucleophilic character (ClO$_4^-$), high cost, long reaction times, and low yields. Moreover, many Lewis acids are either decomposed or deactivated due to the formation of water during
imine formation. InCl₃ is readily available and found to retain its activity even in the presence of amines, water and other active functional groups such as NO₂, COOH, CN in the substrates. In the imino Diels–Alder reactions, it is necessary to activate the imine double bond. This is due to the low electrophilicity of the imines as compared to the corresponding carbonyl compounds. The activation of the imine can be achieved by coordination of InCl₃ at the imine nitrogen.

Indium trichloride has been effectively employed as a Lewis acid catalyst for various transformations in organic synthesis, such as aldol condensations, imino Diels–Alder reactions, rearrangement of epoxides and Prins-type cyclization. In continuation of our research interest on the catalytic applications of InCl₃, we herein describe another remarkable catalytic activity of InCl₃ in the synthesis of tetrahydrochromano[4,3-b]quinolines from aromatic amines and O-allyl derivatives of salicylaldehydes via the intramolecular [4+2] cyclization of imines in acetonitrile at room temperature in shorter time with excellent yields.

In the presence of 20 mol% InCl₃, arylimine derived in situ from aniline and the O-prenyl derivative of salicylaldehyde in acetonitrile at room temperature gave tetrahydrochromanoquinolines in 87–98% yield as a mixture of diastereoisomers 3 and 4 (Scheme 1). In all cases, the products were obtained as a mixture of cis and trans isomers in a 1:1 ratio, determined from the ¹H NMR spectrum of the crude product. These isomers were isolated by column chromatography on silica gel. Several other aromatic imines underwent smooth cycloaddition to give the corresponding tetrahydrochromanoquinolines in good yields (Table 1). The cis- and trans-stereochemistry of the products was assigned on the basis of coupling constants of the protons in the ¹H NMR spectra and also by direct comparison with literature data wherever available.

\[ \text{R'NH} + \text{R'O} = \text{CHO} \xrightarrow{\text{InCl}_3 (20\text{mol\%})} \text{CH}_3\text{CN, r.t.}} \]

Scheme 1
Table 1. InCl₃ catalyzed synthesis of tetrahydrochromano[4,3-b]quinolines via IMIDA reaction

<table>
<thead>
<tr>
<th>Entry</th>
<th>R (1a-j)</th>
<th>R’ (2a-j)</th>
<th>Time (min)</th>
<th>Yield (%)ᵇ</th>
<th>Overall yield (%) (3 + 4)</th>
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<tbody>
<tr>
<td>a</td>
<td>H</td>
<td>H</td>
<td>5</td>
<td>52</td>
<td>46  98</td>
</tr>
<tr>
<td>b</td>
<td>3-CH₃O</td>
<td>H</td>
<td>5</td>
<td>45</td>
<td>49  94</td>
</tr>
<tr>
<td>c</td>
<td>H</td>
<td>2-CH₃</td>
<td>8</td>
<td>44</td>
<td>48  92</td>
</tr>
<tr>
<td>d</td>
<td>H</td>
<td>4-CH₃O</td>
<td>10</td>
<td>47</td>
<td>49  96</td>
</tr>
<tr>
<td>e</td>
<td>H</td>
<td>4-Br</td>
<td>10</td>
<td>45</td>
<td>48  93</td>
</tr>
<tr>
<td>f</td>
<td>H</td>
<td>4-NO₂</td>
<td>15</td>
<td>42</td>
<td>47  89</td>
</tr>
<tr>
<td>g</td>
<td>H</td>
<td>4-CO₂H</td>
<td>15</td>
<td>42</td>
<td>49  91</td>
</tr>
<tr>
<td>h</td>
<td>H</td>
<td>4-CN</td>
<td>10</td>
<td>46</td>
<td>41  87</td>
</tr>
<tr>
<td>i</td>
<td>5-Cl</td>
<td>H</td>
<td>5</td>
<td>50</td>
<td>44  94</td>
</tr>
<tr>
<td>j</td>
<td>H</td>
<td>-C₄H₄⁻</td>
<td>10</td>
<td>40ᵈ</td>
<td>48ᵈ  88</td>
</tr>
</tbody>
</table>

ᵃ All the products were characterized by IR, ¹H, ¹³C NMR and mass spectroscopy and by comparison with reported data.¹²
ᵇ Yield refers to the 1:1 mixture of diastereoisomers of products 3 and 4 isolated in pure form by column chromatography.
ᶜ 2j = Naphthylamine.

Results and Discussion

We found that the intramolecular cyclization can be carried out very conveniently as a one-pot reaction starting from the O-allyl salicylaldehydes and arylamines without isolation of the intermediate imines. Both imine formation and cyclization could be achieved in one sequential transformation. This would be a highly desirable method for the preparation of hetero-polycyclic systems, in which isolation and purification of intermediates could be avoided.¹⁹ It can be concluded that InCl₃ is an efficient catalyst for cyclization of aromatic amines with O-allyl salicylaldehyde derivatives in a one-pot reaction to afford tetrahydrochromanoquinolines. In addition to its efficiency, simplicity and mild reaction conditions and only a small amount (20 mol%) is needed. This method provides high yields of products in short reaction times, making it a useful process for the synthesis of hetero-polycyclic systems.
**Experimental Section**

**General experimental procedure A**

20 mol% InCl$_3$ (0.6 mmol, 206 mg) was added to a mixture of $O$-allyl salicylaldehyde 1a (3 mmol, 570 mg) and arylamine 2a (1 equiv. 279 mg) in acetonitrile (20 mL). The reaction mixture was stirred at room temperature for 5 min. On completion, as indicated by TLC, the mixture was quenched with water and extracted with ethyl acetate, the organic layer was washed with brine and dried over Na$_2$SO$_4$. The solvent was evaporated in vacuo and the crude product was chromatographed on silica gel (EtOAc: hexane mixture) to afford analytically pure diastereoisomers 3 and 4 in 98% yield.

**cis-7,7-Dimethyl-(6aS,12aR)-6a,7,12,12a-tetrahydro-6H-chromano[4,3-b]quinoline (3a).** Prepared from $O$-prenyl derivative of salicylaldehyde 1a (3 mmol) and aryl amine 2a (1 eq.) by following procedure A. The pure 3a was obtained as a yellow (coloured solid from the first fraction. Mp: 123-125 °C. Yield: 52%. IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$ 3396 (NH), 3022, 2968, 2922, 2844, 1605, 1585, 1492, 1299, 1234, 748.$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.37 (s, 3H, CH$_3$), 1.45 (s, 3H, CH$_3$), 2.00 (dt, 1H, H$_6$a, $J = 11.7$, 3.9 Hz), 3.82 (dd, 2H, H$_6$, $J = 11.7$, 2.4 Hz, including NH), 4.25 (dd, 1H, H$_6'$, $J = 10.7$, 2.4 Hz), 4.55 (d, 1H, H12a, $J = 2.9$ Hz), 6.40 (d, 1H, Ar, $J = 7.3$ Hz), 6.65 (t, 1H, Ar, $J = 7.3$ Hz) 6.86-7.25 (m, 6H, Ar). 13C NMR (100 MHz, CDCl$_3$) $\delta$ 25.6, 33.3, 34.0, 40.6, 45.6, 63.6, 113.4, 116.8, 117.1, 120.3, 123.9, 125.7, 126.8, 127.2, 129.3, 129.5, 140.4, 153.9. MS $m/z$: 265 (M$^+$). Anal. Calcd. for C$_{18}$H$_{19}$NO: C, 81.47; H, 7.22; N, 5.28 Found: C, 81.28; H, 7.29; N, 5.23.

**trans-7,7-Dimethyl-(6aS,12aS)-6a,7,12,12a-tetrahydro-6H-chromano[4,3-b]quinoline (4a).** Prepared from $O$-prenyl derivative of salicylaldehyde 1a (3 mmol) and aryl amine 2a (1 eq.) by following procedure A. The pure 4a was obtained as a yellow coloured solid from the second fraction. Yield: 46% Mp: 114-116 °C. IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$ 3345 (NH), 3015, 2953, 2918, 2842, 1611, 1581, 1483, 1292, 1218, 742.$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.21 (s, 3H, CH$_3$), 1.47 (s, 3H, CH$_3$), 2.08 (td, 1H, H$_6$a, $J = 10.7$, 2.9 Hz), 3.93 (t, 2H, H$_6$, $J = 11.2$ Hz, including NH), 4.42 (d, 1H, H$_3$, $J = 10.7$), 4.48 (dd, 1H, H$_6'$, $J = 10.7$, 2.9 Hz), 6.67 (d, 1H, J = 7.3 Hz), 6.78 (t, 1H, J = 7.8 Hz), 6.88 (d, 1H, J = 8.3 Hz), 6.98-7.35 (m, 5H, Ar). 13C NMR (100 MHz, CDCl$_3$) $\delta$ 27.2, 27.9, 34.4, 43.8, 47.6, 65.5, 112.9, 116.1, 117.0, 118.8, 120.8, 123.7, 125.6, 126.8, 128.3, 131.4, 143.0, 154.1. MS $m/z$: 265 (M$^+$).

**cis-4-Methoxy-7,7-dimethyl-(6aS,12aR)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (3b).** Prepared from $O$-prenyl derivative of 3-CH$_3$O-salicylaldehyde 1b (3 mmol) and aryl amine 2b (1 eq.) by following procedure A. The pure 3b was obtained as a yellow coloured solid from the first fraction. Yield: 45% Mp: 112-114 °C. IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$ 3392 (NH), 3018, 2965, 2925, 2839, 1612, 1578, 1483, 1291, 1242, 745.$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.35 (s, 3H, CH$_3$), 1.42 (s, 3H, CH$_3$), 2.01 (dt, 1H, H$_6$a, $J = 11.5$, 3.8 Hz), 3.80 (s, 3H, OCH$_3$), 3.84 (dd, 2H, H$_6$, $J = 11.5$, 2.7 Hz, including NH), 4.23 (dd, 1H, H$_6'$, $J = 11.2$, 2.7 Hz), 4.51 (d, 1H, H12a, $J = 2.8$ Hz), 6.52 (d, 1H, J = 7.8 Hz), 6.72-7.21 (m, 6H, Ar). 13C NMR (100 MHz,
trans-4-Methoxy-7,7-dimethyl-(6aS,12aS)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (4b). Prepared from O-prenyl derivative of 3-CH$_3$O- salicylaldehyde 1b (3 mmol) and aryl amine 2b (1 eq.) by following procedure A. The pure 4b was obtained as a yellow coloured solid from the second fraction. Yield: 49%. Mp: 120-122 °C. IR (KBr) $\nu_{max}$ cm$^{-1}$ 3385 (NH), 3015, 2923, 2834, 1611, 1573, 1482, 1298, 1142, 748. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.22 (s, 3H, CH$_3$), 1.43 (s, 3H, CH$_3$), 2.05 (td, 1H, H$_6$a, $J$ = 10.8, 3.0 Hz), 3.82 (s, 3H, OCH$_3$), 3.94 (t, 2H, H$_6$, $J$ = 11.1 Hz, including NH), 4.44 (d, 1H, H$_{12}$a, $J$ = 10.8 Hz), 4.46 (dd, 1H, H$_6'$, $J$ = 10.8, 3.0 Hz), 6.65 (d, 1H, H$_6$, $J$ = 8.2 Hz), 6.75-7.25 (m, 6H, Ar). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 24.8, 32.3, 34.5, 40.6, 43.6, 45.3, 63.1, 114.7, 116.5, 118.1, 120.2, 124.5, 125.3, 126.5, 126.9, 129.2, 129.9, 140.5, 154.3. MS $m/z$: 295 (M$^+\$). Anal. Calcd. for C$_{19}$H$_{21}$NO$_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.31; H, 7.12; N, 4.70.

cis-7,7,11-Trimethyl-(6aS,12aR)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (3c). Prepared from O-prenyl derivative of salicylaldehyde 1c (3 mmol) and 2-CH$_3$-aryl amine 2c (1 eq.) by following procedure A. The pure 3c was obtained as a yellow coloured solid from the first fraction. Yield: 44%. Mp: 127-129 °C IR (KBr) $\nu_{max}$ cm$^{-1}$ 3392 (NH), 3012, 2953, 2915, 2875, 1605, 1506, 1489, 1246, 752. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.27 (s, 3H, CH$_3$), 1.42 (s, 3H, CH$_3$), 1.97 (dt, 1H, H$_6$a, $J$ = 10.7 Hz), 2.15 (s, 3H, ArCH$_3$), 3.81 (t, 2H, H$_6$, $J$ = 10.7 Hz, including NH), 4.19 (dd, 1H, H$_6'$, $J$ = 10.8, 3.3 Hz), 4.45 (d, 1H, H$_{12}$a, $J$ = 3.3 Hz), 6.25-7.22 (m, 7H, Ar). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 25.4, 31.3, 34.7, 40.6, 43.6, 45.3, 63.1, 114.7, 116.5, 118.1, 120.2, 124.5, 125.3, 126.7, 126.8, 129.3, 129.8, 140.1, 154.1. MS $m/z$: 279 (M$^+\$). Anal. Calcd. for C$_{19}$H$_{21}$NO: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.72; H, 7.51; N, 5.08.

trans-7,7,11-Trimethyl-(6aS,12aS)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (4c). Prepared from O-prenyl derivative of salicylaldehyde 1c (3 mmol) and 2-CH$_3$-aryl amine 2c (1 eq.) by following procedure B. The pure 4c was obtained as a yellow coloured solid from the second fraction. Yield: 48%. Mp: 119-121 °C IR (KBr) $\nu_{max}$ cm$^{-1}$ 3315 (NH), 2955, 2873, 1603, 1517, 1481, 1244, 752. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.31 (s, 3H, CH$_3$), 1.42 (s, 3H, CH$_3$), 2.00 (td, 1H, H$_6$a, $J$ = 11.0, 3.2 Hz), 2.30 (s, 3H, ArCH$_3$), 3.60 (brs, 1H, NH), 3.82 (t, 1H, H$_6$, $J$ = 10.9 Hz), 4.21 (dd, 1H, H$_6'$, $J$ = 10.8, 3.2 Hz), 4.55 (d, 1H, H$_{12}$a, $J$ = 3.3 Hz), 6.21-7.38 (m, 7H, Ar). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 24.1, 31.4, 34.5, 40.1, 43.5, 45.4, 63.2, 114.6, 116.7, 118.2, 120.4, 124.5, 125.2, 126.5, 126.7, 129.2, 129.7, 140.2, 153.5. MS $m/z$: 279 (M$^+\$). Anal. Calcd. for C$_{19}$H$_{21}$NO: C, 77.31; H, 7.12; N, 4.70. Found: C, 77.19; H, 7.25; N, 4.78.

cis-7,7,11-Trimethyl-(6aS,12aR)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline-9-yl-methyl ether (3d). Prepared from O-prenyl derivative of salicylaldehyde 1d (3 mmol) and 4-CH$_3$O-aryl amine 2d (1 eq.) by following procedure A. The pure 3d was obtained as a yellow coloured solid from the first fraction. Yield: 47%. Mp: 135-137°C IR (KBr) $\nu_{max}$ cm$^{-1}$ 3315 (NH), 2955, 2873, 1603, 1517, 1481, 1244, 752. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.31 (s, 3H, CH$_3$), 1.42 (s, 3H, CH$_3$), 2.00 (td, 1H, H$_6$a, $J$ = 11.0, 3.2 Hz), 2.30 (s, 3H, ArCH$_3$), 3.60 (brs, 1H, NH), 3.82 (t, 1H, H$_6$, $J$ = 10.9 Hz), 4.21 (dd, 1H, H$_6'$, $J$ = 10.8, 3.2 Hz), 4.55 (d, 1H, H$_{12}$a, $J$ = 3.3 Hz), 6.21-7.38 (m, 7H, Ar). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 24.1, 31.4, 34.5, 40.1, 43.5, 45.4, 63.2, 114.6, 116.7, 118.2, 120.4, 124.5, 125.2, 126.5, 126.7, 129.2, 129.7, 140.2, 153.5. MS $m/z$: 279 (M$^+\$). Anal. Calcd. for C$_{19}$H$_{21}$NO: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.63; H, 7.62; N, 5.03.
trans-7,7-Dimethyl-(6aS,12aS)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline-9-yl-methyl ether (4d). Prepared from O-prenyl derivative of salicylaldehyde 1d (3 mmol) and 4-CH$_3$O-aryl amine 2d (1 eq.) by following procedure A. The pure 4d was obtained as a yellow coloured solid from the second fraction. Yield: 49%. Mp: 112-114 °C. IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$ 3317 (NH), 2958, 2881, 1609, 1521, 1478, 1241, 758. $^1$H NMR: (400 MHz, CDCl$_3$) $\delta$ 1.23 (s, 3H, CH$_3$), 1.43 (s, 3H, CH$_3$), 2.03 (td, 1H, H$_6$a, $J = 11.2$, 3.4 Hz), 3.82 (s, 3H, OCH$_3$), 3.91 (t, 2H, H$_6$, $J = 10.8$ Hz, including NH), 4.42 (dd, 1H, H$_6'$, $J = 11.2$, 3.5 Hz), 4.57 (d, 1H, H$_{12}$a, $J = 11.2$ Hz), 6.71-7.31 (m, 7H, Ar). $^{13}$C NMR: (100 MHz, CDCl$_3$) $\delta$ 26.8, 27.2, 41.7, 47.9, 54.1, 60.8, 64.9, 114.2, 116.6, 118.4, 120.7, 124.5, 125.8, 126.4, 126.9, 129.4, 129.6, 140.4, 154.5. MS $m/z$: 295 (M$^+$. Anal. Calcd. for C$_{19}$H$_{21}$NO$_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.21; H, 7.26; N, 4.65.

cis-7,7-Dimethyl-(6aS,12aR)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline-9-yl-bromide (3e). Prepared from O-prenyl derivative of salicylaldehyde 1e (3 mmol) and 4-Br-aryl amine 2e (1 eq.) by following procedure B. The pure 3e was obtained as a yellow coloured solid from the first fraction. Yield: 45%. Mp: 143-145 °C. IR: (KBr) $\nu_{\text{max}}$ cm$^{-1}$ 3375 (NH) 2962, 2891, 1605, 1523, 1463, 1223, 745. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.41 (s, 3H, CH$_3$), 1.52 (s, 3H, CH$_3$), 1.98 (dt, 1H, H$_6$a, $J = 10.8$, 3.5 Hz), 3.82 (t, 1H, H$_6$, $J = 10.3$ Hz), 3.83 (brs, 1H, NH), 4.30 (dd, 1H, H$_6'$, $J = 10.5$, 3.3 Hz), 4.60 (d, 1H, H$_{12}$a, $J = 3.5$ Hz), 6.51-7.38 (m, 7H, Ar). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 27.3, 27.6, 43.8, 47.9, 60.3, 65.8, 112.5, 112.8, 113.5, 117.1, 120.3, 120.7, 125.9, 129.9, 132.3, 132.8, 140.6, 154.6. MS $m/z$: 344 (M$^+$), 346 (M$^+$2) Anal. Calcd. for C$_{18}$H$_{18}$NO: C, 62.80; H, 5.27; N, 4.07. Found: C, 62.91; H, 5.20; N, 4.12.

cis-7,7-Dimethyl-9-yl-nitro-(6aS,12aR)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (3f). Prepared from O-prenyl derivative of salicylaldehyde 1f (3 mmol) and 4-O$_2$N-aryl amine 2f (1 eq.) by following procedure A. The pure 3f was obtained as a yellow coloured solid from the first fraction. Yield: 42%. Mp: 184-186 °C. IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$ 3363 (NH), 3081,
2969, 2936, 2878, 1606, 1559, 1522, 1467, 1327, 1226, 1124, 1018, 755. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.37 (s, 3H), 1.53 (s, 3H), 2.10 (dt, 1H, H$_6$a, $J$ = 12.0, 2.3 Hz), 3.57 (t, 2H, H$_6$, $J$ = 12.0 Hz, including NH), 4.25 (dd, 1H, H$_6$' $J$ = 10.9, 2.3 Hz), 4.66 (d, 1H, H$_{12}$a, $J$ = 3.5 Hz), 6.36 (d, 1H, $J$ = 8.6 Hz), 6.88 (d, 1H, $J$ = 8.6 Hz), 6.95-7.02 (m, 2H), 7.25-7.28 (m, 1H), 7.91 (dd, 1H, $J$ = 9.2, 2.3 Hz), 8.09 (d, 1H, $J$ = 6.3 Hz). 13C NMR (100 MHz, CDCl$_3$) $\delta$ 25.3, 32.9, 33.7, 39.7, 46.4, 63.1, 112.5, 117.3, 121.0, 122.1, 122.9, 124.7, 125.9, 129.4, 130.3, 138.2, 146.3, 153.9. MS m/z: 310 (M$^+$). Anal. Calcd. for C$_{18}$H$_{18}$N$_2$O$_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.59; H, 5.91; N, 9.09.

trans-7,7-Dimethyl-9-yl-nitro-(6aS,12aS)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (4f). Prepared from O-prenyl derivative of salicylaldehyde 1f (3 mmol) and 4-O$_2$N-aryl amine 2f (1 eq.) by following procedure A. The pure 4f was obtained as a yellow coloured solid from the second fraction. Yield: 47%. Mp: 175-177 °C. IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$ 3355 (NH), 3025, 2961, 2915, 1618, 1575, 1502, 1285, 1225, 1015, 759. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.31 (s, 3H, CH$_3$), 1.61 (s, 3H, CH$_3$), 2.03 (td, 1H, H$_6$a, $J$ = 11.8, 2.9 Hz), 3.58 (t, 2H, H$_6$, $J$ = 11.7 Hz, including NH), 4.58 (d, 1H, H$_{12}$a, $J$ = 10.9 Hz), 4.61 (dd, 1H, H$_6$' $J$ = 11.8, 3.0 Hz), 6.57 (d, 1H, $J$ = 7.6 Hz), 6.98 (d, 1H, $J$ = 7.6 Hz), 7.03-7.12 (m, 3H, Ar), 7.67 (t, 1H, Ar, $J$ = 7.83 Hz), 7.89 (s, 1H, Ar), 12.01 (s, 1H, COOH). 13C NMR (100 MHz, CDCl$_3$) $\delta$ 25.4, 31.8, 33.6, 39.8, 46.5, 64.0, 112.5, 117.4, 121.5, 122.7, 122.9, 124.8, 125.9, 129.3, 130.5, 138.3, 146.3, 154.2. MS m/z: 310 (M$^+$). Anal. Calcd. for C$_{18}$H$_{18}$N$_2$O$_3$: C, 69.72; H, 5.81; N, 9.11.

cis-7,7-Dimethyl-9-yl-carboxy-(6aS,12aR)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (3g). Prepared from O-prenyl derivative of salicylaldehyde 1g (3 mmol) and 4-O$_2$C-aryl amine 2g (1 eq.) by following procedure A. The pure 3g was obtained as a yellow coloured solid from the first fraction. Yield: 42%. Mp: 189-191 °C. IR (KBr) $\nu_{\text{max}}$ cm$^{-1}$ 3349 (NH), 3023, 2965, 2917, 1602, 1573, 1501, 1281, 1227, 1021, 751. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.32 (s, 3H, CH$_3$), 1.67 (s, 3H, CH$_3$), 2.05 (td, 1H, H$_6$a, $J$ = 11.2, 3.5 Hz), 3.67 (t, 1H, H$_6$, $J$ = 10.8 Hz), 4.57 (d, 2H, H$_{12}$a, $J$ = 11.2 Hz, including NH), 4.61 (dd, 1H, H$_6$' $J$ = 10.7, 3.4 Hz), 6.60 (d, 1H, $J$ = 7.8 Hz), 6.88 (d, 1H, $J$ = 7.9 Hz), 7.05-7.14 (m, 3H, Ar), 7.71 (t, 1H, J =...
7.8 Hz), 7.91 (s, 1H), 12.02 (s, 1H, COOH). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 24.9, 31.2, 33.7, 39.4, 45.8, 64.2, 112.3, 117.5, 121.7, 122.3, 122.8, 124.3, 125.4, 129.3, 130.5, 138.1, 148.2, 153.9, 169.2. MS $m/z$: 309 (M$^+$). Anal. Calcd. for C$_{19}$H$_{19}$NO$_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.83; H, 6.13; N, 4.61.

cis-7,7-Dimethyl-9-yl-cyano-(6aS,12aR)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (3h). Prepared from O-prenyl derivative of salicylaldehyde 1h (3 mmol) and aryl amine 2h (1 eq.) by following procedure A. The pure 3h was obtained as a yellow coloured solid from the first fraction. Yield: 46%. Mp: 168-170 ºC. IR (KBr) $\nu$ max cm$^{-1}$ 3365 (NH), 3085, 2972, 2932, 2873, 2210 (CN), 1603, 1554, 1520, 1452, 1328, 1221, 1120, 1015, 754. $^1$H NMR (400 MHz, CDCl$_3$) δ 1.35 (s, 3H, CH$_3$), 1.54 (s, 3H, CH$_3$), 2.12 (dt, 1H, H$_6$a, $J$ = 12.0, 2.5 Hz), 3.54 (t, 2H, H$_6$, $J$ = 11.8 Hz, including NH), 4.27 (dd, 1H, H$_6'$, $J$ = 10.8, 2.4 Hz), 4.66 (d, 1H, H$_{12}$a, $J$ = 2.5 Hz), 6.87 (d, 1H, $J$ = 8.7 Hz), 6.94-7.01 (m, 2H), 7.25-7.29 (m, 2H), 7.81 (dd, 1H, $J$ = 9.3, 2.5 Hz), 8.05 (d, 1H, $J$ = 7.8 Hz). $^{13}$C NMR: (100 MHz, CDCl$_3$) δ 25.7, 32.4, 33.2, 40.1, 46.3, 63.2, 113.1, 117.3, 121.3, 122.3, 122.9, 124.7, 125.9, 129.5, 130.4, 138.4, 146.3, 154.3, 165.4. MS $m/z$: 290 (M$^+$). Anal. Calcd. for C$_{19}$H$_{18}$N$_2$O: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.50; H, 6.31; N, 9.72.

trans-7,7-Dimethyl-9-yl-cyano-(6aS,12aS)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (4h). Prepared from O-prenyl derivative of salicylaldehyde 1h (3 mmol) and aryl amine 2h (1 eq.) by following procedure A. The pure 4h was obtained as a yellow coloured solid from the second fraction. Yield: 41%. Mp: 153-155 ºC. IR (KBr) $\nu$ max cm$^{-1}$ 3363 (NH), 3080, 2975, 2937, 2871, 2212 (CN), 1605, 1559, 1530, 1457, 1321, 1228, 1017, 752. $^1$H NMR (400 MHz, CDCl$_3$) δ 1.32 (s, 3H, CH$_3$), 1.56 (s, 3H, CH$_3$), 2.21 (td, 1H, H$_6$a, $J$ = 11.5, 2.7 Hz), 3.57 (t, 2H, H$_6$, $J$ = 11.4 Hz, including NH), 4.31 (d, 1H, H-3, $J$ = 11.5 Hz), 4.47 (dd, 1H, H$_{12}$a, $J$ = 10.9, 2.7 Hz), 6.75 (d, 1H, $J$ = 8.8 Hz), 6.94-7.10 (m, 2H), 7.24-7.26 (m, 2H), 7.81 (dd, 1H, $J$ = 9.3, 2.5 Hz), 8.05 (d, 1H, $J$ = 7.8 Hz). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 24.8, 33.1, 33.5, 40.1, 45.9, 63.3, 113.1, 117.5, 121.4, 122.6, 122.8, 124.3, 125.7, 129.3, 130.4, 138.4, 146.3, 154.7, 167.4. MS $m/z$: 290 (M$^+$). Anal. Calcd. for C$_{19}$H$_{18}$N$_2$O: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.50; H, 6.31; N, 9.72.

cis-2-Chloro-7,7-dimethyl-(6aS,12aR)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (3i). Prepared from O-prenyl derivative of salicylaldehyde 1i (3 mmol) and aryl amine 2i (1 eq.) by following procedure A. The pure 3i was obtained as a yellow coloured solid from the first fraction. Yield: 50%. Mp: 152-154 ºC. IR (KBr) $\nu$ max cm$^{-1}$ 3355 (NH), 3080, 2975, 2935, 2867, 1602, 1551, 1525, 1213, 767. $^1$H NMR (400 MHz, CDCl$_3$) δ 1.32 (s, 3H, CH$_3$), 1.46 (s, 3H, CH$_3$), 1.98 (dt, 1H, H$_6$a, $J$ = 10.9, 2.4 Hz), 3.87 (t, 2H, H$_6$, $J$ = 10.8 Hz, including NH), 4.23 (dd, 1H, H$_6'$, $J$ = 10.8, 2.3 Hz), 4.63 (d, 1H, H$_{12}$a, $J$ = 3.4 Hz), 6.26-7.26 (m, 7H, Ar). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 27.1, 27.6, 43.5, 47.8, 60.3, 65.7, 112.3, 112.5, 114.3, 121.5, 124.3, 126.1, 127.2, 127.4, 129.1, 133.9, 142.2, 154.6. MS $m/z$: 299 (M$^+$), 301 (M+2). Anal. Calcd. for C$_{18}$H$_{18}$ClNO: C, 72.11; H, 6.05; N, 4.67. Found: C, 72.19; H, 6.01; N, 4.52.

trans-2-Chloro-7,7-dimethyl-(6aS,12aS)-6a,7,12,12a-tetrahydro-6H-chromeno[4,3-b]quinoline (4i). Prepared from O-prenyl derivative of salicylaldehyde 1i (3 mmol) and aryl
amine 2i (1 eq.) by following procedure A. The pure 4i was obtained as a yellow coloured solid from the second fraction. Yield: 44%. Mp: 117-119°C. IR (KBr) νmax cm⁻¹ 3354 (NH), 3072, 2978, 2931, 2868, 1601, 1523, 1214, 1017, 768. ¹H NMR (400 MHz, CDCl₃) δ 1.33 (s, 3H, CH₃), 1.75 (s, 3H, CH₃), 2.10 (td, 1H, H₆ₐ, J = 10.8, 2.9 Hz), 3.87 (t, 2H, H₆, J = 10.6 Hz, including NH), 4.39 (dd, 1H, H₆', J = 10.6, 2.8 Hz), 4.65 (d, 1H, H₁₂a, J = 10.8 Hz), 6.65-7.26 (m, 7H, Ar). IR (KBr) νmax cm⁻¹ 3382 (NH), 3091, 2965, 2932, 2891, 1604, 1552, 1465, 1325, 1213, 1015, 748. ¹H NMR (400 MHz, CDCl₃) δ 1.28 (s, 3H, CH₃), 1.41 (s, 3H, CH₃), 2.01 (td, 1H, H₆ₐ, J = 10.8, 3.8 Hz), 3.86 (t, 2H, H₆, J = 10.8 Hz, including NH), 4.44 (dd, 1H, H₆', J = 10.7, 3.5 Hz), 4.59 (d, 1H, H₁₂a, J = 3.8 Hz), 6.81-7.79 (m, 10H, Ar). ¹H NMR (500 MHz, CDCl₃) δ 26.1, 26.2, 40.5, 46.4, 60.3, 63.8, 113.9, 115.9, 116.9, 119.8, 120.4, 121.1, 122.3, 122.5, 123.9, 124.8, 125.3, 126.4, 127.8, 136.8, 146.9, 154.3. MS m/z: 315 (M⁺). Anal. Calcd. for C₂₂H₂₁NO: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.67; H, 6.79; N, 4.48.  

cis-7,7-Dimethyl-(6aS,14aR)-6a,7,14,14a-tetrahydro-6H-benzo|h|chromeno[4,3-b]quinoline (3j). Prepared from O-prenyl derivative of salicylaldehyde 1j (3 mmol) and aryl amine 2j (1 eq.) by following procedure A. The pure 3j was obtained as a yellow coloured solid from the first fraction. Yield: 40%. IR (neat) νmax cm⁻¹ 3382 (NH), 3091, 2965, 2932, 2891, 1604, 1552, 1465, 1325, 1213, 1015, 748. ¹H NMR (400 MHz, CDCl₃) δ 1.28 (s, 3H, CH₃), 1.41 (s, 3H, CH₃), 2.01 (td, 1H, H₆ₐ, J = 10.8, 3.8 Hz), 3.86 (t, 2H, H₆, J = 10.8 Hz, including NH), 4.44 (dd, 1H, H₆', J = 10.7, 3.5 Hz), 4.59 (d, 1H, H₁₂a, J = 3.8 Hz), 6.81-7.79 (m, 10H, Ar). ¹H NMR (400 MHz, CDCl₃) δ 26.1, 26.2, 40.5, 46.4, 60.3, 63.8, 113.9, 115.9, 116.9, 119.8, 120.4, 121.1, 122.3, 122.5, 123.9, 124.8, 125.3, 126.4, 127.8, 136.8, 146.9, 154.3. MS m/z: 315 (M⁺). Anal. Calcd. for C₂₂H₂₁NO: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.67; H, 6.79; N, 4.48.  

trans-7,7-Dimethyl-(6aS,14aS)-6a,7,14,14a-tetrahydro-6H-benzo|h|chromeno|4,3-b|quinoline (4j). Prepared from O-prenyl derivative of salicylaldehyde 1j (3 mmol) and aryl amine 2j (1 eq.) by following procedure B. The pure 4j was obtained as a yellow coloured solid from the second fraction. Yield: 48%. IR (neat) νmax cm⁻¹ 3380 (NH), 3088, 2961, 2930, 2895, 1608, 1548, 1461, 1325, 1215, 1021, 745. ¹H NMR (500 MHz, CDCl₃) δ 1.21 (s, 3H, CH₃), 1.34 (s, 3H, CH₃), 2.14 (td, 1H, H₆ₐ, J = 11.4, 3.5 Hz), 3.98 (t, 2H, H₆, J = 10.9 Hz, including NH), 4.46 (d, 1H, H₁₂a, J = 11.4 Hz), 4.54 (dd, 1H, H₆', J = 9.8, 3.4 Hz), 6.85-7.92 (m, 10H, Ar). ¹H NMR (125 MHz, CDCl₃) δ 26.2, 26.3, 40.6, 40.7, 60.5, 63.4, 113.7, 115.6, 116.9, 119.7, 120.5, 121.2, 122.4, 122.7, 123.8, 124.9, 125.6, 126.5, 127.2, 136.7, 146.2, 154.6. MS m/z: 315 (M⁺). Anal. Calcd. for C₂₂H₂₁NO: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.85; H, 6.63; N, 4.37.  

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