Notes

Site-Specific Methylation of Coordinated 1,2,4-Triazoles: A Novel Route to Sterically Hindered $Ru(bpy)_2$ Complexes

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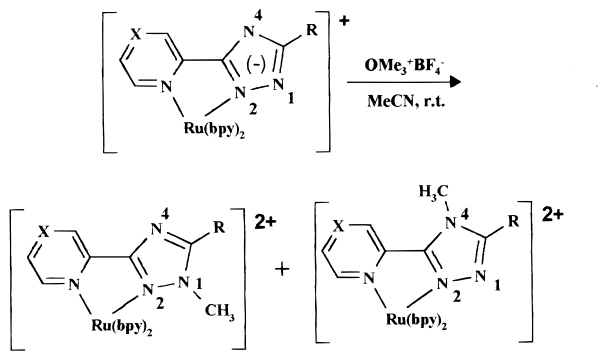
Introduction

In the last few years it has been shown that chelating 1,2,4-triazoles such as pyridine− and pyrazine−triazoles are interesting building blocks for supramolecular systems.[1,2] So far most attention has been paid to the study of the photophysical and electrochemical properties of $[Ru(bpy)_2pt]^+$ type complexes (bpy = 2,2′-bipyridyl and pt = a pyridine− or a pyrazine−triazole), containing *negatively* charged (deprotonated) triazole rings. The results obtained have shown that the presence of a negative charge on the ligand gives rise to compounds with unusual photophysical properties.[2,3] To assess the importance of this factor we are now investigating metal complexes containing N-methylated (*neutral*) triazoles.[4] In the traditional route to these complexes, the N-methylated ligand is prepared first and subsequently used to prepare the appropriate metal complex.[5]

In this contribution, we wish to report a novel synthetic route to such complexes. This method is based on the direct methylation of the appropriate precursor metal complex with trimethyl oxonium tetrafluoroborate ($OMe_3^+BF_4^-$). The methylation process was found to be remarkably site-specific, leading to the target complex in a single step under very mild conditions. Surprisingly, the main product of the reaction is always the sterically hindered N1 methylated isomer, which was never obtained using the aforementioned "traditional route". The methylation of heteroaromatic nitrogens has been successfully applied during the synthesis of sophisticated supramolecular assemblies,[6,7] and the methylation of ruthenium complexes has been observed before.[6b] However, this contribution is the first example of the synthesis of sterically hindered ruthenium(II) polypyridyl substrates otherwise not synthetically accessible.

Scheme 1. Reaction Pathway and Complex Structures



1	X = C, R = H	**5**	X = N, R = H
2	X = C, R = Me	**6**	X = C, R = o-hydroxyphenyl
3	X = C, R = Br	**7**	X = C, R = 9,10-phenothiazine
4	X = C, R = p-toluyl	**8**	X = C, R = p-chloromethoxyphenyl

Experimental Section

Materials. All precursor complexes were available from earlier studies.

Methylation of Complex 1−8. The reaction pathway and ligand structures are shown in Scheme 1. To a stirring suspension of the required metal complex (0.07 mmol) and K_2CO_3 (28 mg, 0.21 mmol) in dry acetonitrile (10 mL) was added $OMe_3^+BF_4^-$ (15 mg, 0.1 mmol) in one portion at room temperature. The resulting mixture was stirred under N_2 for 1 h, after which the solvent was removed under reduced pressure. The residue was dissolved in a mixture of acetone and water from which the product was precipitated as a $[Ru(bpy)_2Mept](PF_6)_2$ salt by the addition of few drops of a NH_4PF_6 saturated water solution. An overall yield (N1 and N4 isomers combined) of 80−88% is obtained for all systems studied. The main isomer (N1 methylated) could be obtained in pure form by double recrystallization from an acetone−water mixture or by semipreparative cation-exchange HPLC.[8]

Results and Discussion

We have applied this direct methylation method to eight different $[Ru(bpy)_2pt]^+$ complexes. As shown in Scheme 1, the triazole moiety in the parent complexes is bound through the N2 atom of the ring, leaving the N1 and N4 positions available for methylation. It is known from previous studies[5,8,9] that for N2-coordinated triazole rings the N4 and N1 methyl groups give rise to ^1H NMR signals around 4.15 and 3.10 ppm, respectively. One can, therefore, conveniently determine the location of the methylation and quantify the N1/N4 product ratio by ^1H NMR

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Table 1. N1/N4 Selectivites Obtained for the Compounds Investigated

		N−Me δ ^{1}H NMR[a]		
complex	η (%)	N1	N4	N1/N4 selectivity[b]
1	100	3.15	4.21	90/10
2	100	3.08	4.12	90/10
3	100	3.07	4.14	90/10
4	100	3.21	4.16	95/5
5	100	3.17	4.26	70/30
6	70	2.97	4.01	95/5
7	100	3.09	4.13	85/15
8	100	3.16	4.22	85/15

spectroscopy. UV/vis and emission spectra were also recorded, but since these do not differentiate between the different methylation sites, they are not discussed here. All products obtained were NMR and HPLC pure.

Previous studies have shown that when a N1-methylated pt ligand is reacted with a $Ru(bpy)_2$ substrate, coordination took place almost exclusively through the N4 position. Yields for the N2 isomer as identified by HPLC were typically 10% or less.[8] The reason for this behavior was ascribed to the steric hindrance caused on the N2 position by the methyl group in N1. Therefore, one would expect the methylation reaction here described to give exclusively the N4-methylated isomer. However, the data given in Table 1 show that the reaction is remarkably site-specific with a high selectivity for methylation at the N1 position, suggesting that the N1 position is more nucleophilic and that steric hindrance is not an overriding factor for these reactions.

The analysis of the results obtained shows some other interesting features. The selectivity toward the N1 position is hardly affected by the nature of the R substituent. In addition, no sign of products other than the N1- and N4-methyl derivatives was seen for entries **5**, **6**, and **7**, where additional methylation sites are present. The drop on the selectivity observed for entry **5** could be explained in the light of previous studies which suggested a high degree of delocalization of the negative charge on the triazole ring onto the pyrazine grouping.[10]

A 100% conversion was observed for all the complexes under investigation but complex **6**. The lower yield observed for compound **6** is possibly explained by the presence of an hydrogen bond between the hydroxyl group and the N4 nitrogen of the triazole, thereby reducing the negative character of the triazole ring.[11]

A study of the photochemical properties of some of the complexes synthesized yielded interesting results. When the N2-bound/N1-methylated complex **1** is irradiated with white light for 24 h in acetone, it is quantitatively isomerized into the N4-bound/N1-methylated isomer. This isomer is photostable, and neither decomposition nor isomerization is observed after further irradiation. The N2-bound/N4-methylated isomer is also photostable under the same conditions. These results clearly suggest that the N2-bound/N1-methylated isomer is the less stable thermodynamically, an observation that makes the selectivity found even more remarkable. More detailed photochemical and photophysical studies are underway to further investigate this unusual behavior.

In conclusion, the method reported represents a new and simple route for the high yield synthesis of sterically hindered $[Ru(bpy)_2]$ complexes by direct methylation of the appropriate metal complex. The interest of this method resides in the high selectivity achieved and in the fact that the less thermodynamically stable isomer, so far only obtained in very small amounts, is the main product of the reaction. These observations represent a significant example on how "classical" organic reactions could be applied to solve synthetic problems during the synthesis of ruthenium polypyridyl complexes. In the continuing search for larger supramolecular systems, this new approach adds to the synthetic pathways available.

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