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Functionalization of dihydrodipyridopyrazines involving palladium-catalyzed coupling reactions

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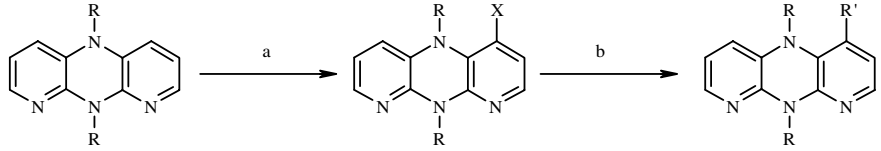
Abstract—Various 4-substituted dihydrodipyridopyrazines were synthesized by palladium-mediated cross-coupling reactions. Starting from the corresponding 4-iodo or 4-bromo derivatives, the incorporation of aryl, vinyl, alkynyl and methoxycarbonyl groups is described.

Unprecedented dihydrodipyridopyrazines (DHDPP) were easily obtained by hetarynic dimerization of 2-alkylamino-3-halogenopyridines in the presence of the complex base $NaNH_2$–*t*-BuONa.[1]

From the literature it appears that, among anticancer agents, planar nitrogen aromatic heterocycles constitute an important family.[2] We previously found that the dihydrodipyridopyrazines have interesting properties in this area.[3] On the other hand such heterocycles were practically unknown when we published our first synthesis.[1] So we thought that it would be of interest to know if their reactivity could be deduced from the chemical properties of other nitrogen heterocycles as well as to obtain new substrates for biological studies. In the present publication we report our results aimed at reaching these targets.

We investigated the possible functionalization of some halogenated 5,10-dihydrodipyrido[2,3-*b*:3,2-*e*]pyrazines by palladium-catalyzed coupling reactions.[4] To this end 4-iododihydrodipyridopyrazines **2a**,**b** and 4-bromodihydrodipyridopyrazine **2c** (Scheme 1) were used as starting materials. These derivatives were previously obtained[5] from dihydrodipyridopyrazines **1a** and **1b** by lithiation with *n*-butyllithium followed by reaction with the appropriate halogenating reagent.

The Suzuki reaction of **2a**–**c** with 4-(methoxyphenyl)-boronic acid catalyzed by $Pd(PPh_3)_4$ in refluxing



1a, R=Me
1b, R=Bu

2a, R=Me, X=I
2b, R=Bu , X=I
2c, R=Me, X=Br

3a-7a, R=Me
3b-7b, R=Bu

Scheme 1. (a) *n*-BuLi, I_2 or CBr_4, THF, −78 °C, 1 h (59–63%); (b) see Table 1.

Keywords: Dihydrodipyridopyrazines; Cross-coupling; Stille reaction; Suzuki reaction; Sonogashira reaction; Heck reaction; Palladium-catalyzed carbonylation.
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Table 1. Synthesis of 4-substituted dihydrodipyridopyrazines by palladium-mediated cross-coupling reactions

Entry	Substrate	Coupling partner	Conditions	Time (h)	Product	R	R′	Yield (%)
1	**2a**	4-$MeOC_6H_4B(OH)_2$	$Pd(PPh_3)_4$, aq Na_2CO_3, DME, reflux	1	**3a**	Me	$-C_6H_4$-4-OMe	90
2	**2b**	4-$MeOC_6H_4B(OH)_2$	$Pd(PPh_3)_4$, aq Na_2CO_3, DME, reflux	2	**3b**	Bu	$-C_6H_4$-4-OMe	87
3	**2c**	4-$MeOC_6H_4B(OH)_2$	$Pd(PPh_3)_4$, aq Na_2CO_3, DME, reflux	2	**3a**	Me	$-C_6H_4$-4-OMe	69
4	**2a**	$H_2C{=}C(OEt)SnBu_3$	$Pd(PPh_3)_4$, toluene, reflux, then HCl 10%	3	**4a**	Me	–COMe	76[a]
5	**2b**	$H_2C{=}C(OEt)SnBu_3$	$Pd(PPh_3)_4$, toluene, reflux, then HCl 10%	3	**4b**	Bu	–COMe	78[a]
6	**2c**	$H_2C{=}C(OEt)SnBu_3$	$Pd(PPh_3)_4$, toluene, reflux, then HCl 10%	3	**4a**	Me	–COMe	75[a]
7	**2c**	$H_2C{=}C(OEt)SnBu_3$	$Pd(PPh_3)_4$, toluene, reflux	3	**4c**	Me	$-C(OEt){=}CH_2$	59
8	**2a**	$H_2C{=}CHCO_2Me$	$PdCl_2$(dppf), TBAI, Et_3N/DMF/H_2O, 50 °C	2	**5a**	Me	$-CH{=}CHCO_2Me$	77
9	**2b**	$H_2C{=}CHCO_2Me$	$PdCl_2$(dppf), TBAI, Et_3N/DMF/H_2O, 50 °C	6	**5b**	Bu	$-CH{=}CHCO_2Me$	61
10	**2c**	$H_2C{=}CHCO_2Me$	$PdCl_2$(dppf), TBAI, Et_3N/DMF/H_2O, 50 °C	8	**5a**	Me	$-CH{=}CHCO_2Me$	24[b]
11	**2a**	$HC{\equiv}C\text{-}CH_2NMe_2$	$Pd(PPh_3)_2Cl_2$, CuI, Et_3N/DMF, rt	12	**6a**	Me	$-C{\equiv}C\text{-}CH_2NMe_2$	71
12	**2b**	$HC{\equiv}C\text{-}CH_2NMe_2$	$Pd(PPh_3)_2Cl_2$, CuI, Et_3N/DMF, rt	12	**6b**	Bu	$-C{\equiv}C\text{-}CH_2NMe_2$	68
13	**2a**	CO/MeOH	$Pd(OAc)_2$, $(Ph_2P)_2(CH_2)_3$, DMSO, Et_3N, 100 °C	5	**7a**	Me	$-CO_2Me$	85
14	**2b**	CO/MeOH	$Pd(OAc)_2$, $(Ph_2P)_2(CH_2)_3$, DMSO, Et_3N, 100 °C	7	**7b**	Bu	$-CO_2Me$	70

[a] Without isolation of vinyl compounds.
[b] Starting material (56%) was recovered.

dimethoxyethane led to the expected coupling products **3a**,**b** in 69–90% yield (Table 1, entries 1–3).[6]

On the other hand **2a** and **2c** under typical Stille conditions afforded the coupling product **4c**[7] (Table 1, entry 7), which when treated with 10% aq HCl, furnished **4a** in 76% yield (Table 1, entries 4 and 6). Under the same conditions **2b** gave access to the corresponding **4b** (Table 1, entry 5).[8]

The interesting Heck cross-coupling reaction of **2a**–**c** with methyl acrylate was performed in the presence of a catalytic amount of dichloro[1,1′-bis(diphenylphosphino)-ferrocene]palladium(II) and gave access to the methyl propenoates **5a**,**b** (Table 1, entries 8–10).[9] Compound **2c** was of rather low reactivity and led to the expected product **5a** in only 24% yield while 56% of starting material was recovered (Table 1, entry 10).

Under Sonogashira reaction conditions **2a**,**b** reacted with *N*,*N*-dimethylpropargylamine in the presence of CuI and $Pd(Ph_3)_2Cl_2$ to give **6a**,**b** in good yields (Table 1, entries 11 and 12).[10] Finally, palladium-catalyzed carbonylation[11] of **2a**,**b** with CO and MeOH/Et_3N in the presence of $Pd(OAc)_2$ and 1,3-bis(diphenylphosphino)-propane gave access to the corresponding methyl esters **7a**,**b** in excellent yields (Table 1, entries 13 and 14).[12]

In conclusion, using palladium-mediated cross-coupling reactions, we have realized the functionalization of the 4-position of dihydrodipyridopyrazines.

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6. General procedure for the synthesis of 4-(methoxyphenyl)dihydrodipyridopyrazines **3a**,**b**. A heterogeneous mixture of 4-halogeno-dihydrodipyrido pyrazines **2a**–**c** (1 equiv), $Pd(PPh_3)_4$ (0.1 equiv), 2 M aq Na_2CO_3 (5 mL), and 4-(methoxyphenyl)boronic acid (2.5 equiv) in DME (20 mL) was refluxed under nitrogen for 1–2 h. The reaction mixture was cooled, extracted (CH_2Cl_2), dried ($MgSO_4$), filtered and evaporated. Flash chromatography (silica gel, petroleum ether/ethyl acetate 70:30) of the residue gave pure products as indicated below. Compound **3a**: IR(NaCl): 1418, 1610 cm^{-1}; MS: 319 (M+1); ^1H NMR ($CDCl_3$, 250 MHz) δ 2.54 (s, 3H, CH_3), 3.40 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 6.35 (dd, 1H, H-6, $J = 1.4$ Hz, $J = 7.6$ Hz), 6.50–6.57 (m, 2H, H-3, H-7), 6.92–6.96 (m, 2H, $2H_{Ar}$), 7.23–7.29 (m, 2H, $2H_{Ar}$), 7.57–7.60 (m, 2H, H-2, H-8); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 28.6 (CH_3), 42.2 (CH_3), 55.5 (OCH_3), 114.1 (2CH, CH_{Ar}), 117.0, 118.3, 120.4 (3CH, C-3, C-6, C-7), 128.3 (C, C-4), 129.6 (2CH, CH_{Ar}), 131.3, 133.4, 135.1 (3C, C_{Ar}, C-4a, C-5a), 139.1 (2CH, C-2, C-8), 150.0, 152.0 (C, C-9a, C-10a), 159.3 (C, C-O). Compound **3b**: IR(NaCl): 1421, 1606 cm^{-1}; MS: 403.5 (M+1); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.66 (t, 3H, CH_3, $J = 7.4$ Hz), 0.93 (t, 3H, CH_3, $J = 7.4$ Hz), 1.08–1.17 (m, 2H, CH_2), 1.31–1.49 (m, 4H, $2CH_2$), 1.63–1.72 (m, 2H, CH_2), 2.81 (t, 2H, CH_2, $J = 7.2$ Hz), 3.85 (s, 3H, OCH_3), 4.15 (t, 2H, CH_2, $J = 7.2$ Hz), 6.53 (d, 1H, H-3, $J = 5.2$ Hz), 6.58–6.60 (m, 2H, H-6, H-7), 6.62–6.69 (m, 2H, $2H_{Ar}$), 7.34–7.39 (m, 2H, $2H_{Ar}$), 7.65–7.69 (m, 2H, H-2, H-8); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 13.7 ($2CH_3$), 19.7, 20.4 ($2CH_2$), 29.3 ($2CH_2$), 40.1, 53.9 ($2CH_2$), 55.4 (OCH_3), 114.3 (2CH, CH_{Ar}), 116.8, 119.2, 123.1 (3CH, C-3, C-6, C-7), 128.1 (C, C-4), 129.2 (2CH, CH_{Ar}), 131.1, 133.2, 136.2 (3C, C_{Ar}, C-4a, C-5a), 140.1, 140.2 (2CH, C-2, C-8), 151.4, 153.1 (2C, C-9a, C-10a), 159.4 (C, C-O).
7. Procedure for the synthesis of 4-(1-ethoxyethenyl) dihydrodipyridopyrazine **4c**. A solution of **2a** (1 equiv), tributyl(1-ethoxyvinyl)tin (1.25 equiv) and $Pd(PPh_3)_4$ (0.1 equiv) in toluene (6 mL) was refluxed for 3 h. The mixture was cooled, treated with Bu_4 NF (2 mL, 1 M in THF) and stirred for 2 h at rt. After addition of CH_2Cl_2, the mixture was washed with H_2O, dried ($MgSO_4$), filtered and evaporated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 90:10). Compound **4c**: IR(NaCl): 1415, 1605 cm^{-1}; MS: 283 (M+1); ^1H NMR ($CDCl_3$, 250 MHz) δ 1.32 (t, 3H, CH_3, $J = 7.0$ Hz), 2.98 (s, 3H, CH_3), 3.33 (s, 3H, CH_3), 3.80 (q, 2H, CH_2, $J = 7.0$ Hz), 4.21 (d, 1H, H-a, $J = 2.3$ Hz), 4.30 (d, 1H, H-b, $J = 2.3$ Hz), 6.33 (dd, 1H, H-6, $J = 1.4$ Hz, $J = 7.6$ Hz), 6.49–6.51 (m, 2H, H-3, H-7), 7.45 (d, 1H, H-2, $J = 5.4$ Hz), 7.53 (dd, 1H, H-8, $J = 1.4$ Hz, $J = 5.2$ Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 14.7 (CH_3), 28.6, 38.5 ($2CH_3$), 63.4 (CH_2), 86.7 ($CH_2=$), 117.0, 117.2, 119.4 (3CH, C-3, C-6, C-7), 128.4, 129.6 (2C, C-4a, C-5a), 134.5 (C, C-4), 138.1, 138.7 (2CH, C-2, C-8), 149.5, 151.5 (2C, C-9a, C-10a), 159.2 (C, C=O).
8. Procedure for the synthesis of 4-(ethanoyl) dihydrodipyridopyrazines **4a**, **b**. A solution of **2a**,**b** (1 equiv), tributyl(1-ethoxyvinyl)tin (1.25 equiv) and $Pd(PPh_3)_4$ (0.1 equiv) in toluene (6 mL) was refluxed for 3 h. The mixture was cooled, treated with 10% aq HCl solution and stirred for 30 min at rt. After addition of NaOH for basification, the aqueous phase was separated and extracted with CH_2Cl_2, the extracts were dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash chromatography (petroleum ether/EtOAc, 90:10). Compound **4a**: IR(NaCl): 1417, 1681 cm^{-1}; MS: 255 (M+1); ^1H NMR ($CDCl_3$, 250 MHz) δ 2.49 (s, 3H, CH_3), 2.74 (s, 3H, CH_3), 3.35 (s, 3H, CH_3), 6.45 (dd, 1H, H-6, $J = 1.4$ Hz, $J = 7.5$ Hz), 6.55–6.62 (m, 2H, H-3, H-7), 7.48 (d, 1H, H-2, $J = 5.4$ Hz), 7.59 (dd, 1H, H-8, $J = 1.4$ Hz, $J = 5.0$ Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 28.3, 29.2 ($2CH_3$), 44.7 (CH_3), 115.5, 117.2, 119.1 (3CH, C-3, C-6, C-7), 124.7 (C, C-4), 131.6, 133.4 (2C, C-4a, C-5a), 138.1, 140.3 (2CH, C-2, C-8), 148.7, 152.1 (2C, C-9a, C-10a), 199.5 (C, C=O). Compound **4b**: 1419, 1679 cm^{-1}; MS: 339.5 (M+1); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.75 (t, 3H, CH_3, $J = 7.4$ Hz), 0.91 (t, 3H, CH_3, $J = 7.4$ Hz), 1.27–1.33 (m, 2H, CH_2), 1.36–1.45 (m, 2H, CH_2), 1.48–1.69 (m, 4H, $2CH_2$), 2.46 (s, 3H, CH_3), 3.19 (t, 2H, CH_2, $J = 7.2$ Hz), 4.09 (t, 2H, CH_2, $J = 7.2$ Hz), 6.59–6.64 (m, 2H, H-3, H-7), 6.68 (dd, 1H, H-6, $J = 1.4$ Hz, $J = 7.6$ Hz), 7.58 (d, 1H, H-2, $J = 5.2$ Hz), 7.68 (dd, 1H, H-8, $J = 1.4$ Hz, $J = 4.8$ Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 13.7, 14.2 ($2CH_3$), 19.7, 20.4 ($2CH_2$), 28.6 (CH_3), 28.7, 28.9 ($2CH_2$), 40.2, 56.1 ($2CH_2$), 115.5, 117.1, 123.4 (3CH, C-3, C-6, C-7), 130.8, 131.1, 132.6 (3C, C-4, C-4a, C-5a), 139.8, 141.2 (2CH, C-2, C-8), 150.3, 152.9 (2C, C-9a, C-10a), 200.6 (C, C=O).
9. General procedure for the synthesis of methyl 4-(prop-2-enoate)dihydrodipyridopyrazines **5a**,**b**. 4-Iodo-dihydrodipyridopyrazines **2a**,**b** was dissolved in a mixture of DMF/H_2O/Et_3N (12:2:2). To this solution were added methyl acrylate (10 equiv), $PdCl_2$(dppf) (0.2 equiv) and tetrabutylammonium iodide (2 equiv). The resulting mixture was heated at 50 °C for the appropriate time. After cooling to room temperature, the excess of methyl acrylate was evaporated and the crude product was submitted to chromatographic separation eluting with a 90:10 petroleum ether/AcOEt to give **5a** or **5b**. Compound **5a**: IR(NaCl): 1417, 1716 cm^{-1}; MS: 297 (M+1); ^1H NMR ($CDCl_3$, 250 MHz) δ 3.19 (s, 3H, CH_3), 3.36 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 6.25 (d, 1H, CH=, $J = 15.9$ Hz), 6.58 (d, 1H, H-3, $J = 5.4$ Hz), 6.61–6.65 (m, 2H, H-6, H-7), 7.53 (d, 1H, H-2, $J = 5.4$ Hz), 7.54 (d, 1H, CH=, $J = 15.9$ Hz), 7.64 (dd, 1H, H-8, $J = 2.4$ Hz, $J = 4.0$ Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 28.2, 45.2 ($2CH_3$), 52.0 (OCH_3), 114.9, 117.1, 119.6 (3CH, C-3, C-6, C-7), 120.8 (CH=), 126.4 (C, C-4), 132.5, 133.9 (2C, C-4a, C-5a), 139.6, 140.6 (3CH, CH=, C-2, C-8), 149.3, 152.0 (2C, C-9a, C-10a), 167.2 (C, C=O). Compound **5b**: IR(NaCl): 1419, 1720 cm^{-1}; MS: 381.5 (M+1); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.72 (t, 3H, CH_3, $J = 7.4$ Hz), 0.91 (t, 3H, CH_3, $J = 7.4$ Hz), 1.16–1.28 (m, 2H, CH_2), 1.36–1.45 (m, 2H, CH_2), 1.49–1.58 (m, 2H, CH_2), 1.61–1.70 (m, 2H, CH_2), 3.37 (t, 2H, CH_2, $J = 7.2$ Hz), 3.81 (s, 3H, OCH_3), 4.13 (t, 2H, CH_2, $J = 7.2$ Hz), 6.34 (d, 1H, CH=, $J = 16.1$ Hz), 6.64–6.69 (m, 2H, H-3, H-7), 6.92 (dd, 1H,

H-6, $J = 1.6$ Hz, $J = 7.7$ Hz), 7.60–7.68 (m, 2H, H-2 and CH═), 7.66 (dd, 1H, H-8, $J = 1.6$ Hz, $J = 5.0$ Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 13.7, 14.2 ($2CH_3$), 19.8, 20.4 ($2CH_2$), 29.2, 29.4 ($2CH_2$), 40.0 ($2CH_2$), 52.0 (OCH_3), 114.2, 117.1, 119.9 (3CH, C-3, C-6, C-7), 125.9 (CH═), 130.1, 131.5, 131.6 (3C, C-4, C-4a, C-5a), 139.8, 141.0, 141.6 (3CH, CH═, C-2, C-8), 150.9, 153.0 (2C, C-9a, C-10a), 167.3 (C, C═O).

10. General procedure for the synthesis of 4-(3-dimethylaminoprop-1-ynyl)dihydrodipyridopyrazines **6a**,**b**. 4-Iododihydrodipyridopyrazines **2a**,**b** (1 equiv), $Pd(PPh_3)_2$ Cl_2 (0.1 equiv), CuI (0.1 equiv), alkyne (1.2 equiv), Et_3N (10 mL) and DMF (5 mL) were stirred under argon overnight. The mixture was then poured into water and extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel). Compound **6a**: IR(NaCl): 1417 cm^{-1}; MS: 294 (M+1); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.33 (s, 6H, $2CH_3$, NMe_2), 3.29 (s, 3H, CH_3), 3.33 (s, 3H, CH_3), 3.44 (s, 2H, CH_2), 6.40 (dd, 1H, H-6, $J = 1.4$ Hz, $J = 7.7$ Hz), 6.47 (d, 1H, H-3, $J = 5.4$ Hz), 6.51 (dd, 1H, H-7, $J = 5.0$ Hz, $J = 7.7$ Hz), 7.37 (d, 1H, H-2, $J = 5.4$ Hz), 7.53 (dd, 1H, H-8, $J = 1.4$ Hz, $J = 5.0$ Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 28.3, 40.1 ($2CH_3$), 44.4 ($2CH_3$, NMe_2), 48.9 (CH_2), 83.2, 91.1 (2C, C≡), 112.8 (C, C-4), 117.1, 117.8, 121.6 (3CH, C-3, C-6, C-7), 133.6, 133.8 (2C, C-4a, C-5a), 138.3, 139.6 (2CH, C-2, C-8), 149.4, 151.2 (2C, C-9a, C-10a). Compound **6b**: IR(NaCl): 1422 cm^{-1}; MS: 378.5 (M+1); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.82 (t, 3H, CH_3, $J = 7.2$ Hz), 0.91 (t, 3H, CH_3, $J = 7.2$ Hz), 1.31–1.41 (m, 4H, $2CH_2$), 1.59–1.65 (m, 4H, $2CH_2$), 2.36 (s, 6H, $2CH_3$, NMe_2), 3.49 (s, 2H, CH_2), 3.81 (t, 2H, CH_2, $J = 7.2$ Hz), 4.03 (t, 2H, CH_2, $J = 7.2$ Hz), 6.50 (d, 1H, H-3, $J = 5.2$ Hz), 6.54 (dd, 1H, H-7, $J = 4.8$ Hz, $J = 7.8$ Hz), 6.61 (dd, 1H, H-6, $J = 1.6$ Hz, $J = 7.8$ Hz), 7.44 (d, 1H, H-2, $J = 5.2$ Hz), 7.6 (dd, 1H, H-8, $J = 1.6$ Hz, $J = 4.8$ Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 13.9, 14.2 ($2CH_3$), 19.9, 20.3 ($2CH_2$), 29.0, 29.5 ($2CH_2$), 40.0 (CH_2), 44.0 ($2CH_3$, NMe_2), 48.8 (CH_2), 52.6 (CH_2), 83.6, 90.9 (2C, C≡), 115.5 (C, C-4), 116.9, 120.9, 122.0 (3CH, C-3, C-6, C-7), 132.2, 132.9 (2C, C-4a, C-5a), 139.2, 140.3 (2CH, C-2, C-8), 150.3, 151.8 (2C, C-9a, C-10a).

11. (a) Sakakura, T.; Yamashita, H.; Kobayashi, T.-A.; Hayashi, T.; Tanaka, M. *J. Org. Chem.* **1987**, *52*, 5733; (b) Allegretti, M.; Arcadi, A.; Marinelli, F.; Nicolini, L. *Synlett* **2001**, 609.

12. General procedure for the synthesis of 4-(carbomethoxy)dihydrodipyridopyrazines **7a**,**b**. A solution of 4-iodo-dihydrodipyridopyrazines **2a**,**b** (1 equiv), Et_3N (3 equiv) and 1,3-bis(diphenylphosphino) propane (0.1 equiv) in DMSO and MeOH was stirred under argon for 30 min. After the addition of the $Pd(OAc)_2$ (0.1 equiv), the mixture was pressurized with carbon monoxide and heated at 100 °C. After cooling to room temperature and concentration of the solution under reduced pressure, the crude product was chromatographed on silica to give the derivatives **7a**,**b** indicated below. Compound **7a**: IR (NaCl): 1418, 1715 cm^{-1}; MS: 271 (M+1); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.86 (s, 3H, CH_3), 3.35 (s, 3H, CH_3), 3.86 (s, 3H, OCH_3), 6.43 (dd, 1H, H-6, $J = 1.3$ Hz, $J = 7.6$ Hz), 6.53 (dd, 1H, H-7, $J = 5.1$ Hz, $J = 7.6$ Hz), 6.68 (d, 1H, H-3, $J = 5.5$ Hz), 7.42 (d, 1H, H-2, $J = 5.5$ Hz), 7.57 (dd, 1H, H-8, $J = 1.3$ Hz, $J = 5.1$ Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 28.2, 40.3 ($2CH_3$), 52.5 (OCH_3), 116.9, 117.1, 118.6 (3CH, C-3, C-6, C-7), 120.1 (C, C-4), 132.6, 133.1 (2C, C-4a, C-5a), 137.8, 140.1 (2CH, C-2, C-8), 148.7, 151.8 (2C, C-9a, C-10a), 166.9 (C, C═O). Compound **7b**: IR(NaCl): 1427, 1722 cm^{-1}; MS: 355.5 (M+1); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.78 (t, 3H, CH_3, $J = 7.4$ Hz), 0.91 (t, 3H, CH_3, $J = 7.4$ Hz), 1.25–1.45 (m, 4H, $2CH_2$), 1.51–1.66 (m, 4H, $2CH_2$), 3.26 (t, 2H, CH_2, $J = 7.2$ Hz), 3.87 (s, 3H, OCH_3), 4.06 (t, 2H, CH_2, $J = 7.2$ Hz), 6.59 (m, 2H, H-6 and H-7), 6.77 (d, 1H, H-3, $J = 5.3$ Hz), 7.49 (d, 1H, H-2, $J = 5.3$ Hz), 7.62 (dd, 1H, H-8, $J = 4.1$ Hz, $J = 2.5$ Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 13.7, 14.2 ($2CH_3$), 19.8, 20.4 ($2CH_2$), 28.4, 28.9 ($2CH_2$), 40.2 (CH_2), 52.5 (OCH_3), 53.3 (CH_2), 116.8, 116.9, 122.1 (3CH, C-3, C-6, C-7), 130.9, 132.6 (2C, C-4a, C-5a), 138.5, 140.4 (2CH, C-2, C-8), 149.9 (C, C-4), 150.0, 152.8 (2C, C-9a, C-10a), 166.7 (C, C═O).