Experimental Section

Lithiation Directed by Amino Alkoxydes. Application to the Synthesis of New Disubstituted Dihydrodipyridopyrazines

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Materials and Methods

Mps were determined on a Tottoli or a Kofler melting point apparatus and are uncorrected.

¹H and ¹³C NMR spectra were recorded in CDCl₃ with a Bruker 250 MHz spectrometer (Attached Proton Test Method, APT) or a Bruker instrument Avance DPX 250 at 250.131 and 62.9 MHz, respectively. Chemical Shifts (δ values) were reported in parts per million and coupling constants (*J* values) in Hz. TMS was the internal standard.

Infrared spectra were recorded using NaCl films or KBr pellets techniques on a Perkin-Elmer 841 instrument.

Mass spectra (MS) were recorded on a Perkin-Elmer mass spectrometer SCIEX API 300 by ion spray (IS).

TLC was performed with plates coated with Kieselgel G (Merck). The silica gel used for flash chromatography was Kieselgel of 0.04-0.063 mm particle size.

Reagent-grade THF was first distilled from potassium hydroxide, then from sodium benzophenone ketyl and stored over sodium until used.

General procedure for preparation of compound 1a and 1b

At 0 °C, under inert atmosphere, to a solution of 5.10-dihydrodipyrido[2,3-*b* : 3,2-*e*]pyrazine¹ **1a** or **1b** (1 equiv.) in THF (10 mL), was added dropwise 2 equiv. of *n*-BuLi (1.6 M in hexane). After stirring at the same temperature for 1 h, *N,N*-dimethylformamide (4 equiv.) was added. The mixture was allowed to warm at room temperature, quenched with water and extracted with CH₂Cl₂. The combined extracts were dried over MgSO₄, filtered and concentrated *in vacuo*. The crud solid was purified by flash chromatography (silica gel, petroleum ether/ethyl acetate 90/10).

1a

Compound **1a**: Mp 184-185 °C; IR (KBr): 1608 cm⁻¹; MS: *m/z* = 241 (*M*+1); ¹H NMR (CDCl₃, 250 MHz): δ = 3.13 (s, 3H, CH₃), 3.37 (s, 3H, CH₃), 6.62-6.65 (m, 2H, H₆, H₇), 6.78 (d, 1H, H₃, *J* = 5.3 Hz), 7.52 (d, 1H, H₂, *J* = 5.3 Hz), 7.67 (dd, 1H, H₈, *J* = 4.4 Hz, *J* = 1.9 Hz), 9.86 (s, 1H, CHO); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 28.2 (CH₃), 43.9 (CH₃), 116.2, 117.1 (C₃, C₇), 119.9 (C₆), 142.2, 132.4 (C_{4a}, C_{5a}), 134.4 (C₄), 138.0, 141.0 (C₂, C₈), 148.2, 151.5 (C_{9a}, C_{10a}), 188.5 (CHO).

¹ Blanchard, S.; Rodriguez, I.; Kuehm-Caubère, C.; Renard, P.; Pfeiffer, B.; Guillaumet, G.; Caubère, P. *Tetrahedron* **2002**, 58, 3513.

Compound **1b**: Mp 153-154 °C; IR (KBr): 1427, 1660 cm^{-1} ; MS: $m/z = 325$ ($M+1$); ^1H NMR (CDCl_3 , 250 MHz): $\delta = 0.77$ (t, 3H, CH_3 , $J = 7.3$ Hz); 0.92 (t, 3H, CH_3 , $J = 7.1$ Hz); 1.24-1.33 (m, 2H, CH_2); 1.37-1.46 (m, 2H, CH_2); 1.60-1.67 (m, 4H, 2CH_2); 3.54 (t, 2H, NCH_2 , $J = 6.9$ Hz); 4.10 (t, NCH_2 , $J = 7.1$ Hz); 6.64 (dd, 1H, H_7 , $J = 4.9$ Hz, $J = 7.7$ Hz); 6.79 (dd, 1H, H_6 , $J = 1.5$ Hz, $J = 7.7$ Hz); 6.82 (d, 1H, H_3 , $J = 5.3$ Hz); 7.61 (d, 1H, H_2 , $J = 5.3$ Hz); 7.73 (dd, 1H, H_8 , $J = 1.5$ Hz, $J = 4.9$ Hz); 9.92 (s, 1H, CHO); ^{13}C NMR (CDCl_3 , 62.9 MHz): $\delta = 13.7$, 14.1 (2CH_3), 19.7, 20.3 (2CH_2), 28.9, 29.1 (2CH_2), 40.3, 58.9 (2NCH_2), 114.8, 117.1, 124.2 (C_3 , C_7 , C_6), 127.4, 130.3, 135.2 (C_4 , C_{4a} , C_{5a}), 139.7, 141.7 (C_2 , C_8), 149.9, 152.8 (C_{9a} , C_{10a}), 188.7 (CHO).

General procedure for preparation of compounds 2-10

To a solution of 1.5 equiv. of *N,N,N'*-trimethylethylenediamine in 3 mL of THF at -50 °C was added 1.4 equiv. of *n*-BuLi (1.6 M in hexane). After 15 min, 1 equiv. of dihydropyridopyrazine-4-carbaldehyde **1a** or **1b** was added and the mixture was allowed to stir for an additional 15 min. A hexane solution of *n*-BuLi (2.2 equiv.) was added and the solution was stirred for an additional 2 h at -50 °C. Keeping the temperature at -50°C (in the case of iodine the temperature was decreased -78 °C), the electrophile (6 equiv.) was added dropwise and the solution was allowed to warm to room temperature (30 min). The mixture was then poured into water and extracted with CH_2Cl_2 . The organic extracts were dried (MgSO_4), filtered and concentrated. The crude product was purified by flash chromatography (petroleum ether/ethyl acetate 90/10).

Compound **2**: Mp 105-107 °C; IR (KBr): 1407, 1682 cm^{-1} ; MS: $m/z = 255$ ($M+1$); ^1H NMR (CDCl_3 , 250 MHz): $\delta = 2.29$ (s, 3H, CH_3), 3.19 (s, 3H, NCH_3), 3.51 (s, 3H, NCH_3), 6.66 (d, 1H, H_3 , $J = 5.1$ Hz), 6.99 (d, 1H, H_7 , $J = 5.3$ Hz), 7.82 (d, 1H, H_2 , $J = 5.1$ Hz), 7.91 (d, 1H, H_8 , $J = 5.3$ Hz), 10.26 (s, 1H, CHO); ^{13}C NMR (CDCl_3 , 62.9 MHz): $\delta = 17.8$ (CH_3), 28.8 (NCH_3), 50.1 (NCH_3), 114.2 (C_3), 120.6 (C_7), 130.3, 130.4, 136.3 (3C , C_4 , C_{4a} , C_{5a}), 138.4 (C_6), 142.2, 142.9 (C_8 , C_2); 150.9, 153.8 (C_{9a} , C_{10a}), 189.3 (CHO).

Compound **3**: Mp 122-123 °C; IR (KBr): 1400, 1684 cm⁻¹; MS: m/z = 313.5 (M+1); ¹H NMR (CDCl₃, 250 MHz): δ = 0.38 (s, 9H, 3xCH₃, SiMe₃), 3.09 (s, 3H, NCH₃), 3.56 (s, 3H, NCH₃), 6.92 (d, 1H, H₃, *J* = 4.7 Hz), 7.06 (d, 1H, H₇, *J* = 5.1 Hz), 7.96 (d, 1H, H₂, *J* = 4.7 Hz), 8.02 (d, 1H, H₈, *J* = 5.1 Hz), 10.48 (s, 1H, CHO); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 0.1 (SiMe₃), 28.8 (NCH₃), 52.7 (NCH₃), 113.2 (C₃), 123.8 (C₇), 132.8, 135.5, 135.9 (C₄, C_{4a}, C_{5a}), 143.0 (C₂), 143.5 (C₆), 143.6 (C₈), 150.7, 153.5 (C_{9a}, C_{10a}), 189.7 (CHO).

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Compound **4**: oil (gum); IR (NaCl): 1400, 1684 cm⁻¹; MS: m/z = 531 (M+1); ¹H NMR (CDCl₃, 250 MHz): δ = 0.82 (s, 3H, 3xCH₃, *J* = 7.5 Hz), 1.11-1.18 (m, 6H, 3xCH₂), 1.26-1.35 (m, 6H, 3xCH₂), 1.45-1.55 (m, 6H, 3xCH₂), 3.14 (s, 3H, NCH₃), 3.52 (s, 3H, NCH₃), 6.87 (d, 1H, H₃, *J* = 4.7 Hz), 7.00 (d, 1H, H₇, *J* = 5.3 Hz), 7.86 (d, 1H, H₂, *J* = 4.7 Hz), 7.92 (d, 1H, H₈, *J* = 5.3 Hz), 10.33 (s, 1H, CHO); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 10.8 (3CH₂), 13.7 (3xCH₃), 27.3 (3xCH₂), 28.6 (NCH₃), 29.1 (3xCH₂), 52.1 (NCH₃), 113.4, 126.1 (C₃, C₇), 131.2, 135.9, 137.3 (C₄, C_{4a}, C_{5a}), 142.1, 142.6 (C₂, C₈), 145.4 (C₆), 149.9, 153.2 (C_{9a}, C_{10a}).

5

Compound **5**: Mp 129-130 °C; IR (KBr): 1396, 1686 cm⁻¹; MS: m/z = 367 (M+1); ¹H NMR (CDCl₃, 250 MHz): δ = 3.27 (s, 3H, CH₃), 3.54 (s, 3H, CH₃), 7.10 (d, 1H, H₃, *J* = 5.1 Hz), 7.27 (d, 1H, H₇, *J* = 5.1 Hz), 7.61 (d, 1H, H₂, *J* = 5.3 Hz), 8.03 (d, 1H, H₈, *J* = 5.1 Hz), 10.43 (s, 1H, CHO); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 28.9 (CH₃), 50.6 (CH₃), 102.4 (C₆), 113.6 (C₇), 128.1 (C₃), 132.5, 133.1, 135.4 (C_{4a}, C_{5a}, C₄), 143.6, 144.1 (C₂, C₈), 151.5, 153.6 (C_{9a}, C_{10a}), 189.7 (CHO).

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Compound **6**: Mp 158-159 °C; IR (KBr): 1414, 1680 cm⁻¹; MS: m/z = 269 (M+1); ¹H NMR (CDCl₃, 250 MHz): δ = 3.37 (s, 3H, CH₃), 3.51 (s, 3H, CH₃), 7.02 (d, 2H, H₃, H₇, *J* = 5.1 Hz), 7.91 (d, 2H, H₂, H₈, *J* = 5.1 Hz), 10.16 (s, 2H, 2xCHO); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 28.9, 52.6 (2NCH₃), 116.0 (C₃, C₇), 129.8 (C₄, C₆), 133.9 (C_{4a}, C_{5a}), 142.4 (C₂, C₈), 152.1 (C_{9a}, C_{10a}), 189.0 (2xCHO).

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Compound **7**: Mp 144-145 °C; IR (KBr): 1402, 1686 cm⁻¹; MS: m/z = 287 (M+1); ¹H NMR (CDCl₃, 250 MHz): δ = 2.47 (s, 3H, SCH₃), 3.19 (s, 3H, CH₃), 3.53 (s, 3H, CH₃), 6.65 (d, 1H, H₃, *J* = 5.3 Hz), 7.04 (d, 1H, H₇, *J* = 5.1 Hz), 7.90 (d, 1H, H₂, *J* = 5.3 Hz), 7.97 (d, 1H, H₈, *J* = 5.1 Hz), 10.38 (s, 1H, CHO); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 14.0 (SCH₃), 28.7 (NCH₃), 48.9 (NCH₃), 113.4 (C₃, C₇), 126.8, 132.1, 125.9 (C₄, C_{4a}, C_{5a}), 142.8 (C₆), 143.1, 143.5 (C₂, C₈), 150.7, 153.9 (C_{9a}, C_{10a}), 189.7 (CHO).

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Compound **8**: Mp 166-167 °C; IR (KBr): 1410, 1698, 3314 cm^{-1} ; MS: $m/z = 423.5$ ($M+1$); ^1H NMR (CDCl_3 , 250 MHz): $\delta = 2.30$ (s, 3H, CH_3), 3.65 (s, 3H, CH_3), 6.34 (d, 1H, H_3 , $J = 5.3$ Hz), 7.11-7.15 (m, 2H, 2CH_{arom}), 7.18 (d, 1H, H_7 , $J = 4.8$ Hz), 7.23-7.26 (m, 3H, 3CH_{arom}), 7.33-7.45 (m, 3H, 3CH_{arom}), 7.60-7.63 (m, 2H, 2CH_{arom}), 7.78 (s, 1H, OH), 7.97 (d, 1H, H_2 , $J = 5.3$ Hz), 8.27 (d, 1H, H_8 , $J = 4.8$ Hz), 10.17 (s, 1H, CHO); ^{13}C NMR (CDCl_3 , 62.9 MHz): $\delta = 29.3$, 47.45 (2CH_3), 82.6 (COH), 117.4, 120.2 (C_3 , C_7), 127.1 (C_4), 127.5 (2CH_{arom}), 127.7, 127.8 (2CH_{arom}), 128.0 (2CH_{arom}), 128.5 (2CH_{arom}), 128.6 (2CH_{arom}), 131.0, 133.7 (C_{4a} , C_{5a}), 143.8 (C_2), 145.3 (C_{arom}), 145.4 (C_8), 145.9 (C_{arom}), 150.7 (C_6), 153.2, 153.5 (C_{9a} , C_{10a}), 189.9 (CHO).

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Compound **9**: Mp 88-89 °C; IR (KBr): 1417, 1695 cm^{-1} ; MS: $m/z = 353$ ($M+1$); ^1H NMR (CDCl_3 , 250 MHz): $\delta = 0.71$ (s, 3H, CH_3 , $J = 7.3$ Hz), 0.95 (s, 3H, CH_3 , $J = 7.3$ Hz), 1.14-1.20 (m, 2H, CH_2), 1.39-1.49 (m, 4H, $2\times\text{CH}_2$), 1.63-1.67 (m, 2H, CH_2), 3.51 (t, 2H, CH_2N , $J = 7.5$ Hz), 4.25 (t, 2H, CH_2N , $J = 7.5$ Hz), 7.05 (d, 2H, H_3 , H_7 , $J = 5.1$ Hz), 7.97 (d, 2H, H_2 , H_8 , $J = 5.1$ Hz), 10.23 (s, 2H, 2CHO); ^{13}C NMR (CDCl_3 , 62.9 MHz): $\delta = 13.7$, 14.1 (2CH_3), 19.8, 20.3 (2CH_2), 28.9, 29.5 (2CH_2), 40.8, 66.1 (2CH_2), 115.0 (C_3 , C_7), 131.7 (C_4 , C_6), 132.5 (C_{4a} , C_{5a}), 143.1 (C_2 , C_8), 153.0 (C_{9a} , C_{10a}), 188.9 (2CHO).

10

Compound **10**: oil (gum) IR (NaCl): 1408, 1695 cm^{-1} ; MS: $m/z = 397.5$ ($M+1$); ^1H NMR (CDCl_3 , 250 MHz): $\delta = 0.37$ (s, 3H, CH_3 , SiMe_3), 0.71 (t, 3H, CH_3 , $J = 7.3$ Hz), 0.93 (t, 3H, CH_3 , $J = 7.3$ Hz), 1.04-1.12 (m, 2H, 2CH_2), 1.35-1.49 (m, 4H, 2CH_2), 1.63 (m, 2H, CH_2), 3.08-3.20 (m, 1H, CH, NCH_2), 3.35-3.45 (m, 1H, CH, CH_2N), 4.29 (t, 2H, NCH_2 , $J = 7.3$ Hz), 6.91 (d, 1H, H_3 , $J = 4.9$ Hz), 7.05 (d, 1H, H_7 , $J = 5.1$ Hz), 7.94 (d, 1H, H_2 , $J = 4.9$ Hz), 7.99 (d, 1H, H_8 , $J = 5.1$ Hz), 10.45 (s, 1H, CHO); ^{13}C NMR (CDCl_3 , 62.9 MHz): $\delta = 0.2$ (3CH_3 , SiMe_3), 13.8, 14.1 (2CH_3), 20.1, 20.5 (2CH_2), 28.4, 29.34 (2CH_2), 40.4 (NCH_2), 66.2 (NCH_2), 112.7, 123.8 (C_3 , C_7), 133.4, 134.1, 134.4 (C_{4a} , C_{5a} , C_4), 142.7, 143.3 (C_2 , C_8), 143.4 (C_6), 151.2, 154.1 (C_{9a} , C_{10a}), 189.9 (CHO).

Procedure for the synthesis of 11

11

A heterogeneous mixture of 6-iodo-dihydropyridopyrazine-4-carbaldehyde **5** (1 equiv.), Pd(PPh₃)₄ (0.1 equiv.), 2 M aqueous Na₂CO₃ (5 mL), and 4-(methoxyphenyl)boronic acid (2.5 equiv.) in DME (20 mL) was refluxed under nitrogen for 1 h. The reaction mixture was cooled, extracted (CH₂Cl₂), dried (MgSO₄), filtered and evaporated. The crude product was purified by column chromatography (silica gel, petroleum ether/ethyl acetate 90/10) to give **11**.

Compound **11**: Mp 177-178 °C; IR (KBr): 1408, 1683 cm⁻¹; MS: m/z = 347 (M+1); ¹H NMR (CDCl₃, 250 MHz): δ = 2.77 (s, 3H, OCH₃), 3.54 (s, 3H, NCH₃), 3.87 (s, 3H, CH₃, NCH₃), 6.71 (d, 1H, H₃, J = 5.1 Hz), 6.92 (d, 1H, H₇, J = 5.3 Hz), 6.99-7.03 (m, 2H, 2CH_{arom}), 7.42-7.46 (m, 2H, 2CH_{arom}), 7.79 (d, 1H, H₂, J = 5.1 Hz), 7.87 (d, 1H, H₈, J = 5.3 Hz); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 28.8 (NCH₃), 50.2 (NCH₃), 55.4 (OCH₃), 114.3 (C₃), 114.5 (2CH_{arom}), 119.6 (C₇), 129.0 (C₄), 129.1 (C₆), 129.5 (2CH_{arom}), 129.8 (C_{arom}), 136.8, 138.8 (2C_{4a}, C_{5a}), 141.0, 142.7 (C₂, C₈), 151.3, 153.4 (C_{9a}, C_{10a}), 159.9 (CO), 189.1 (CHO).

Procedure for the synthesis of 12

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6-Iodo-dihydropyridopyrazine-4-carbaldehyde **5** (1 equiv.), Pd(PPh₃)₂Cl₂ (0.1 equiv.), CuI (0.1 equiv.), phenylacetylene (1.25 equiv.), Et₃N (6 mL) and DMF (3 mL) were stirred under argon overnight. The mixture was then poured into water and extracted three times with CH₂Cl₂. The combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated on reduced pressure. The crude product was purified by column chromatography (silica gel, CH₂Cl₂/MeOH/NH₄OH 100/1/0.5).

Compound **12**: Mp 153-154 °C; IR (KBr): 1407, 1687 cm⁻¹; MS: m/z = 341 (M+1); ¹H NMR (CDCl₃, 250 MHz): δ = 3.46 (s, 3H, CH₃), 3.55 (s, 3H, CH₃), 6.79 (d, 1H, H₃, J = 5.0 Hz), 6.94 (d, 1H, H₇, J = 5.3 Hz), 7.38-7.56 (m, 3H, 3CH_{arom}), 7.57-7.60 (m, 2H, 2CH_{arom}), 7.76 (d, 1H, H₂, J = 5.0 Hz), 7.79 (d, 1H, H₈, J = 5.3 Hz), 10.1 (s, 1H, CHO); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 28.7, 50.3 (2NCH₃), 85.2, 98.6 (2C≡), 114.9, 120.3 (C₃, C₇), 122.3 (C₄), 128.3 (C₆, C_{arom}), 128.8 (2CH_{arom}), 129.4 (CH_{arom}), 131.6 (2CH_{arom}), 133.6, 136.0 (C_{4a}, C_{5a}), 141.1, 141.8 (C₂, C₈), 150.7, 152.7 (C_{9a}, C_{10a}), 189.0 (CHO).

Procedure for the synthesis of 13

6-Iodo-dihydrodipyriddyridopyrazine-4-carbaldehyde **5** (1 equiv.) was dissolved in 5 mL of dry DMF. To this solution were added methyl acrylate (1.2 equiv.), The resulting mixture was refluxed under nitrogen for 8 h and after cooling to room temperature was hydrolyzed, extracted (CH₂Cl₂), dried (MgSO₄), filtered and evaporated. The crude product was submitted to chromatographic separation eluting with an 80/20 petroleum ether/AcOEt to give **13**.

Compound **13**: Mp 125-126 °C; IR (KBr): 1414, 1714 cm⁻¹; MS: m/z = 325 (M+1); ¹H NMR (CDCl₃, 250 MHz): δ = 3.21 (s, 3H, NCH₃), 3.53 (s, 3H, NCH₃), 3.86 (s, 1H, OCH₃), 6.49 (d, 1H, HC=, *J* = 16.1 Hz), 6.85 (d, 1H, H₃, *J* = 5.2 Hz), 7.04 (d, 1H, H₇, *J* = 5.2 Hz), 7.73 (d, 1H, HC=, *J* = 16.1 Hz), 7.96 (d, 1H, H₂, *J* = 5.2 Hz), 7.95 (d, 1H, H₈, *J* = 5.2 Hz), 10.31 (s, 1H, CHO); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 28.8 (NCH₃), 52.0 (NCH₃), 52.2 (OCH₃), 114.9, 115.0 (C₃, C₇), 122.5 (HC=), 130.8, 131.1, 132.8, 135.0 (C_{4a}, C_{5a}, C₄, C₆), 138.4 (HC=), 142.7, 143.1 (C₂, C₈), 151.7, 152.9 (C_{9a}, C_{10a}), 166.8 (CO), 189.0 (CHO).

Procedure for the synthesis of 14

A solution of 6-iodo-dihydrodipyriddyridopyrazine-4-carbaldehyde **5** (1 equiv.), tributyl(1-ethoxyvinyl)tin (1.25 equiv.) and Pd(PPh₃)₄ (0.1 equiv.) in toluene (6 mL) was refluxed for 3 h. The mixture was cooled, treated with Bu₄NF (2 mL, 1M in THF) and stirred for 2 h at the r.t. After addition of CH₂Cl₂, the mixture was washed with H₂O, dried (MgSO₄), filtered and evaporated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc/NH₄OH, 90/10/1).

Compound **14**: Mp 101-102 °C; IR (KBr): 1410, 1682 cm⁻¹; MS: m/z = 311 (M+1); ¹H NMR (CDCl₃, 250 MHz): δ = 1.37 (t, 3H, CH₃, *J* = 7.1 Hz), 3.23 (s, 3H, CH₃), 3.47 (s, 3H, CH₃), 3.89 (q, 2H, OCH₂, *J* = 7.1 Hz), 4.46 (d, 1H, =CH₂, *J* = 2.5 Hz), 4.49 (d, 1H, =CH, *J* = 2.5 Hz), 6.73 (d, 1H, H₃, *J* = 5.1 Hz), 6.90 (s, 1H, H₇, *J* = 5.3 Hz), 7.73 (d, 1H, H₂, *J* = 5.1 Hz), 7.77 (d, 1H, H₈, *J* = 5.3 Hz), 10.00 (s, 1H, CHO); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 14.6 (CH₃), 28.8 (NCH₃), 49.0 (NCH₃), 63.8 (OCH₂), 87.5 (CH₂=), 114.3, 118.6 (C₃, C₇), 128.1, 129.3 (C₄, C₆), 133.9, 136.8 (C_{4a}, C_{5a}), 140.5, 141.9 (C₂, C₈), 151.0, 153.0 (C_{9a}, C_{10a}), 158.0 (CO), 189.2 (CHO).

Procedure for the synthesis of 15

15

A solution of **5** (1equiv.), tributyl(1-ethoxyvinyl)tin (1.25 equiv.) and Pd(PPh₃)₄ (0.1eq.) in toluene (6 mL) was refluxed for 3 h. The mixture was cooled, treated with 10% aqueous HCl solution and stirred for 30 min at room temperature. After addition of NaOH for basification, the aqueous phase was separated and extracted with CH₂Cl₂, the extracts was dried (MgSO₄), filtered and evaporated. The residue was purified by flash chromatography (petroleum ether/EtOAc, 90/10).

Compound **15**: Mp 129-130 °C; IR (KBr): 1410, 1682 cm⁻¹; MS: m/z = 283 (M+1); ¹H NMR (CDCl₃, 250 MHz): δ = 2.61 (s, 3H, CH₃), 3.12 (s, 3H, CH₃), 3.49 (s, 3H, CH₃), 6.75 (d, 1H, H₃, *J* = 5.1 Hz), 6.37 (d, 1H, H₇, *J* = 5.3 Hz), 7.84 (2d, 2H, H₂, H₈, *J* = 5.1 Hz, *J* = 5.3 Hz), 10.06 (s, 1H, CHO); ¹³C NMR (CDCl₃, 62.9 MHz): δ = 28.9, 29.4 (2CH₃), 50.3 (CH₃), 115.7, 116.1 (C₃, C₇), 129.1, 130.5, 134.4, 135.1 (C_{4a}, C_{5a}, C₄, C₆), 141.6, 142.3 (C₂, C₈), 151.6, 152.3 (C_{9a}, C_{10a}), 189.2 (CHO), 200.7 (CO).