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Preliminary communication

Nucleophilic additions to palladium(II)-activated C=C bonds: synthesis of cyclopalladated 8-substituted quinoline derivatives

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Abstract

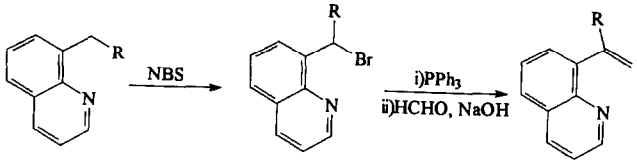
8-Vinylquinoline and α-methyl-8-vinylquinoline have been prepared in 40–67% overall yield from 8-methyl- and 8-ethyl-quinoline, respectively. These unsaturated compounds undergo nucleophilic addition with carbon and oxygen nucleophiles at the terminal vinyl carbon atom in the presence of Pd^{II} compounds affording, exclusively, five-membered metallacyclic rings.

Keywords: Synthesis; Palladium; Cyclopalladated compounds; Nucleophilic additions; Metallacycle; Alkene

The use of metallacyclic complexes with a M–C bond stabilised by intramolecular coordination of a heteroatom to the metal as reagents for organic synthesis is a subject of rapidly growing interest [1]. Such complexes of Pd have been used as starting materials for the stoichiometric synthesis of N- or S- heterocycles through their reactions with alkynes [1–3]. These reagents are usually obtained via direct C–H bond activation of compounds containing a Group 15 or 16 donor atom by Pd^{II} [4]. However, an alternative synthesis, among other involves the carbo- and alkoxy-palladation of allyl and homo-allyl amines and sulphides [5].

We describe here an extension of these last reactions for the synthesis of a variety of cyclopalladated 8-substituted quinolines that are potential precursors of 1*H*-pyrrolo-[2,1,5-*de*]quinolizines [3].

The reaction of 8-methyl- or 8-ethyl-quinoline [6] with *N*-bromosuccimide in the presence of benzoyl peroxide in carbon tetrachloride at reflux temperature for 6 h affords the bromo derivatives **1** and **2**, respectively, in more than 85% yield [7]. Reaction of **1** or **2** with triphenylphosphine in chloroform at reflux temperature for 8 h produces quantitatively the phosphonium salts that, by a Wittig reaction with formaldehyde in the presence of aqueous sodium hydroxide, produces the desired olefins **3** and **4** [8] in 40% and 67% overall yield, respectively.



1, R= H
2, R= Me

3, R= H
4, R= Me

The addition of **3** (1.1 equiv.) to a stirred solution of $[PdCl_2(PhCN)_2]$ (1.0 equiv.) in THF at room temperature followed by sodium dimethylmalonate (1.1 equiv.) affords a green–yellow solution. After 2 h a yellow solid **5a** was isolated, upon addition of hexanes, in 75% yield. The ^1H NMR spectrum of **5a** in $CDCl_3$ [8] shows the presence of at least four nonequivalent carbomethoxy groups suggesting a mixture of isomers [9]. However the ^{1}NMR spectrum of the monomeric compound derived from **5a** (prepared in situ by the addition of pyridine-d_5 to a solution of **5a** in the NMR tube), shows only one set of signals, indicating a single isomer. The triplet at 3.94 ppm for the α CH of the quinoline ring establishes unambiguously that nucleophilic addition has proceeded at the terminal olefinic carbon atom with high regioselectivity. The reaction of **4** with dimethyl malonate requires 5–6 h, under the same reaction conditions, affording the compound **6a** [8] in 83% yield.

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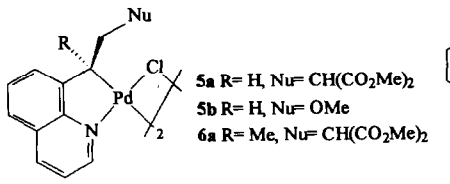
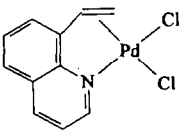


5a R= H, Nu= $CH(CO_2Me)_2$
5b R= H, Nu= OMe
6a R= Me, Nu= $CH(CO_2Me)_2$



7

The reaction temperature is crucial, for the addition of the methoxide anion (NaOMe) to the olefin since at room temperature forms of palladium metal were observed together with unreacted vinylquinoline, **3**. However, at 0°C the nuclear cyclopalladated complex **5b** [8] was isolated in 43% yield from the reaction of **3** (1.1. equiv.) and $PdCl_2(PhCN)_2$ (1.0 equiv.) in the presence of NaOMe (1.1 equiv.). This can be rationalized in terms of two competitive reactions, external nucleophilic attack on the coordinated alkene, and the substitution of the Cl^- by methoxide. The latter reaction probably leads to palladium methoxide species that decomposes to Pd metal. Indeed, when this reaction is performed in the presence of an excess (> 2 eqiv.) of NaOMe, only metallic palladium and an uncharacterisable mixture of organic products were isolated.

It is very likely that these nucleophilic additions proceed through a palladium adduct of 8-vinylquinoline in which both the nitrogen and the double bond are coordinated. Indeed, we have isolated the yellow compound **7** [8] from the reaction of $Na_2[PdCl_4]$ with the vinylquinoline **3** in the absence of nucleophilic reagents. The ^1H NMR spectrum of complex **7** in DMSO-d_6 (it is insoluble in other common organic solvents) shows the signals of the free vinylquinoline only. This indicates strongly that the ligand is weakly coordinated to the metal and is easily displaced by coordinating solvent (DMSO). The regiochemistry observed in these reactions is consistent with that observed earlier for the carbopalladation of allyl- and homo-allylamines and sulfides, i.e. the more thermodynamically stable five-membered palladocycle is formed preferentially [10].

The reactions of these new cyclopalladated complexes with alkynes and isocyanides is currently being investigated.

Acknowledgments

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References and notes

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[8] All new organometallic compounds gave satisfactory CHN analyses. Selected spectroscopic data as follows (FTIR, KBr pellets and ^1H NMR, 200 MHz at 20°C): Compound **3**: IR 1620 cm^{-1} (νC=C); ^1H NMR ($CDCl_3$):8.94 (dd, 1H, $^3J_{HH}$ = 4.1Hz, $^4J_{HH}$ = 1.8Hz, *o*-quinoline); 8.15–7.60 (m, 5H, aromatic); 7.52, 5.98 and 5.47 (3dd, 3H, ABX system, vinylic H). Compound **4**: IR1608 cm^{-1} (νC=C); ^1H NMR ($CDCl_3$): 8.80 (dd, 1H, $^3J_{HH}$ = 4.1 Hz, $^4J_{HH}$ = 1.8 Hz, *o*-quinoline); 7.93 (dd, 1H, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 1.7 Hz aromatic); 7.57–7.21 (m, 4H, aromatic); 5.32 (d, 1H, vinylic, $^2J_{HH}$ = 1.5 Hz), 5.10 (d, 1H, vinylic), 2.25 (s, 3H, Me). Compound **5a**: IR 1730 cm^{-1} (νC=O); ^1H NMR ($CDCl_3 + \epsilon$Py-d_5): 8.91 (d, 1H, $^3J_{HH}$ = 4.9 Hz, *o*-quinoline); 7.95 (d, 1H, $^3J_{HH}$ = 7.9 Hz, aromatic); 7.80–7.29 m, 4H, aromatic), 3.94 (t, 1H, C<u>H</u>$(CO_2Me)_2$); 3.75 and 3.30 (2s, 6H, CO_2Me); 2.1 (m, 1H, $CHCH_2$); 1.85 (m, 2H, $CHCH_2$). Compound **5b**: IR 1095 cm^{-1} (νC–O); ^1H NMR ($CDCl_3 + \epsilon$Py-d_5): 8.88 (d, 1H, $^3J_{HH}$ = 5.9 Hz, *o*-quinoline); 8.28 (d, 1H, $^3J_{HH}$ = 8.0 Hz, aromatic); 7.82–7.33 (m, 4H, aromatic), 4.01 and 3.25 (2dd, 2H, AB part of an ABX system); 3.45 (t, 1H, X part of an ABX system); 3.17 (s, 3H, OMe). Compound **6a**: IR 1730 cm^{-1} (νC=O); ^1H NMR ($CDCl_3 + \epsilon$Py-d_5): 9.60 (dd, 1H, $^3J_{HH}$ = 4.1Hz, $^4J_{HH}$ = 1.8 Hz, *o*-quinoline); 8.21 (dd, 1H, $^3J_{HH}$ = 8.3 Hz, $^4J_{HH}$ = 2.0 Hz aromatic); 7.79–7.30 (m, 4H, aromatic); 3.73 and 3.14 (2s, 6H, CO_2Me); 3.49 (t, 1H, X part of an ABX system, C<u>H</u>$(CO_2Me)_2$), 2.42 and 1.38 (2dd, 2H, AB part of an ABX system); 1.17 (s, 3H, Me).

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