$InCl_3$ as an efficient catalyst for intramolecular imino Diels–Alder reactions: synthesis of tetrahydrochromanoquinolines

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Dedicated to Professor S. Swaminathan on his 80th 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

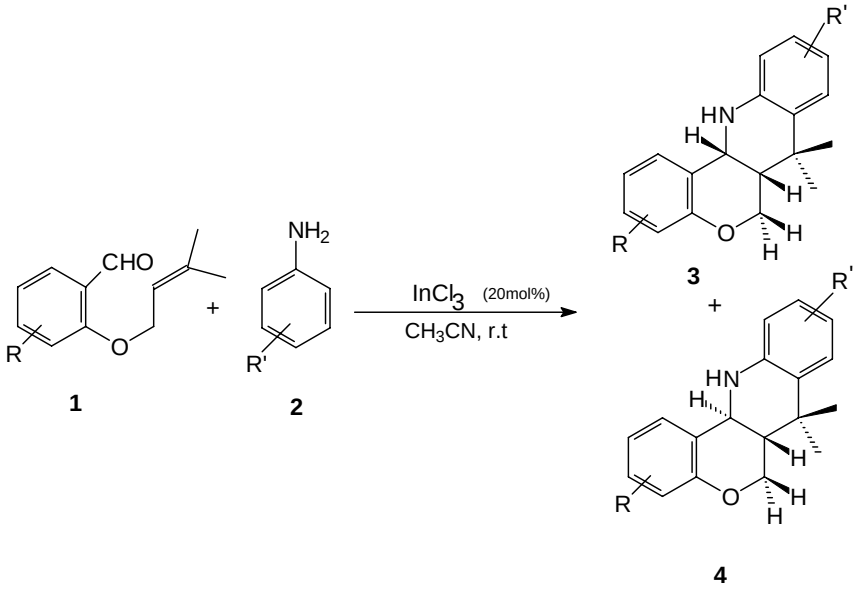
Introduction

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 $BF_3{\cdot}Et_2O$,[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 aldimines 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. $InCl_3$ is readily available and found to retain its activity even in the presence of amines, water and other active functional groups such as NO_2, COOH, CN in the substrates.[13] 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 $InCl_3$ at the imine nitrogen.

Indium trichloride has been effectively employed as a Lewis acid catalyst for various transformations[14] in organic synthesis, such as aldol condensations, imino Diels–Alder reactions, rearrangement of epoxides and Prins-type cyclization.[15] In continuation of our research interest on the catalytic applications of $InCl_3$,[16] we herein describe another remarkable catalytic activity of $InCl_3$ 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% $InCl_3$, 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 ^{1}H 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 ^{1}H NMR spectra and also by direct comparison with literature data wherever available.[17,18]



1 **2** **3** **4**

Scheme 1

Table 1. $InCl_3$ catalyzed synthesis of tetrahydrochromano[*4,3-b*]quinolines *via* IMIDA reaction[a]

Entry	R (**1a-j**)	R' (**2a-j**)	Time (min)	Yield (%)[b] **3**	**4**	Overall yield (%) (**3** + **4**)
a	H	H	5	52	46	98
b	3-CH_3O	H	5	45	49	94
c	H	2-CH_3	8	44	48	92
d	H	4-CH_3O	10	47	49	96
e	H	4-Br	10	45	48	93
f	H	4-NO_2	15	42	47	89
g	H	4-CO_2H	15	42	49	91
h	H	4-CN	10	46	41	87
i	5-Cl	H	5	50	44	94
j	H	-C_4H_4-[c]	10	40[d]	48[d]	88

[a] All the products were characterized by IR, ^1H, ^{13}C NMR and mass spectroscopy and by comparison with reported data.[12]

[b] Yield refers to the 1:1 mixtture of diastereoisomers of products **3** and **4** isolated in pure form by column chromatography.

[c] **2j** = Naphthylamine.

[d] **4j**= Benzo*[h]*chromeno-[4,3-*b*]quinoline.

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 $InCl_3$ is an eficient 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_2SO_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-6*H*-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) ν_{max} cm^{-1} 3396 (NH), 3022, 2968, 2922, 2844, 1605, 1585, 1492, 1299, 1234, 748.^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 2.00 (dt, 1H, H6a, *J* = 11.7, 3.9 Hz), 3.82 (dd, 2H, H6, *J* = 11.7, 2.4 Hz, including NH), 4.25 (dd, 1H, H6', *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).^{13}C NMR (100 MHz, $CDCl_3$) δ 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-6*H*-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) ν_{max} cm^{-1} 3345 (NH), 3015, 2953, 2918, 2842, 1611, 1581, 1483, 1292, 1218, 742. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 2.08 (td, 1H, H6a, *J* = 10.7, 2.9 Hz), 3.93 (t, 2H, H6, *J* = 11.2 Hz, including NH), 4.42 (d, 1H, H-3, *J* = 10.7), 4.48 (dd, 1H, H6', *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). ^{13}C NMR (100 MHz, $CDCl_3$) δ 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-6*H*-chromeno[4,3-b]quinoline (3b).** Prepared from *O*-prenyl derivative of 3-CH_3O- 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) ν_{max} cm^{-1} 3392 (NH), 3018, 2965, 2925, 2839, 1612, 1578, 1483, 1291, 1242, 745. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.01 (dt, 1H, H6a, *J* = 11.5, 3.8 Hz), 3.80 (s, 3H, OCH_3), 3.84 (dd, 2H, H6, *J* = 11.5, 2.7 Hz, including NH), 4.23 (dd, 1H, H6', *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).^{13}C NMR (100 MHz,

$CDCl_3$) δ 25.2, 33.4, 34.3, 40.2, 43.5, 45.2, 63.8, 114.1, 116.2, 117.5, 120.6, 122.0, 125.9, 126.7, 127.3, 129.7, 129.9, 140.6, 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.

***trans*-4-Methoxy-7,7-dimethyl-(6aS,12aS)-6a,7,12,12a-tetrahydro-6*H*-chromeno[4,3-b]quinoline (4b).** Prepared from *O*-prenyl derivative of 3-CH_3O- 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) ν_{max} cm^{-1} 3385 (NH), 3015, 2963, 2923, 2834, 1611, 1573, 1482, 1298, 1243, 748. ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 2.05 (td, 1H, H6a, *J* = 10.8, 3.0 Hz), 3.82 (s, 3H, OCH_3), 3.94 (t, 2H, H6, *J* = 11.1 Hz, including NH), 4.44 (d, 1H, H12a, *J* = 10.8 Hz), 4.46 (dd, 1H, H6', *J* = 10.8, 3.0 Hz), 6.65 (d, 1H, *J* = 8.2 Hz), 6.75-7.25 (m, 6H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ 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, 153.8.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, 77.19; H, 7.25, N, 4.78.

***cis*-7,7,11-Trimethyl-(6aS,12aR)-6a,7,12,12a-tetrahydro-*6H*-chromeno[4,3-b]quinoline (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) ν_{max} cm^{-1} 3392 (NH), 3012, 2953, 2915, 2875, 1605, 1506, 1489, 1246, 752. ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.99 (dt, 1H, H6a, *J* = 10.7 Hz), 2.25 (s, 3H, $ArCH_3$), 3.81 (t, 2H, H6, *J* = 10.7 Hz, including NH), 4.19 (dd, 1H, H6', *J* = 10.8, 3.3 Hz), 4.55 (d, 1H, H12a, *J* = 3.3 Hz), 6.25-7.22 (m, 7H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.4, 31.3, 34.7, 40.2, 43.5, 45.4, 63.2, 114.6, 116.6, 118.1, 120.3, 124.4, 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-6*H*-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) ν_{max} cm^{-1} 3389 (NH), 3010, 2958, 2875, 1602, 1510, 1485, 1247, 752. ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.00 (td, 1H, H6a, *J* = 11.0, 3.2 Hz), 2.30 (s, 3H, $ArCH_3$), 3.60 (brs, 1H, NH), 3.82 (t, 1H, H6, *J* = 10.9 Hz), 4.21 (dd, 1H, H6', *J* = 10.8, 3.2 Hz), 4.50 (d, 1H, H12a, *J* = 11.0 Hz), 6.21-7.38 (m, 7H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 31.4, 34.5, 40.1, 43.7, 45.2, 63.4, 114.5, 116.6, 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.

***cis*-7,7,Dimethyl-(6aS,12aR)-6a,7,12,12a-tetrahydro-6*H*-chromeno[4,3-b]quinoline-9-yl-methyl ether (3d).** Prepared from *O*-prenyl derivative of salicylaldehyde **1d** (3 mmol) and 4-CH_3O-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) ν_{max} cm^{-1} 3315 (NH), 2955, 2873, 1603, 1517, 1481, 1244, 752. ^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 3H, CH_3), 1.42

(s, 3H, CH_3), 2.01 (dt, 1H, H6a, *J* = 10.7, 3.9 Hz), 3.73 (s, 3H, OCH_3), 3.81 (t, 2H, H6, *J* = 10.4 Hz, including NH), 4.21 (dd, 1H, H6', *J* = 10.5, 3.8 Hz), 4.37 (d, 1H, H12a, *J* = 3.9 Hz), 6.41-7.31 (m, 7H, Ar). ^{13}C NMR: (100 MHz, $CDCl_3$) δ 26.7, 27.4, 41.8, 47.9, 54.1, 60.8, 64.9, 113.9, 116.7, 118.5, 120.5, 124.3, 125.9, 126.7, 126.8, 129.3, 129.5, 140.2, 154.2. 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.

***trans*-7,7,Dimethyl-(6aS,12aS)-6a,7,12,12a-tetrahydro-6*H*-chromeno[4,3-b]quinoline-9-yl-methyl ether (4d).** Prepared from *O*-prenyl derivative of salicylaldehyde **1d** (3 mmol) and 4-CH_3O- 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) ν_{max} cm^{-1} 3317 (NH), 2958, 2881, 1609, 1521, 1478, 1241, 758. ^{1}H NMR: (400 MHz, $CDCl_3$) δ 1.23 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 2.03 (td, 1H, H6a, *J* = 11.2, 3.4 Hz), 3.82 (s, 3H, OCH_3), 3.91 (t, 2H, H6, *J* = 10.8 Hz, including NH), 4.42 (dd, 1H, H6', *J* = 11.2, 3.5 Hz), 4.57 (d, 1H, H12a, *J* = 11.2 Hz), 6.71-7.31 (m, 7H, Ar). ^{13}C NMR :(100 MHz, $CDCl_3$) δ 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, 77.32; H, 7.14; N, 4.79.

***cis*-7,7-Dimethyl-(6aS,12aR)-6a,7,12,12a-tetrahydro-6*H*-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) ν_{max} cm^{-1} 3375 (NH) 2962, 2891, 1605, 1523, 1463, 1223, 745. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.98 (dt, 1H, H6a, *J* = 10.8, 3.5 Hz), 3.82 (t, 1H, H6, *J* = 10.3 Hz), 3.83 (brs, 1H, NH), 4.30 (dd, 1H, H6', *J* = 10.5, 3.3 Hz), 4.60 (d, 1H, H12a, *J* = 3.5 Hz), 6.51-7.38 (m, 7H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ 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.

***trans*-7,7-Dimethyl-(6aS,12aS)-6a,7,12,12a-tetrahydro-6*H*-chromeno[4,3-b]quinoline-9-yl-bromide (4e).** Prepared from *O*-prenyl derivative of salicylaldehyde **1e** (3 mmol) and 4-Br-aryl amine **2e** (1 eq.) by following *procedure* A. The pure **4e** was obtained as a yellow coloured solid from the second fraction. Yield: 48%. Mp: 115-117 °C IR: (KBr) ν_{max} cm^{-1} 3372 (NH), 2965, 2897, 1601, 1526, 1462, 1221, 741. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.98 (td, 1H, H6a, *J* = 10.7, 3.5 Hz), 3.86 (t, 1H, H6, *J* = 10.6 Hz), 4.15 (brs, 1H, NH), 4.33 (d, 1H, H12a, *J* = 10.7 Hz), 4.45 (dd, 1H, H6', *J* = 10.6, 3.5 Hz), 6.31-7.38 (m, 7H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2, 27.4, 43.7, 47.8, 60.2, 65.9, 112.5, 112.7, 113.4, 117.1, 120.4, 120.8, 125.9, 132.5, 132.8, 140.3, 154.5. 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, 62.71; H, 5.32; N, 4.02.

***cis*-7,7-Dimethyl-9-yl-nitro-(6aS,12aR)-6a,7,12,12a-tetrahydro-6*H*-chromeno[4,3-b]quinoline (3f).** Prepared from *O*-prenyl derivative of salicylaldehyde 1f (3 mmol) and 4-O_2N-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) ν_{max} cm^{-1} 3363 (NH), 3081,

2969, 2936, 2878, 1606, 1559, 1522, 1467, 1327, 1226, 1124, 1018, 755. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 3H), 1.53 (s, 3H), 2.10 (dt, 1H, H6a, *J* = 12.0, 2.3 Hz), 3.57 (t, 2H, H6, *J* = 12.0 Hz, including NH), 4.25 (dd, 1H, H6', *J* = 10.9, 2.3 Hz), 4.66 (d, 1H, H12a, *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). ^{13}C NMR (100 MHz, $CDCl_3$) δ 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 $C_{18}H_{18}N_2O_3$: 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-6*H*-chromeno[4,3-b]quinoline (4f).** Prepared from *O*-prenyl derivative of salicylaldehyde **1f** (3 mmol) and 4-O_2N-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) ν_{max} cm^{-1} 3355 (NH), 3025, 2961, 2915, 16181575, 1502, 1285, 1225, 1015, 759. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 2.02 (td, 1H, H6a, *J* = 11.8, 2.9 Hz), 3.52 (t, 2H, H6, *J* = 11.7 Hz, including NH), 4.58 (d, 1H, H12a, *J* = 10.9 Hz), 4.61 (dd, 1H, H6', *J* = 11.8, 3.0 Hz), 6.38 (d, 1H, *J* = 8.7 Hz), 6.87 (d, 1H, *J* = 8.7Hz), 6.95-7.23 (m, 3H, Ar), 7.93 (dd, 1H, *J* = 9.3, 2.4 Hz), 8.10 (d, 1H, *J* = 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.4, 31.8, 33.5, 39.4, 46.3, 63.5, 112.4, 17.8, 121.5, 122.3, 122.5, 124.8, 125.9, 129.3, 130.5, 138.8, 146.3, 154.2. MS *m/z*: 310 (M^+). Anal. Calcd. for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found : C, 69.72; H, 5.81; N, 9.11.

***cis*-7,7-Dimethyl-9-yl-carboxy-(6aS,12aR)-6a,7,12,12a-tetrahydro-6*H*-chromeno[4,3-b]quinoline (3g).** Prepared from *O*-prenyl derivative of salicylaldehyde **1g** (3 mmol) and 4-HO_2C-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) ν_{max} cm^{-1} 3349 (NH), 3023, 2965, 2917, 1602, 1573, 1501, 1281, 1227, 1021, 751. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 3H, CH_3), 1.61 (s, 3H, CH_3), 2.03 (dt, 1H, H6a, *J* = 10.8, 3.2 Hz), 3.58 (t, 2H, H6, *J* = 10.7 Hz, including NH), 4.59 (dd, 1H, H6', *J* = 10.8, 3.1 Hz), 4.62 (d, 1H, 1H, H12a, *J* = 3.2 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). ^{13}C NMR:(100 MHz, $CDCl_3$) δ 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, 129.5, 130.4, 138.3, 147.1, 154.2, 168.7. 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, 73.68; H, 6.25; N, 4.47.

***trans*-7,7-Dimethyl-9-yl-carboxy-(6aS,12aS)-6a,7,12,12a-tetrahydro-6*H*-chromeno[4,3-b]quinoline (4g).** Prepared from *O*-prenyl derivative of salicylaldehyde **1g** (3 mmol) and 4-HO_2C-aryl amine **2g** (1 eq.) by following *procedure* A. The pure **4g** was obtained as a yellow coloured solid from the second fraction. Yield: 49%. Mp: 209-211 °C. IR (KBr) ν_{max} cm^{-1} 3342 (NH), 3025, 2962, 2914, 1600, 1569, 1505, 1283, 1228, 1025, 758. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 3H, CH_3), 1.67 (s, 3H, CH_3), 2.05 (td, 1H, H6a, *J* = 11.2, 3.5 Hz), 3.67 (t, 1H, H6, *J* = 10.8 Hz), 4.57 (d, 2H, H12a, *J* = 11.2Hz, including NH), 4.61 (dd, 1H, H6', *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-6*H*-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 °C. IR (KBr) ν_{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, H6a, *J* = 12.0, 2.5 Hz), 3.54 (t, 2H, H6, *J* = 11.8 Hz, including NH), 4.27 (dd, 1H, H6', *J* = 10.8, 2.4 Hz), 4.66 (d, 1H, H12a, *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 $C_{19}H_{18}N_2O$: 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-6*H*-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 °C. IR (KBr) ν_{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, H6a, *J* = 11.5, 2.7 Hz), 3.57 (t, 2H, H6, *J* = 11.4 Hz, including NH), 4.31 (d, 1H, H-3, *J* = 11.5 Hz), 4.47 (dd, 1H, H6', *J* = 10.9, 2.7 Hz), 6.75 (d, 1H, *J* = 8.8 Hz), 6.92-7.10 (m, 2H), 7.24-7.28 (m, 2H), 7.82 (dd, 1H, *J* = 7.9, 2.3 Hz), 8.04 (d, 1H, *J* = 7.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 33.1, 33.5, 40.2, 45.9, 63.3, 113.4, 117.5, 121.4, 122.6, 122.8, 124.3, 125.7, 129.3, 130.4, 138.5, 146.6, 154.7, 167.4. MS *m/z*: 290 (M^+). Anal. Calcd. for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.62; H, 6.17; N, 9.57

***cis*-2-Chloro-7,7-dimethyl-(6aS,12aR)-6a,7,12,12a-tetrahydro-6*H*-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 °C. IR (KBr) ν_{max} cm^{-1} 3355 (NH), 3082, 2972, 2935, 2867, 1602, 1551, 1525, 1213, 767. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.98 (dt, 1H, H6a, *J* = 10.9, 2.4 Hz), 3.87 (t, 2H, H6, *J* = 10.8 Hz, including NH), 4.23 (dd, 1H, H6', *J* = 10.8, 2.3 Hz), 4.63 (d, 1H, H12a, *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-6*H*-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) ν_{max} cm^{-1} 3354 (NH), 3072, 2978, 2931, 2868, 1601, 1523, 1214, 1017, 768. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 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). ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7, 27.5, 43.3, 47.8, 60.3, 65.8, 112.4, 112.5, 114.5, 121.8, 124.5, 127.1, 127.8, 127.9, 129.3, 134.1, 143.1, 155.2. 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, 72.02; H, 6.13; N, 4.73.

***cis*-7,7-Dimethyl-(6aS,14aR)-6a,7,14,14a-tetrahydro-6*H*-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) ν_{max} cm^{-1} 3382 (NH), 3091, 2965, 2932, 2891, 1604, 1552, 1465, 1325, 1213, 1015, 748.^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.99 (dt, 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). ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 26.2, 40.5, 46.4, 60.3, 63.8, 113.9, 115.9, 116.8, 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 $C_{22}H_{21}NO$: 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-6*H*-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) ν_{max} cm^{-1} 3380 (NH), 3088, 2961, 2930, 2895, 1608, 1548, 1461, 1325, 1215, 1021, 745. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 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). ^{13}C NMR (125 MHz, $CDCl_3$) 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 $C_{22}H_{21}NO$: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.85; H, 6.63; N, 4.37.

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