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Indium(III) chloride catalyzed in situ generation of enamines and cyclization with imines: a novel route for synthesis of hexahydroxanthene-9-*N*-arylamines

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Abstract—A simple, efficient, and novel method has been developed for the synthesis of hexahydroxanthene-9-*N*-arylamine derivatives through a one-pot reaction of cyclohexanone and morpholine with salicylaldehyde imines in the presence of indium(III) chloride as a catalyst. 1-(4-Morpholino)-cyclohexene enamine prepared in situ from cyclohexanone and morpholine in presence of 20 mol% $InCl_3$ in acetonitrile under reflux condition was used without further purification, for the cyclization reaction with salicylaldehyde Schiff's bases.

1. Introduction

Xanthone derivatives are parent compounds of a large number of naturally occurring, as well as synthetic derivatives, and occupy a prominent position in medicinal chemistry.[1] Ishiguro et al. have reported the isolation of clusone (1,3,4,5,6-pentamethoxy-9*H*-xanthen-9-one) from the fresh flowers of Clusia insignis.[2] 4-Methoxyxanthen-9-amine derivatives have been used for the synthesis of pharmacologically important Clavizepine alkaloids.[3] Boyd et al. have reported that 9-aryl or alkylimino-xanthene derivatives have been used for solid phase synthesis of (*RS*)-1-aminophosphinic acid.[4] Broggini et al. have reported the synthesis of (−)-(1*S*,4a*R*,9*R*,9a*S*)-9-amino-1,2,3,4,4a,9a-hexahydro-9*H*-xanthen-1-ol using intra-molecular nitrone cycloadditions to the cyclohexene ring.[5] Schemidt has reported the synthesis of linear fused cyclohexyl benzopyrans via 4+2 cycloaddition reaction of *o*-hydroxybenzyl carbocation with cyclohexene using $SnCl_4$ as a catalyst.[6]

Enamines have been intensively studied and used in organic synthesis in a wide variety of ways following Stork's report on the application of enamines in the alkylation and acylation of carbonyl compounds.[7] Weidinger et al. have reported that 1,3-diaza-1,3-butadiene have been shown to participate in [4+2] cycloaddition reactions with 1-[4-morpholino]cyclohexene.[8] Enamines have been used in natural product synthesis, for example the total synthesis of fabianine[9] and quaipyridines,[10] including heteroaromatic azadiene Diels–Alder reaction.

Indium trichloride has been effectively employed as a Lewis acid catalyst for various transformations[11] in organic synthesis, such as aldol condensations, imino Diels–Alder reactions, rearrangement of epoxides and prins-type cyclization.[12] $InCl_3$ is readily available and found to retain its activity even in the presence of water and other active functional groups such as NO_2, COOH, CN, NH_2 in the substrates.[13] In continuation of our research interest on the catalytic applications of $InCl_3$,[14] we herein describe another remarkable catalytic activity of $InCl_3$ in the synthesis of novel xanthene-9-*N*-arylamine derivatives from salicylaldehyde imines and 1-(4-morpholino)-cyclohexene enamine in CH_3CN at room temperature in excellent yields within 40 min. 1-(4-Morpholino)-cyclohexene enamine is moisture sensitive and undergoes hydrolysis easily.[15] In order to overcome this difficulty we have attempted the generation of 1-(4-morpholino)-cyclohexene enamine in situ using $InCl_3$ (20 mol%) under reflux conditions.

1-(4-Morpholino)-cyclohexene enamine **3** prepared in situ from cyclohexanone **1** and morpholine **2** in the presence of 20 mol% $InCl_3$ in acetonitrile under reflux conditions for 2–3 h was used without further purification, for the cyclization with salicylaldehyde Schiff's bases **4**. A wide range of salicylaldehyde Schiff's bases **4** with various substituent groups were subjected to this procedure and converted to the corresponding linear fused hexahydroxanthene-9-*N*-arylamines **5** derivatives in high yields (Scheme 1). In all these reactions, a single product **5** was

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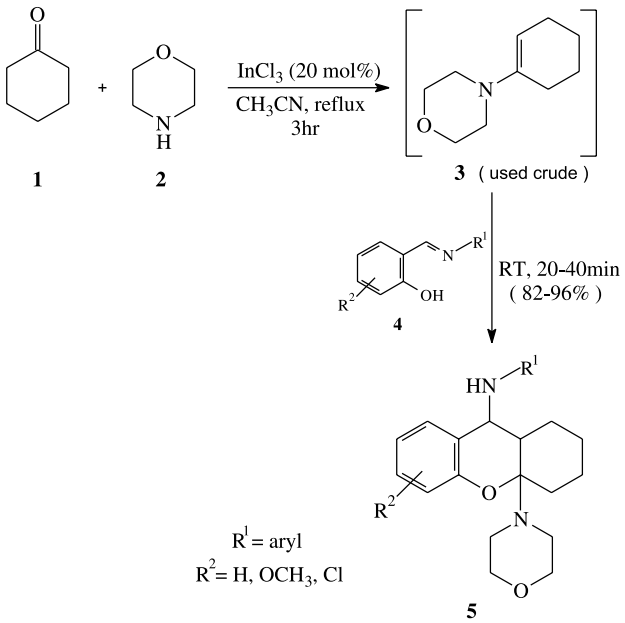


Scheme 1. Synthesis of hexahydroxanthene-9-*N*-arylamine.

Table 1. $InCl_3$ catalyzed formation of hexahydroxanthene-9-*N*-arylamine[a]

Entry	R^1	R^2	Time (min)	Yield (%)	Mp (°C)
a	C_6H_5	H	20	96	156–158
b	2-CH_3–C_6H_4	H	30	89	140–143
c	4-CH_3O–C_6H_4	H	20	93	160–162
d	4-Br–C_6H_4	H	40	90	164–166
e	2-Pyridine	H	30	87	166–168
f	C_6H_5	5-CH_3O	30	95	174–178
g	4-NO_2–C_6H_4	H	35	82	187–189
h	C_6H_5	7-Cl	25	87	132–134
i	4-CH_3–C_6H_4	7-Cl	20	90	148–149
j	4-CH_3–C_6H_4	5-CH_3O	30	92	180–182
k	2-Pyridine	5-CH_3O	40	86	152–154
l	2-Naphthyl	5-CH_3O	20	91	128–130

[a] All the products were characterized by ^1H NMR, ^{13}C NMR, IR and MS. All compounds gave satisfactory CHN values.

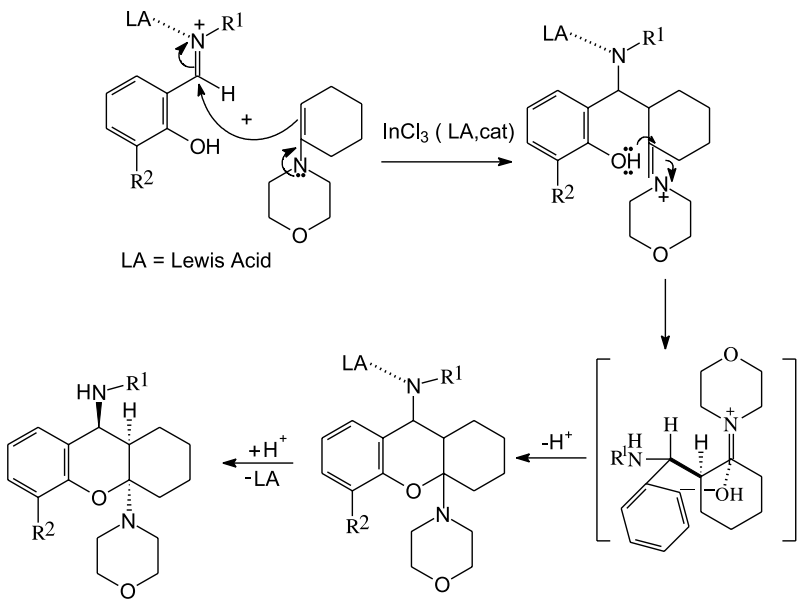
obtained, which upon recrystallization with ethyl acetate yielded pure crystalline products. The results are summarized in Table 1.

The reaction is expected to proceed through the activation of the imine nitrogen by co-ordination of the catalyst $InCl_3$, followed by nucleophilic addition at imine (C═N) bond and subsequent cyclization of the iminium ion, resulting in the formation of the linear fused hexahydroxanthene-9-*N*-arylamines (Scheme 2).

The structures of **5a**–**l** were confirmed by ^1H and ^{13}C NMR spectroscopy. The structure assignment of **5e** was supported by an X-ray crystallography determination.[16] The X-ray crystal structure of **5e** is shown in Figure 1.

The experimental procedure is simple and the products are obtained in excellent yields. However, when the substituent group R^1 was benzyl, cyclohexyl, methyl and ethyl, the cyclization under these reaction conditions was not favoured. We have substituted different cyclic ketones, such as cyclopentanone, cycloheptanone and cyclooctanone instead of cyclohexanone in the reaction with morpholine and salicylaldehydimine, under similar reaction conditions and no reaction was observed, the starting materials, being recovered as such. When the reaction was carried out at ambient temperature using equimolar ratio of reagents and 20 mol% $InCl_3$, the cyclization reaction was not observed which led to the recovery of unchanged starting materials.

The influence of various solvents on the yield of the reaction was investigated using *o*-hydroxy benzaldimine (entry a in Table 1) as the substrate. The results indicate that acetonitrile is the best solvent for the enamine formation and cyclization reaction of 1-(4-morpholino)-cyclohexene enamine with salicylaldehyde Schiff's bases (Table 2). The increased yield in the acetonitrile medium may be attributed to the higher polarity of the solvent and miscibility with water, formed during the enamine formation.



Scheme 2. Mechanism for the $InCl_3$ catalysed synthesis of hexahydroxanthene-9-*N*-arylamines.

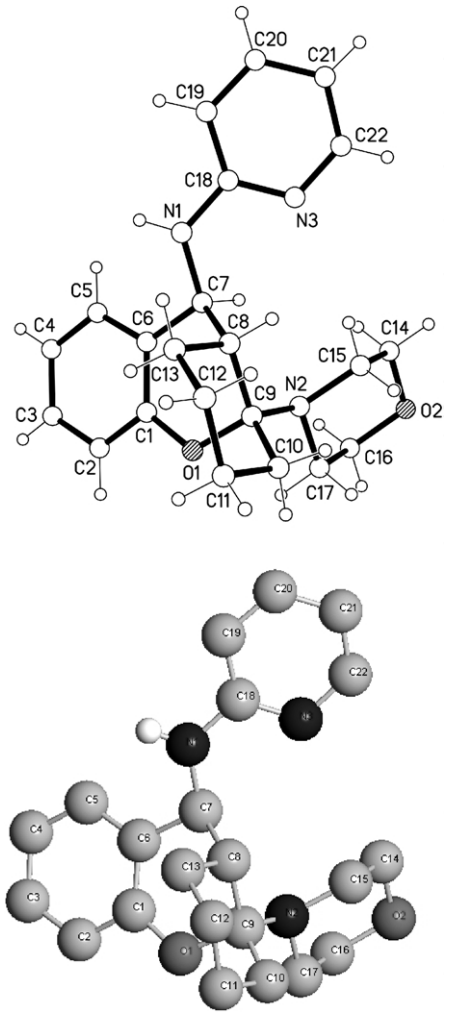


Figure 1. A perspective view of one of the two independent molecules in the asymmetric unit of **5e**.

Table 2. Effect of the solvent medium on the reaction yield of *o*-hydroxy benzaldimine with 20 mol% $InCl_3$

Entry	Solvent	Yield (%)
1	Benzene	94
2	Toluene	89
3	CH_3CN	97
4	$CHCl_3$	65
5	THF	37

In summary, this paper describes a general method for the synthesis of hexahydroxanthene-9-*N*-arylamines from salicylaldimines and 1-(4-morpholino)-cyclohexene enamine using sub-stoichiometric amounts of $InCl_3$. The catalyst is mild which has an advantage in that only 20 mol% is required for the reactions. In addition to its efficiency, operational simplicity, mild reaction conditions and easier work-up procedure make it a useful method for the synthesis of fused hexahydroxanthene-9-*N*-arylamines derivatives.

2. Experimental

o-Hydroxybenzaldimines prepared from appropriate *o*-hydroxybenzaldehyde and aniline. Salicylaldehyde, substituted anilines, cyclohexanone and morpholine were purchased from s. d. Fine Chem Ltd, India. Reagent grade acetonitrile and other solvents were used as supplied. The procedure does not require anhydrous solvent and inert atmosphere. All the products obtained were purified by recrystallization with ethyl acetate. IR measurements were done as KBr pellets for solids using Perkin Elmer Spectrum RXI FT-IR. The ^1H and ^{13}C NMR was recorded in $CDCl_3$ with JEOL 400 MHz (model GSX 400) high resolution NMR spectrometer. $CDCl_3$ was used as the solvent for the NMR spectral measurements and spectra were recorded in ppm with TMS as internal standards. The products Mass were analyzed by using a VG70-70H instrument. Melting points were determined in capillary tubes and are uncorrected. Analytical TLC was performed on precoated plastic sheets of silica gel G/UV-254 of 0.2 mm thickness (Macherey-Nagel, Germany).

2.1. Preparation of hexahydroxanthene-9-*N*-arylamines: general procedure

To a mixture of cyclohexanone (0.3 g, 3.06 mmol) and morpholine (0.27 g, 3.10 mmol), in acetonitrile (20 mL), was added a catalytic amount of $InCl_3$ (0.136 g, 20 mol%). The reaction mixture was refluxed on a water bath under nitrogen atmosphere for 3 h and then allowed to cool to room temperature before the addition of *o*-hydroxy benzaldimine **1a** (0.6 g, 3.05 mmol). The stirring was continued for 20 min. After completion of the reaction as indicated by TLC, the reaction mixture was quenched by addition of water (30 mL) and extracted with ethylacetate (2×30 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent evaporated in vacuo, kept at 0 °C overnight in a fridge to obtain the crude product. The crude solid was recrystallized from ethylacetate to give the corresponding xanthene derivative **5a** (1.064 g, 96%).

2.1.1. Product 5a: *N*-phenyl-*N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-9-yl) amine. Yield 1.064 g (96%); colorless solid, mp 156–158 °C; IR (KBr) 3361 (NH), 3050, 3015, 2926, 2855, 2821, 1599, 1488, 1450, 1360, 1299, 1260, 1234, 1151, 1112, 1064, 1026, 973, 973, 770, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48–6.57 (m, 9H), 4.12 (d, 1H, J=9.8 Hz), 3.60–3.67 (m, 4H), 2.55–2.70 (m, 3H), 2.35–2.38 (m, 2H), 2.02 (t, 2H, J=13.2 Hz), 1.72–1.10 (m, 7H, including NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6, 146.9, 129.6, 128.5, 123.3, 121.1, 116.9, 112.9, 112.2, 89.6, 67.4, 52.4, 45.3, 35.8, 29.0, 26.7, 25.1, 21.9; MS (*m*/*z*): 364 (M^+). Anal. calcd for $C_{23}H_{28}N_2O$: C, 75.79; H, 7.74; N, 7.69. Found: C, 75.92; H, 7.69; N, 7.58%.

2.1.2. Product 5b: *N*-(2-methylphenyl)-*N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-9-yl) amine. Yield 0.797 g (89%); colorless solid, mp 140–143 °C; IR (KBr) 3438 (NH), 3064, 3021, 2919, 2886, 2848, 2754, 1604, 1582, 1514, 1482, 1450, 1294, 1257, 1234, 1203, 1146, 1116, 1029, 975, 957, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, 1H, J=7.82 Hz), 7.23 (m, 3H), 6.95 (t, 1H, J=7.3 Hz), 6.83–6.81 (m, 1H), 6.69–6.62 (m, 2H), 5.26 (brs, 1H), 3.68–3.63 (m, 4H), 2.74–2.64 (m, 3H),

2.35–2.34 (m, 2H), 2.18 (s, 3H, CH_3), 2.09–2.00 (m, 2H), 1.68–1.12 (m, 7H, including NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 145.4, 130.6, 128.2, 127.3, 126.7, 124.5, 121.8, 120.8, 116.8, 116.4, 108.9, 90.9, 67.5, 47.4, 45.4, 34.1, 27.0, 24.6, 21.9, 21.8, 17.7; MS (*m*/*z*): 378 (M^+). Anal. calcd for $C_{24}H_{30}N_2O$: C, 76.16; H, 7.79; N, 7.40. Found: C, 76.29; H, 7.67; N, 7.29%.

2.1.3. Product 5c: *N*-(4-methoxyphenyl)-*N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro 1*H*-xanthen-9-yl) amine. Yield 0.807 g (93%); colorless solid, mp 160–162 °C; IR (KBr) 3375 (NH), 3375, 3049, 3004, 2943, 2855, 2826, 1589, 1511, 1455, 1297, 1240, 1182, 1149, 1116, 1038, 975, 944, 819, 772 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89–7.29 (m, 4H), 6.81 (d, 2H, *J*=8.8 Hz), 6.55 (d, 2H, *J*=8.8 Hz), 4.03 (d, 1H, *J*=10.3 Hz), 3.76 (s, 3H), 3.59 (m, 4H), 2.57 (m, 4H), 2.39–1.27 (m, 10H, including NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 150.5, 141.3, 130.7, 128.5, 123.5, 121.0, 116.9, 115.2, 113.7, 89.6, 67.4, 55.7, 53.4, 45.5, 35.6, 29.1, 26.8, 25.1, 21.9; MS (*m*/*z*): 394 (M^+) Anal. calcd for $C_{24}H_{30}N_2O_3$: C, 73.07; H, 7.66; N, 7.10. Found: C, 73.31; H, 7.77; N, 7.18%.

2.1.4. Product 5d: *N*-(4-bromophenyl)-*N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-9-yl) amine. Yield 0.722 g (90%); colorless solid, mp 164–166 °C; IR (KBr) 3398 (NH), 3050, 3011, 2926, 2856, 1593, 1493, 1454, 1312, 1261, 1238, 1147, 1114, 1070, 976, 950, 811, 772 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, 2H, *J*=8.3 Hz), 7.25–7.17 (m, 2H), 6.95–6.80 (m, 2H), 6.46 (d, 2H, *J*=8.8 Hz) 4.05 (d, 1H, *J*=10.3 Hz), 3.57 (m, 4H), 2.63–2.54 (m, 3H), 2.34–2.30 (m, 2H), 2.06–2.02 (m, 2H), 1.70–1.24 (m, 7H, including NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.5, 145.9, 132.3, 130.6, 128.8, 122.8, 121.2, 117.1, 113.8, 108.5, 89.5, 67.5, 52.7, 48.1, 45.3, 35.7, 29.0, 26.7, 25.1, 21.9; MS (*m*/*z*):443 (M^+). Anal. calcd for $C_{23}H_{27}N_2O_2Br$: C, 62.31; H, 6.14; N, 7.10. Found: C, 62.18; H, 6.01; N, 7.23%.

2.1.5. Product 5e: *N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-9-yl) pyridin-2-amine. Yield 0.802 g (87%); colorless solid, mp 164–166 °C; IR (KBr) 3348 (NH), 3062, 2936, 2854, 2817, 2744, 1607, 1513, 1487, 1450, 1344, 1283, 1241, 1198, 1139, 1108, 1033, 956, 850, 751 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08–8.06 (m, 1H), 7.44–7.38 (m, 2H), 7.18–7.14 (m, 1H), 6.93–6.91 (m, 1H), 6.89–6.80 (m, 1H), 6.59–6.57 (m, 1H), 6.43 (d, 1H, *J*=8.3 Hz), 4.53 (d, 1H, *J*=9.8 Hz), 3.71–3.62 (m, 2H), 2.86–2.73 (m, 2H), 2.46–2.41 (m, 1H), 2.03–1.99 (m, 2H), 1.87 (brs, 1H, NH), 1.68–1.54 (m, 2H), 1.44–1.36 (m, 2H), 1.18–1.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 152.4, 148.7, 137.6, 128.4, 126.6, 124.4, 120.9, 116.8, 113.3, 107.9, 91.3, 67.9, 46.7, 45.5, 34.8, 27.2, 24.9, 22.3, 22.2; MS (*m*/*z*): 365 (M^+). Anal. calcd for $C_{22}H_{27}N_3O$: C, 72.30; H, 7.45; N, 11.50. Found: C, 72.45; H, 7.53; N, 11.61%.

2.1.6. Product 5f: *N*-(phenyl)-*N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-5-methoxy xanthen-9-yl) amine. Yield 0.825 g (95%); colorless solid, mp 174–178 °C; IR (KBr) 3372 (NH), 3058, 3018, 2949, 2849, 2832, 1582, 1516, 1443, 1245, 1147, 1118, 978, 767 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.19 (m, 2H), 6.93–6.64 (m, 5H), 6.59 (d, 1H, *J*=8.0 Hz), 4.66 (d, 1H, *J*=10.3 Hz), 4.12 (d, 1H, *J*=10.3 Hz), 3.86 (s, 3H), 3.72–3.61 (m, 2H), 2.56 (m, 2H), 2.39–2.12 (m, 3H), 1.80–1.61 (m, 6H), 1.52–1.1 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 147.0, 140.1, 129.8, 124.3, 122.5, 120.6, 117.2, 112.4, 123.0, 110.7, 89.8, 67.7, 56.2, 52.7, 45.5, 36.0, 29.2, 26.9, 25.2; MS (*m*/*z*): 394 (M^+). Anal. calcd for $C_{24}H_{30}N_2O$: C, 73.07; H, 7.66; N, 7.10. Found: C, 72.87; H, 7.57; N, 7.22.

2.1.7. Product 5g: *N*-(4-nitrophenyl)-*N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-9-yl) amine. Yield 0.693 g (82%); pale yellow colored solid, mp 187–189 °C IR (KBr) 3392 (NH), 3053, 3015, 2928, 2849, 1596, 1493, 1459, 1321, 1234, 1119, 981, 773 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12–8.10 (m, 2H), 7.30–7.18 (m, 3H), 6.96–6.83 (m, 2H), 6.61(d, 1H, *J*=9.2 Hz), 5.26 (dd, 1H, J_1=5.8 Hz, J_2=9.8 Hz), 4.60 (d, 1H, *J*=10.3 Hz), 3.67–3.61 (m, 2H), 2.78–2.02 (m, 6H), 1.84–1.14 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 151.9, 138.4, 130.4, 129.5, 129.1, 126.9, 126.5, 122.5, 121.1, 116.9, 90.9, 67.5, 48.2, 45.5, 34.9, 27.0, 24.5, 22.1, 21.1; MS (*m*/*z*): 409 (M^+). Anal. calcd for $C_{23}H_{27}N_3O$: C, 67.46; H, 6.65; N, 10.26. Found: C, 67.23; H, 6.56; N, 10.38%.

2.1.8. Product 5h: *N*-(phenyl)-*N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-7-chloroxanthen-9-yl) amine. Yield 0.749 g (87%); colorless solid, mp 132–134 °C; IR (KBr) 3368 (NH), 3055, 3021, 2926, 2852, 2823, 1591, 1482, 1457, 1298, 1235, 1117, 975, 775 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, 1H, *J*=2.2 Hz), 7.25–7.13 (m, 4H), 6.78–6.71 (m, 2H), 6.57–6.56 (d, 1H, *J*=7.4 Hz), 3.76–3.47 (m, 1H), 2.69–2.53 (m, 3H), 2.37–2.02 (m, 2H), 1.72–1.24 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.3, 146.6, 130.4, 129.8, 128.8, 125.9, 125.1, 118.4, 117.5, 112.3, 90.0, 67.5, 52.4, 46.1, 35.7, 29.1, 26.7, 25.1, 21.9; MS (*m*/*z*): 398 (M^+). Anal. calcd for $C_{23}H_{27}N_2O_2Cl$: C, 69.25; H, 6.82; N, 7.02. Found: C, 69.18; H, 6.89; N, 6.89%.

2.1.9. Product 5i: *N*-(4-methylphenyl)-*N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-7-chloroxanthen-9-yl) amine. Yield 0.757 g (90%); colorless solid, mp 148–149 °C; IR (KBr) 3445 (NH), 3067, 3018, 2915, 2879, 2843, 1603, 1578, 1518, 1469, 1451, 1298, 1238, 1156, 965, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.02 (m, 5H), 6.73 (d, 1H, *J*=8.6 Hz), 6.58 (d, 1H, *J*=8.6 Hz), 5.01 (brs, 1H, NH), 4.49 (d, 1H, *J*=9.2 Hz), 4.05 (d, 1H, *J*=8.6 Hz), 4.49 (d, 1H, *J*=9.2 Hz), 3.69–3.60 (m, 4H), 2.80–2.53 (m, 2H), 2.37–2.25 (m, 2H), 2.37–2.25 (m, 5H), 2.06–1.97 (m,1H), 1.71–1.02 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 144.9, 130.3, 128.7, 128.3, 126.9, 126.3, 125.7, 117.8, 113.4, 112.4, 91.4, 67.5, 52.6, 48.2, 45.3, 34.1, 24.5, 21.8, 21.7, 20.4; MS (*m*/*z*): 412 (M^+). Anal. calcd for $C_{24}H_{29}N_2O_2Cl$: C, 69.80; H, 7.08; N, 6.78. Found: C, 69.92; H, 7.19; N, 6.86%.

2.1.10. Product 5j: *N*-(4-methylphenyl)-*N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-5-methoxyxanthen-9-yl) amine. Yield 0.779 g (92%); colorless solid, mp 180–182 °C; IR (KBr) 3365 (NH), 3052, 3008, 2945, 2851, 2828, 1578, 1518, 1459, 1252, 1141, 1112, 972, 778 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–6.70 (m, 6H), 6.60 (d,

J=8.0 Hz), 6.50 (d, 1H, J=8.0 Hz), 4.61 (d, 1H, J=10.1 Hz), 4.09 (d, 1H, J=9.7 Hz), 3.93 (s, 3H), 3.87–3.38 (m, 3H), 2.97–2.96 (m, 2H), 2.72–2.41 (m, 4H), 2.37 (s, 3H), 2.32–1.03 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 151.5, 148.5, 145.6, 137, 130.1, 129.8, 123.7, 121.1, 119.2, 118.5, 114.5, 90.2, 66.8, 56.2, 48.2, 45.4, 36.4, 29.5, 26.7, 21.9, 21.1; MS (*m*/*z*): 408 (M^+). Anal. calcd for $C_{25}H_{32}N_2O_3$: C, 73.50; H, 7.89; N, 6.86. Found; C, 73.35; H, 7.97; N, 6.77%.

2.1.11. Product 5k: *N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-5-methoxyxanthen-9-yl)pyridin-2-amine. Yield 0.745 g (86%); colorless solid, mp 152–154 °C; IR (KBr) 3355 (NH), 3068, 2938, 2855, 2812, 1605, 1521, 1472, 1461, 1232, 1121, 951, 759 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (m, 1H), 7.32 (m, 1H), 6.88–6.37 (m, 5H), 5.58 (d, 1H, J=5.2 Hz), 3.98–3,49 (m, 2H), 3.35 (s, 3H), 2.64–1.88 (m, 6H), 1.70–1.06 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 148.4, 148.2, 141.5, 137.0, 125.4, 120.1, 118.9, 112.1, 117.0, 109.9, 91.4, 67.3, 56.1, 45.5, 34.2, 31.2, 26.7, 24.6, 22.7, 22.4; MS (*m*/*z*): 395 (M^+). Anal. calcd for $C_{24}H_{29}N_3O_3$: C, 70.74; H, 7.17; N, 10.31. Found: C, 70.72; H, 7.18; N, 10.33%.

2.1.12. Product 5l: *N*-(2-naphthyl)-*N*-(4a-morpholin-4yl-2,3,4,4a,9,9a-hexahydro-1*H*-5-methoxyxanthen-9-yl) amine. Yield 0.726 g (91%); brown colored solid, mp 128–130 °C; IR (KBr) 3349 (NH), 3045, 2932, 2855, 2822, 1593, 1492, 1453, 1281, 1260, 1237, 1122, 975, 772, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66–7.62 (m, 3H), 7.37–6.79 (m, 7H), 4.83 (d, 1H, J=9.7 Hz), 4.25 (d, 1H, J=8.6 Hz), 3.88 (s, 3H), 3.75–3.46 (m, 2H), 3.09 (m, 1H), 2.63–1.24 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 144.6, 140.1, 135.4, 129.6, 127.8, 127.4, 126.6, 125.9, 124.1, 122.5, 122.1, 120.7, 117.8, 110.8, 103.0, 89.8, 68.1, 56.2, 52.7, 44.6, 35.4, 29.2, 26.9, 25.3, 22.2; MS (*m*/*z*): 442 (M^+). Anal. calcd for $C_{28}H_{32}N_2O$: C, 75.65; H, 7.26; N, 6.30. Found: C, 75.78; H, 7.14; N, 6.38%.

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