New 3-(2-pyridyl)-1,2,4-triazole derivatives and their palladium (II) complexes

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The article is devoted to investigation of coordination compounds of palladium (II) with 3-(2-pyridyl)-1,2,4-triazole derivatives containing amino groups. We syntesized 4 ligands and 4 new coordination compounds. An interesting after removing of BOC-protection, NH_2-group is still uncoordinated. In ^1H NMR spectra of complexes was a significant shift of the ortho-pyridine proton in a low-field area, which prove proposed structure. This may be due to its closeness to the lone electron pair of the nitrogen cycle of the second triazole ligand.

Introduction

Heterocyclic ligands play an important role in the development of coordination chemistry. Amongst available five-membered ring systems, triazoles represent an interesting class of compounds due to the presence of three nitrogens [1-3]. 1,2,4-Triazole derivatives show diverse pharmacological activities and have been examined as antitumor [4], antibacterial [5], antifungal [6] and antiviral agents [7].

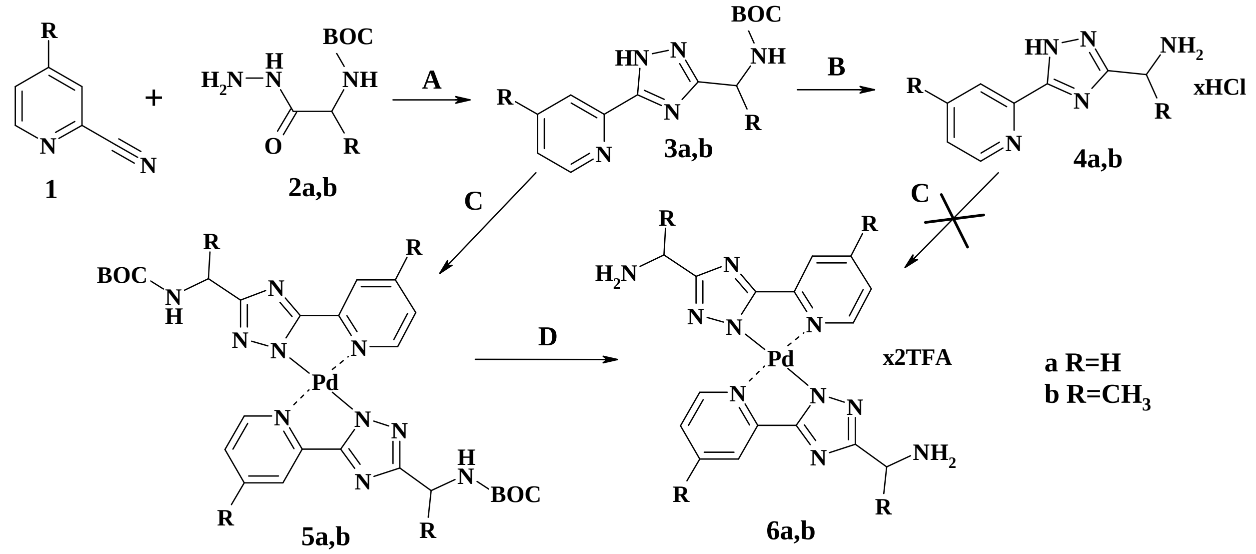
Metal complexes containing triazole may also show biological activity, providing an impetus for the investigation of their coordination chemistry [8-10].

Complexes of 3-(2-pyridyl)-1,2,4-triazoles typically have high stability, owing to the mutual combination of σ-donor and π-acceptor properties. If to compare electronic properties of 3-(2-pyridile)-1,2,4-triazolyl moiety with such wide used ligand as 2,2`-bypyridine, the first one is stronger σ-donor and weaker π-acceptor [11]. Also it should be noted that deprotonation of triazole ring arranges triazole containing ligands to act as a charged bidentate, or even tridentate ligands with simultaneous enhancing of complex stability.

Substantial amount of research has been dedicated to the study of noble metal complexes which incorporate derivatives of 1,2,4-triazole. This is due to their interesting photophysical and photochemical properties. Another possible use of these complexes is as catalysts in different chemical reactions. For example, palladium complexes can be used in cross-coupling reactions in preparative organic chemistry, as well as in obtaining of materials with luminescent properties [1-3].

Results and discussion

The synthesis of ligands **3** are based on acylation of **2** by iminoester **1** with



Scheme 1. *Reagents and conditions:* (A) MeONa, reflux, 10h; (B) HCl, i-PrOH, reflux, 24h; (C) $PdCl_2x2CH_3CN$, Et_3N, CH_3CN; (D) TFA, DCM, reflux, 2h.

subsequent cyclization of the resulting amidrazones into 1,2,4-triazoles (**Scheme 1**). Deprotection of **3** in acidic conditions leads to formation of amines **4**. The attempts to obtain **6** directly from ligands were unsuccessful, because of palladium reduction. Therefore we have synthesized palladium complexes **5** using BOC protected amines. Deprotection of **5** with TFA leads to obtaining of title compounds.

The absence of a ^1H NMR signal for the proton connected to the triazol ring, indicates the deprotonated form of ligands in **5** and **6**. It is noteworthy that the chemical shift of the *ortho*-Py proton in **5a** and **5b** are 9.54 and 9.35 ppm respectively, i.e. this proton becomes less shielded compared to the free ligand ($\Delta\delta_{5a}$=+0.91 ppm, $\Delta\delta_{5b}$=+0.71).

Deprotection of **5** with TFA leads to formation of trifluoroacetates of title compounds **6**. TFA was used for this purpose instead of HCl, because reaction with latter results in $PdCl_2$ formation. Changes in ^1H NMR-spectra of **6** comparing to free ligands is of the same character as in **5**. Δδ For *ortho*-Py proton in **6a** and **6b** is +0.94 and +0.85 ppm respectively. These could be realized in the structure proposed for **5** and **6** (**Fig.1**), where the *ortho*-Py proton is situated in a deshielded region formed by a triazole ring of an opposite ligand molecule, which is an accordance with previously obtained compounds [12].

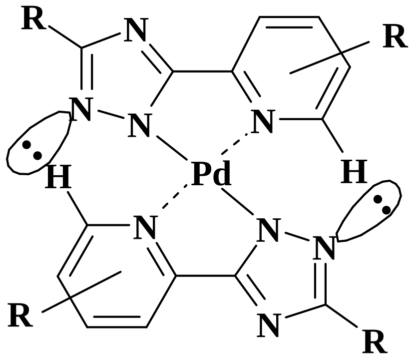


Fig.1. Schematic illustration of **5** and **6** structure.

Conclusion

This article describes synthesis and characterization of four novel palladium (II) complex containing 3-(2-pyridyl)-1,2,4-triazole moiety. Two of them were obtained by deprotection of amino groups in corresponding complexes. The structure of title compounds was proved by means of ^{1}H NMR spectroscopy.

Experimental part

Elemental analyses were carried out at Perkin-Elmer"2400"CHN Analyzer. NMR spectra in DMSO-d_6 solution were recorded on a Varian"400"spectrometer at room temperature.

General procedure A (**3a,b**): 10 ml of sodium methoxide methanolic solution (35 wt%) was added to solution of **1** **(**0.05 mol) in 20 ml of methanol and stirred at room temperature for 1 hour. Then **2** was added to obtained iminoester solution and refluxed for 10 hours. Obtained mixture was cooled to room temperature and solvent removed in vacuo. The resulting suspension was diluted with water and acidified with 2 ml of acetic acid to obtain a white solid. The crystals were separated via filtration, dried and recrystalized from toluene.

3-(2-pyridyl)-5-Boc-methylamino-1,2,4-triazole **(3a):** 6.26 g, (62.0%), white crystals. ^{1}H NMR (DMSO-d^{6}, 400 MHz): dH(ppm) 14.72–14.50 (br s, 1 H), 8.62 (d, 1 H), 8.11 (m, 1 H), 7.97 (m, 1 H), 7.47 (d, 1 H), 7.15 (br s, 1 H), 4.26 (s, 2 H), 1.39 (s, 9 H). Anal. calcd. for $C_{13}H_{17}N_5O_2$, %: C,56.71; H,6.22; N,25.44. Found: C,56.98; H,6.15; N,25.88.

3-(2-pyridyl-4-methyl)-5-Boc-isopropylamine-1,2,4-triazole **(3b):** 6.88 g, (69%), white crystals. ^{1}H NMR (DMSO-d^{6}, 400 MHz): dH(ppm) 14.81–14.66 (br s,1 H), 8.69 (d, 1 H), 8.06 (d, 1 H), 7.52 (s, 1 H), 7.09 (br s, 1 H), 4.29 (s, 1 H), 2.35 (s, 3 H) 1.42 (d, 3 H), 1.34 (s, 9 H). Anal. calcd. for $C_{15}H_{21}N_5O_2$, %: C,59.39; H,6.98; N,23.09. Found: C,59.52; H,6.58; N,23.44.

General procedure B (**4a,b**): 0.9 ml of hydrochloric acid (3.00M) was added to solution of **3** (0.03 mol) in 50 ml of isopropanole and refluxed for 24 h. Solvent was removed under vacuo to obtain a white crystals of **4**.

3-(2-pyridyl)-5-methylamino-1,2,4-triazole **(4a):** 5.01 g, (92.0%), white crystals. ^{1}H NMR (DMSO-d^{6}, 400 MHz): dH(ppm) 15.10–14.85 (br s, 1 H), 8.78 (br s, 3 H), 8.71 (d, 1 H), 8.06-7.97 (m, 2 H), 7.54 (d, 1 H), 4.13 (s, 2 H). Anal. calcd. for $C_8H_{10}ClN_5O_2$, %: C,45.40; H,4.76; N,33.09. Found: C,45.88; H,4.62; N,33.23.

3-(2-pyridyl-4-methyl)-5-isopropylamine-1,2,4-triazole **(4b):** 4,93 g, (89%), white crystals. ^{1}H NMR (DMSO-d^{6}, 400 MHz): dH(ppm) 14.85–14.61 (br s, 1 H), 8.79 (s, 3 H), 8.66 (s, 1 H), 8.02-7.92 (m, 2 H), 4.16 (s, 1 H), 2.53 (m, 3 H), 1.49 (d, 3 H). Anal. calcd. for $C_{10}H_{14}ClN_5$, %: C,50.11; H,5.89; N,29.22. Found: C,50.48; H,5.75; N,29.53.

General procedure C (**5a,b*****):*** $PdCl_2{\times}(CH_3CN)_2$ (0.26 g, 1 mmol) in hot acetonitrile (20 mL) was added to solution of **3** (2 mmol) and Et_3N (0.29 ml, 2 mmol) in acetonitrile (20 ml). Precipitated yellow crystals were collected by filtration, washed with acetonitrile and dried in air.

5a: ^{1}H NMR (DMSO-d^{6}, 400 MHz): dH(ppm) 9.54 (d, 2 H), 8.54 (m, 2 H), 7.96 (m, 2 H), 7.58 (d, 2 H), 4.69 (s, 4 H), 1.49 (s, 18 H). Anal. calcd. for $C_{26}H_{32}N_{10}O_4Pd$, %: C,53.44; H, 4.28; N,22.44. Found: C,53.82; H,4.54; N,22.19.

5b: ^{1}H NMR (DMSO-d^{6}, 400 MHz): dH(ppm) 9.35 (s, 2 H), 7.96-7.58 (m, 4 H), 4.19 (s, 2 H), 2.61 (d, 6 H), 1.57 (s, 6 H), 1.42 (s, 18 H). Anal. calcd. For $C_{30}H_{40}N_{10}O_4Pd$, %: C,50.67; H, 5.68; N,19.71. Found: C,50.82; H,5.59; N,19.33.

General procedure D (*6a,b*). Solution of 1 mmol TFA in DCM was added to suspension of **5** (0,5 mmol) in 20 ml of DCM and then refluxed for 2 h. The mixture was then cooled to room temperature and the solvent was removed to obtain light yellow crystals of **6.**

6a: ^1H NMR (DMSO-d^6, 400 MHz): dH(ppm) 9.71 (d, 2 H), 8.56 (m, 2 H), 7.97 (m, 2 H), 7.61 (d, 2 H), 4.72 (s, 4 H). Anal. calcd. for $C_{20}H_{18}F_6N_{10}O_4Pd$, %: C,35.18; H,2.66; N,20.51. Found: C,34.98; H,2.54; N,20.69.

6b: ^1H NMR (DMSO-d^6, 400 MHz): dH(ppm) 9.64 (d, 2 H), 8.58 (s, 4 H), 7.86 (m, 2 H), 7.52 (d, 2 H), 4.63 (s, 2 H), 2.57 (s, 6 H), 1.67 (d, 6 H). Anal. calcd. for $C_{20}H_{25}N_{10}Pd$, %: C,39.01; H, 3.55; N,18.96. Found: C,38.72; H,3.84; N,18.55.

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