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Step by step palladium mediated syntheses of new 2-(pyridin-2-yl)-6-R-nicotinic acids and esters

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ABSTRACT

Taking advantage of palladium peculiar "rollover" C,N cyclometallation, it is possible to promote C(3) functionalization of 6-alkyl-substituted-2,2′-bipyridines. The carbonylation reaction of rollover species $[Pd(L^n)Cl]_2$, (HL^1 = 6-isopropyl-2,2′-bipy, **1**; HL^2 = 6-neopentyl-2,2′-bipy, **2**; HL^3 = 6-ethyl-2,2′-bipy, **3**; HL^4 = 6-methyl-2,2′-bipy, **4**) allowed the synthesis of 2-(pyridin-2-yl)-6-alkyl-nicotinic acids or esters. These nicotinic derivatives are extremely rare and, as far as we know, quite unreported in the case of the 6-substituted molecules.

1. Results and discussion

Transition metal-mediated reactions are a classical route in organic synthesis since many years ago. Complexes containing metal–carbon σ bonds have found wide application: likely, beside copper, palladium derivatives are the species most frequently involved [1]. The array of reactions in which they can participate includes transmetallation, insertion (e.g. CO, alkenes, alkynes), β elimination, oxidative cleavage and coupling (e.g. C–C) [2]. Although several synthetic approaches are known, the building of a palladium–carbon σ bond by intermolecular reaction of unactivated C–H bonds still is an arduous task. In general much easier is intramolecular activation, which takes advantage of the coordination of a donor atom. Five-membered ring compounds, in particular, more stable than those with four- and six-membered rings, are easily synthesized and often utilized as intermediates [3]. Palladium cyclometallated species [4] with nitrogen, oxygen or sulfur donors, where the palladium–carbon σ bond is part of a five-membered chelate ring, have found many applications in organic synthesis, as reported in a recent review [5]. One of the most important applications is the carbonylation reaction: insertion of CO into the Pd–C bond has been particularly investigated in the case of the cyclometallates with nitrogen ligands. The stoichiometric acylation allows to synthesize heterocyclic ketones and a variety of other carbonyl compounds.

We have previously reported on the reaction of palladium(II) acetate with two 6-alkyl-substituted-2,2′-bipyridines (HL^1 = 6-iso-propyl-2,2′-bipy; HL^2 = 6-neo-pentyl-2,2′-bipy) [6]. In benzene at reflux the reaction gives a crude product which, after treatment with LiCl and recrystallization, allowed us to isolate the cyclometallates $[Pd(L^1)Cl]_2$, **1**, and $[Pd(L^2)Cl]_2$, **2**, in low or moderate yields, respectively. Spectroscopic data (mainly ^1H NMR) and X-ray structure analysis (compound **1**) unambiguously showed that deprotonation of the ligand does not entail activation of a $C(sp^3)$–H bond on the substituent but rather that of the C(3)–H bond of the substituted pyridine ring. Metal-mediated activation of a C–H bond of a bipyridine ring is extremely rare [7]. Although recently other examples of this so called " rollover" metallation have been reported by reaction with platinum(II) electron rich complexes, in the chemistry of palladium, at the best of our knowledge, no other N′,C(3) cyclometallated complex of this type has been reported ever since. We deemed worth to investigate whether such unusual and unique cyclometallated species could find application in the functionalization of the C(3) atom of the substituted pyridine ring. Unsymmetric 2,2′-bipyridines, bearing substituents on one ring alone, are often hard to be achieved by conventional organic methods, particularly in the case of the 3,6-disubstituted ones [8,9].

In this paper we report on the carbonylation reaction of compounds **1–4**, $[Pd(L)Cl]_2$, (**1**, HL^1 = 6-isopropyl-2,2′-bipy; **2**, HL^2 = 6-neopentyl-2,2′-bipy); **3**, HL^3 = 6-ethyl-2,2′-bipy; **4**, HL^4 = 6-methyl-2,2′-bipy), carried out under conditions appropriate to obtain, through insertion of CO into the C(3)–Pd σ bond, C(3)-substituted alkylesters or carboxylic acids. The resulting molecules

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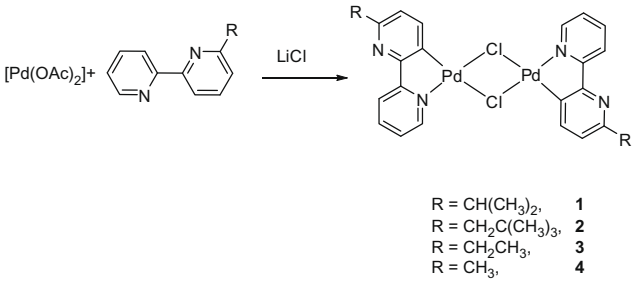
contain the core of the nicotinic acid and therefore should be of biological and pharmaceutical interest.

Compounds **1**, $[Pd(L^1)Cl]_2$, (HL^1 = 6-iso-propyl-2,2′-bipy), and **2**, $[Pd(L^2)Cl]_2$, (HL^2 = 6-neo-pentyl-2,2′-bipy) were prepared as previously reported by reaction of the ligand with palladium acetate in benzene at reflux [6]. As often is the case, purification of the crude product met with difficulty and hence the acetate was exchanged with a chloride when treated with LiCl in acetone/H_2O. Thus analytically pure compounds **1** and **2** were obtained after crystallization,



(1)

Compounds **1** and **2** were fully characterized spectroscopically and in the case of **1** by X-ray analysis.

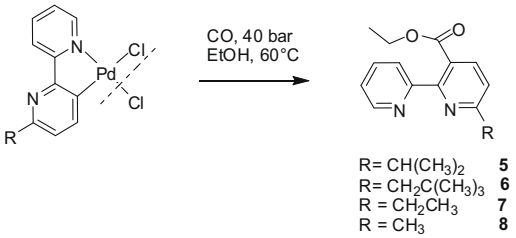
Under our conditions, in the case of HL^1 and HL^2, yields are low as activation of the C(3)–H bond by palladium acetate is not selective: in the reaction mixture, in addition to simple adducts, (molar ratio Pd/HL = 1/1), we also observed species arising from activation of a C(sp^3)–H bond of the substituent, likely favored by the formation of an N,N,C terdentate ligand. As afore noted, activation of a C–H bond of the ring of a bipyridine is extremely rare: the palladium cyclometallates here under consideration are unique being obtained from an inorganic precursor, {$Pd(OAc)_2$}.

Under different conditions, e.g. from $Na_2[PdCl_4]$ in water the more common N,N,C cyclometallates are obtained [3b].

Given the rarity and novelty of compounds **1** and **2**, we now investigated the behavior of other 2,2′-bipyridines, namely 6-ethyl-, and 6-methyl-2,2′-bipy as well as the unsubstituted 2,2′-bipy. In the reaction of palladium acetate with 2,2′-bipy we had no evidence of C(3)–H activation. In contrast, reaction with 6-ethyl-2,2′-bipy, HL^3, and 6-methyl-2,2′-bipy, HL^4, after exchange with LiCl, gave the cyclometallated complexes $[Pd(L^3)Cl]_2$, **3,** and $[Pd(L^4)Cl]_2$, **4**, analogous to **1** and **2**. Yields are moderate (ca. 60–65%), but higher than for **1** and **2,** likely due to minor competition with N,N,C cyclometallation; the reactions however take a longer time and require reflux in toluene in place of benzene. A substituent in 6 position seems to be crucial for the C(3)–H activation, possibly to make hard, along the reaction path, robust coordination of the nitrogen atom of the substituted pyridine ring and favoring rotation around the C(2)–C(2′) bond. The new complexes **3** and **4**, isolated as yellow solids, have satisfactory elemental analyses (C,H,N) and were characterized by ^1H NMR spectroscopy: significant is the lack of the resonance assignable to the C(3)–H proton (see Section 3).

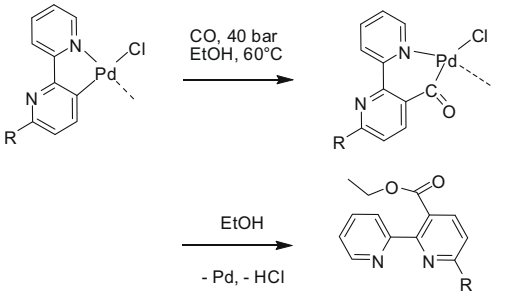
The reaction of the cyclometallates $[Pd(L)Cl]_2$, **1–4**, with CO, carried out under very mild conditions, i.e. bubbling CO at room temperature into a chloroform solution entails cleavage of the chloride bridge to give mononuclear species [Pd(L–H)Cl(CO)], which show in the IR spectra a band in the region typical of a terminal carbonyl, e.g. 2131 cm^{-1} ($CHCl_3$), complex **4**.

The carbonylation reaction was first carried out on compound **1** in ethanol at room temperature, under 40 bar of CO: no insertion of CO into the palladium–carbon bond was achieved, the only organic product of the reaction being the free ligand, HL^1. Insertion of CO was gained in complexes **1–4** when the reaction was performed under harsher conditions, i.e. working in the same solvent at 60 °C and 40 bar.



(2)

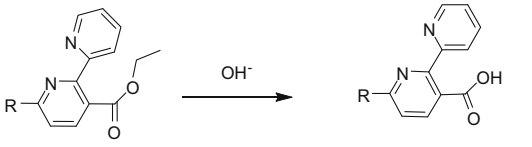
After work up of the reaction mixture the organic molecules **5–8** were isolated as oils: high yields are granted provided the reaction conditions are carefully checked, particularly as for the purity of the palladium reagents and of the solvent. The organic compounds **5–8** were characterized analytically, spectroscopically (IR, ^1H,$^{13}C\{^1H\}$ NMR) and by mass spectra. The spectroscopic data, taken together, fit the proposed formulas: in the IR spectra a strong band around 1725 cm^{-1} (Nujol) supports a –COOR group and in the mass spectra peaks at *m*/*z* corresponding to $[M+H]^+$ a.u. are observed. The ^1H NMR spectra display in the aromatic region an AX system for the H_4 and H_5 protons consistent with a three-substituted pyridine ring. The chemical shift of the H_4 proton, δ ca. 7.9, is slightly deshielded with respect to the free ligands, δ ca. 7.7 [3b], as expected due to the –COOR group in *ortho*. As previously mentioned [5], the carbonylation reaction of palladium C,N cyclometallates is an important reaction in the application of five-membered ring compounds: many heterocyclic ketones are synthesized by carbonyl insertion into a palladium–carbon σ bond, followed by demetallation. At variance, in presence of nucleophilic solvents such as alcohols, in place of the intramolecular attack of nitrogen to the acyl group, attack of the alcohol can occur to give uncyclized esters. Generally it is assumed that, after breaking of the bridge bond brought about by CO, the reaction entails, as key step of the process, insertion of CO into the palladium–carbon bond, to give an unstable six-membered acyl species. Nucleophilic attack of ethanol on the carbonyl of the acylic group, extrusion of the organic product and reductive elimination of palladium account for the outcome of the reaction (Eq. (3)). This pattern is in keeping with the path originally proposed by Thompson and Heck many years ago [10].



(3)

As far as we know the synthesis of 2,2′-bipyridines C(3)-carboxylates is a troublesome matter [9], the metal-mediated reaction seems to be a suitable approach to achieve selective functionalisation of the C(3) atom.

Alkaline hydrolysis of the esters **5–8** renders the corresponding 2-(pyridin-2-yl)-6-R-nicotinic acids, **9–12** in good yields (Eq. (4)). The acids have been isolated as white solids or oils and characterized analytically and spectroscopically, IR, ^1H and ^{13}C NMR.



(4)

2. Conclusions

We have shown in this paper that, taking advantage of palladium peculiar C,N cyclometallates, it is possible to promote C(3) functionalization of 6-alkyl-substituted-2,2′-bipyridines: the carbonylation reaction allowed us to synthesize 2-(2-pyridin-2-yl)-6-alkyl-nicotinic acids or esters. These nicotinic derivatives are extremely rare and, as far as we know, quite unreported in the case of the 6-substituted molecules. Functionalized nicotinic acid derivatives, including amide, ester, and oxazoline, are of paramount biological and pharmaceutical interest. In addition they also find application in quite different fields [11].

3. Experimental

The 2,2′-bipyridines L^1–L^4 and complexes **1** and **2** were prepared according to the literature [3b]. All the solvents were purified and dried according to standard procedures [12]. Elemental analyses were performed with a PerkinElmer 240B elemental analyzer by Mr. Antonello Canu (Dipartimento di Chimica, Università degli studi di Sassari, Sassari, Italy). ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded with a Varian VXR 300 spectrometer operating at 300.0 and 75.4 MHz, respectively. Chemical shifts are given in ppm relative to internal TMS. J values are given in Hz. Infrared spectra were recorded with a FT-IR Jasco 480P instrument using Nujol mulls. The ESI Mass spectra were performed with a GC MS Hewlett Packard G1800B GCD plus instrument.

3.1. Synthesis of $[Pd(L^3\text{-}H)\mu{-}Cl]_2$ (3)

A solution of L^3 (6-ethyl-2,2′-bipyridine, 1.50 mmol) and $Pd(CH_3COO)_2$ (1.50 mmol) in toluene (40 ml) was refluxed for 24 h, then filtered over celite and evaporated to dryness. The residue was treated with a mixture of water/acetone 1:3 (40 ml) containing LiCl (excess) and stirred for other 24 h. The suspension was concentrated to small volume and extracted with 3×15 mL of CH_2Cl_2. Organic layer was then collected and treated with Na_2SO_4 and filtered. The residue solution was concentrated to small volume and treated with Et_2O to give analytical sample as a yellow solid. Yield: 60%. M.p. > 250 °C. Anal. Calc. for $C_{24}H_{22}Cl_2N_4Pd_2$: C, 44.33; H, 3.41; N, 8.62. Found: C, 44.49; H, 3.32; N, 8.72%, ^1H NMR CD_2Cl_2: 8.71 (m, 1H, J_{H-H} = 5.4 Hz $H_{6'}$), 8.09 (d, 1H, J_{H-H} = 7.6 Hz, $H_{3'}$), 7.95 (td, 1H, J_{H-H} = 1.5 Hz, J_{H-H} = 7.6 Hz, $H_{4'}$), 7.58 (d, 1H, J_{H-H} = 8.1 Hz, H_4), 7.31 (m, 1H, J_{H-H} = 5.4 Hz, J_{H-H} = 7.6 Hz, $H_{5'}$), 6.86 (d, 1H, J_{H-H} = 8.1 Hz, H_5), 2.76 (q, 2H, J_{H-H} = 7.7 Hz, CH_2), 1.31 (t, 3H, J_{H-H} = 7.7 Hz, CH_3).

3.2. Synthesis of $[Pd(L^4\text{-}H)\mu Cl]_2$ (4)

A solution of L^4 (6-methyl-2,2′-bipyridine, 0.588 mmol) and $Pd(CH_3COO)_2$ (0.588 mmol) in toluene (40 mL) was refluxed for 24 h, then filtered over celite and evaporated to dryness. The residue was treated with a mixture of water/acetone 1:3 (40 ml) containing LiC1 (excess) and stirred for 24 h. The precipitate formed was filtered, washed with EtOH and Et_2O to give the analytical sample as a yellow solid. Yield: 66%. M.p. > 250 °C. Anal. Calc. for $C_{22}H_{18}Cl_2N_4Pd_2$: C, 42.74; H, 2.92; N, 9.01%. Found: C, 42.47; H, 3.06; N, 8.63%, ^1H NMR CD_2Cl_2: 8.74 (m, 1H, J_{H-H} = 5.8 Hz, $H_{6'}$), 8.09 (dd, 1H, J_{H-H} = 7.9 Hz, $H_{3'}$), 7.91 (td, 1H, J_{H-H} = 7.9 Hz, $H_{4'}$), 7.60 (d, 1H, J_{H-H} = 8.0 Hz, H_4), 7.26 (m, 1H, $H_{5'}$ partially overlapping with $CDCl_3$), 6.83 (d, 1H, J_{H-H} = 8.0 Hz, H_5), 2.50 (s, 3H, CH_3).

3.3. Synthesis of ethyl 6-R-2-(pyridin-2-yl)pyridine-3-carboxylate, R = isopropyl (**5**); neopentyl (**6**); ethyl (**7**); Methyl (8)

A suspension of $[Pd(bipy^R\text{-}H)Cl]_2$, (100 mg) in 40 mL of EtOH was stirred at 60 °C, under 40 bar of CO for 24 h. The residue suspension was treated with Na_2CO_3 for 30′ then filtered over celite and filtered. The solvent was removed under vacuum and the residue oil was extracted with Et_2O. The residue solution was then evaporated to give analytical sample as a oil, in almost quantitative yield.

3.3.1. R = isopropyl (5)

^1H NMR $CDCl_3$: 8.57 (dd, 1H, J_{H-H} = 5.6, 1.2 Hz, $H_{6'}$), 8.15 (dd, 1H, J_{H-H} = 7.9 Hz, $H_{3'}$), 7.87 (d, 1H, J_{H-H} = 7.9 Hz, H_4), 7.85 (td, 1H, J_{H-H} = 1.9 Hz, J_{H-H} = 7.9 Hz, $H_{4'}$), 7.32 (m, 1H, J_{H-H} = 7.9, 1.2 Hz, $H_{5'}$), 7.26 (d, 1H, J_{H-H} = 7.9 Hz, H_5), 4.20 (dd, 2H, J_{H-H} = 7.1 Hz, O–CH_2), 3.15 (sept, 1H, J_{H-H} = 7.0 Hz, C*H*$(CH_3)_2$), 1.33 (d, 6H, J_{H-H} = 7.0 Hz, CH(CH_3)$_2$), 1.11 (t, 3H, J_{H-H} = 7.0 Hz, CH_2-CH_3), FT-IR (nujol): 1726 cm^{-1}, s. MS, m/z = 271 $[M+H]^+$.

3.3.2. R = neopentyl (6)

^1H NMR $CDCl_3$: 8.57 (dd, 1H, J_{H-H} = 5.8, 1.2 Hz, $H_{6'}$), 8.15 (dd, 1H, J_{H-H} = 7.9 Hz, $H_{3'}$), 7.89 (d, 1H, J_{H-H} = 8.1 Hz, H_4), 7.82 (td, 1H, J_{H-H} = 1.8 Hz, J_{H-H} = 8.1 Hz, $H_{4'}$), 7.31 (m, 1H, partially overlapping with $CDCl_3$, $H_{5'}$), 7.18 (d, 1H, J_{H-H} = 8.1 Hz, H_5), 4.20 (q, 2H, J_{H-H} = 7.2 Hz, O–CH_2), 2.79 (s, 2H, C*H*$_2$C$(CH_3)_3$), 1.16 (t, 3H, J_{H-H} = 7.2 Hz, CH_2-CH_3), 1.01 (s, 9H, , $CH_2C(CH_3)_3$), FT-IR (nujol): 1725 cm^{-1}, s. MS, m/z = 299 $[M+H]^+$.

3.3.3. R = ethyl (7)

^1H NMR $CDCl_3$: 8.59 (dd, 1H, J_{H-H} = 5.8, 1.5 Hz, $H_{6'}$), 8.06 (dd, 1H, J_{H-H} = 7.9 Hz, J_{H-H} = 1.2 Hz, $H_{3'}$), 7.91 (d, 1H, J_{H-H} = 7.9 Hz, H_4), 7.80 (td, 1H, J_{H-H} = 7.6 Hz, J_{H-H} = 1.5 Hz, $H_{4'}$), 7.29 (m, 1H, partially overlapping with $CDCl_3$, $H_{5'}$), 7.23 (d, 1H, J_{H-H} = 7.9 Hz, H_5), 4.21 (q, 2H, J_{H-H} = 7.0 Hz, O–CH_2), 2.91 (q, 2H, J_{H-H} = 7.5 Hz, C*H*$_2$CH$_3$), 1.35 (t, 3H, J_{H-H} = 7.5 Hz, CH_2*CH*$_3$), 1.12 (t, 3H, J_{H-H} = 7.0 Hz, O–CH_2*CH*$_3$), ^{13}C NMR ($CDCl_3$): δ 13.92 (CH_3); 31.64 (CH_2); 121.26, 123.05, 123.51 (C5, C5′, C3′); 126.10 (C3); 136.83; 137.79 (C4, C4′); 148.61 (C6); 155.79, 157.32 (C2, C2′); 165.08 (C6); 169.19 (CO). FT-IR (nujol): 1725 cm^{-1}, s. MS, m/z = 257 $[M+H]^+$.

3.3.4. R = Methyl (8)

^1H NMR $CDCl_3$: 8.60 (dd, 1H, J_{H-H} = 5.8 Hz, J_{H-H} = 1.2 Hz, $H_{6'}$), 8.00 (dd, 1H, J_{H-H} = 7.9 Hz, J_{H-H} = 1.1 Hz, $H_{3'}$), 7.90 (d, 1H, J_{H-H} = 7.9 Hz, H_4), 7.81 (td, 1H, J_{H-H} = 7.5 Hz, J_{H-H} = 1.9 Hz, $H_{4'}$), 7.25 (m, 2H, partially overlapping with $CDCl_3$, H_5, $H_{5'}$), 4.21 (q, 2H, J_{H-H} = 7.0 Hz, O–CH_2), 2.60 (s, 1H, CH_3), 1.21 (t, 3H, J_{H-H} = 7.0 Hz, OCH_2CH_3), ^{13}C NMR ($CDCl_3$): δ 168.92 CO; 160.17 (C6); 157.33, 156.10 (C2, C2′); 148.67 (C6′); 137.81, 136.83 (C4, C4′); 125.87 (C3); 123.49, 123.07, 122.51 (C5, C5′, C3′); 61.46 (CH_2); 24.88 (CH_3); 14.07 (CH_3-CH_2). FT-IR (nujol): 1725 cm^{-1}, s. MS, m/z = 243 $[M+H]^+$.

3.4. Synthesis of 6-R-2-(pyridin-2-yl)pyridine-3-carboxylic acid, (2-(pyridin-2-yl)-6-R nicotinic acid)

A suspension of ethyl 6-R-2-(pyridin-2-yl)pyridine-3-carboxylate, (0.20 mmol) in 30 mL of an EtOH/H_2O mixture (1:1) and an excess of NaOH was stirred overnight at 80 °C. The residue solution

was acidified with CH_3COOH and then extracted with 3 × 30 mL of Et_2O. The residue solution was dried with Na_2SO_4, filtered and evaporated to dryness, to give the analytical sample as a white solid or oil.

3.4.1. R = isopropyl (9)

Yield = 69%. ^1H NMR $CDCl_3$: 8.85 (d, 1H, J_{H-H} = 8.3 Hz, $H_{3'}$), 8.74 (d, 1H, J_{H-H} = 8.2 Hz, H_4), 8.57 (dd, 1H, J_{H-H} = 5.4 Hz, $H_{6'}$), 8.11 (td, 1H, J_{H-H} = 1.5 Hz, J_{H-H} = 7.9 Hz, $H_{4'}$), 7.56 (m, 1H, J_{H-H} = 6.6 Hz, $H_{5'}$), 7.38 (d, 1H, J_{H-H} = 8.2 Hz, H_5), 3.19 (sept, H, J_{H-H} = 6.7 Hz, $CH(CH_3)_2$), 1.38 (d, 9H, J_{H-H} = 6.8 Hz, CH_3); ^{13}C NMR $CDCl_3$: δ 22.19; 36.16; 71.66; 121.74; 124.69; 126.09; 127.54; 139.81; 143.74; 143.90; 149.72; 155.79; 168.20, 168.97. FT-IR nujol: 1712 cm^{-1}.

3.4.2. R = neopentyl (10)

Yield: 65%, Anal. Calc. for $C_{16}H_{18}N_2O_2 \cdot H_2O$: C, 66.65; H, 6.99; N, 9.72. Found: C, 66.96; H, 6.07; N, 8.69%.:^1H NMR $CDCl_3$: 8.77 (d, 1H, J_{H-H} = 8.0 Hz, $H_{3'}$), 8.70 (d, 1H, J_{H-H} = 8.2 Hz, H_4), 8.58 (dd, 1H, J_{H-H} = 5.4 Hz, $H_{6'}$), 8.10 (td, 1H, J_{H-H} = 1.8 Hz, J_{H-H} = 8.0 Hz, $H_{4'}$), 7.56 (m, 1H, J_{H-H} = 6.3 Hz, $H_{5'}$), 7.31 (d, 1H, J_{H-H} = 8.2 Hz, H_5), 2.81 (s, 2H, CH_2), 1.01 (s, 9H, CH_3). ^{13}C NMR (CDCl): δ 29.41 (CH_3); 32.14 (Cq^{np}); 51.53 (CH_2); 124.63, 125.21, 125.86 (C5, C5′, C3′); 127.4 (C3); 139.84; 142.53; 143.90; 149.56 (C2); 155.22 (C2′); 162.12 (C6); 168.65 (CO). FT-IR (nujol): 1716 cm^{-1}.

3.4.3. R = ethyl (11)

Yield: 70%, ^1H NMR $CDCl_3$: 8.81 (d, 1H, J_{H-H} = 8.2 Hz, $H_{3'}$), 8.72 (d, 1H, J_{H-H} = 8.2 Hz, H_4), 8.57 (dd, 1H, J_{H-H} = 5.4 Hz, $H_{6'}$), 8.11 (td, 1H, J_{H-H} = 7.9 Hz, $H_{4'}$), 7.56 (td, 1H, J_{H-H} = 5.5 Hz, $H_{5'}$), 7.37 (d, 1H, J_{H-H} = 8.2 Hz, H_5), 2.90 (q, 2H, J_{H-H} = 7.7 Hz, CH_2), 1.40 (t, 3H, J_{H-H} = 7.7 Hz, CH_3). ^{13}C NMR ($CDCl_3$): δ 13.54 (CH_3); 31.36 (CH_2); 122.69, 124.53, 125.70 (C5, C5′, C3′); 128.67 (C3); 139.33; 141.96; 145.30; 151.14 (C2); 156.43 (C2′); 164.90 (C6); 170.59 (CO). FT-IR (nujol): 1713 cm^{-1}.

3.4.4. R = Methyl (12)

Yield: 62%, ^1H NMR $CDCl_3$: 8.70 (d, 1H, J_{H-H} = 8.1 Hz, $H_{3'}$), 8.63 (d, 1H, J_{H-H} = 8.2 Hz, H_4), 8.57 (dd, 1H, J_{H-H} = 5.4 Hz, $H_{6'}$), 8.10 (td, 1H, J_{H-H} = 7.9 Hz, J_{H-H} = 8.0 Hz, $H_{4'}$), 7.53 (m, 1H, J_{H-H} = 5.9 Hz, $H_{5'}$), 7.35 (d, 1H, J_{H-H} = 8.2 Hz, H_5), 2.70 (s, 3H, CH_3). FT-IR (nujol): 1720 cm^{-1}.

Acknowledgements

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