

Synthesis and characterization of new N-Heterocyclic-BF₃ adducts and their reactivity vs water

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ABSTRACT

Species derived from N-Heterocycles with BF₃ Lewis acids generate adducts that are redox active.

Here we report the synthesis and characterization of 5 N-Heterocycle-BF₃ adducts: Py-(BF₃)₂, Q-(BF₃)₂, Ph-(BF₃)₂, TMQ-(BF₃), and Dipy-(BF₃)₂. The new adducts were structurally characterized by ¹H, ¹¹B, and ¹⁹F NMR. As an example, the Q-BF₃ adduct is stable in an inert environment but in the presence of oxygen or water, its voltammetric profile decays, suggesting chemical decomposition of the adduct. Furthermore, this decomposition is accompanied by the generation of BF₄⁻. The crystalline structure of the reaction product of TMQ-(BF₃) with traces of water was obtained, showing that the BF₃ generates BF₄⁻ counterion. Based on our observations, we proposed a plausible reaction mechanism for the generation of BF₄⁻.

Keywords: BF₃ adducts, N-Heterocycles adducts, BF₃ reactivity with water.

1. Introduction

Redox-active organic molecules are used in a wide variety of applications, ranging from energy storage, use as photochemical sensitizers, as homogeneous (electro)catalysts, and in biomedical applications.¹⁻⁶ The generation of charged organic molecules facilitates their solubility in aqueous and nonaqueous solvents. We are particularly interested in boron compounds. The generation of

boron-containing zwitter-ions,^{7, 8} where the organic compound carry simultaneously positive and negative charges within their structure make them of great interest for their solubility. In the last decade, boron fluoride adducts of N-heterocyclic carbene (NHC) were reported. These can also be described as a zwitterionic imidazolium trifluoroborate, which is highly resistant to hydrolysis and can be recrystallized from boiling water.⁹⁻¹¹ Chansaenpak and co-workers reported that the trifluoroborate moiety can be significantly stabilized against hydrolysis by a proximal cationic functionality, such as a phosphonium unit, allowing for in vivo imaging.¹² However, these are particular cases where it is possible to stabilize the BF₃ adducts against water.

Quinoxalines, pyrazines, and pyridines form redox-active materials^{13, 14} when they are coordinated to BF₃ in the nitrogen of the N-Heterocycle. However, the reactivity of these materials against traces of water in nonaqueous electrolytes presents a challenge. As reported¹⁵ by Wamsler, the mechanism of the formation of HBF₄ from Lewis acid BF₃ in the presence of water, shows a series of intermediate stages, which are summarized in equations 1 to 3.



where successive reactions with water leads to the formation of boric acid, hydrofluoric acid, and tetra fluoroboric acids.

Herein, we synthesized five N-heterocycles BF₃ adducts (Figure 1). We replicate the synthesis of Py-(BF₃)₂ (**1**) and Q-(BF₃)₂ (**2**). Additionally, we reported the synthesis of three new BF₃ adducts;

Ph-(BF₃)₂ (**3**), TMQ-(BF₃) (**4**), and Dipy-(BF₃)₂ (**5**). We characterized these adducts, as well as, the reaction of the adducts with traces of water generating BF₄⁻ as the counterion. Based on it, we propose a plausible mechanism of BF₄⁻ formation from the N-heterocycles BF₃ adduct.

2. Experimental

2.1 Chemicals. All reactive and solvents used were of high purity. 4,4'-Dipyridyl (99.5%), phenazine (98%), quinoxaline (>98%), 2,6,7-trimethylquinoxaline (97%), pyrazine (99%), BF₃-etherate, LiTFSI (>99%), Propylene carbonate anhydrous (99.7%), CH₂Cl₂, THF, CD₃CN and CDCl₃ were purchased from Sigma-Aldrich. Methylene chloride and diethyl ether were purchased from Merck. Tetrabutylammonium hexafluorophosphate (TBAPF₆) was recrystallized previous to use and was purchased from Sigma-Aldrich.

2.2 Apparatus. ¹H, ¹¹B, and ¹⁹F NMR spectra were obtained in CD₃CN and CDCl₃ solvents on Varian Unity 500 MHz equipment. TBAPF₆ was used as a standard for the ¹⁹F NMR experiment and BF₃-etherate was used for reference for the ¹¹B NMR experiments. Crystallography data were collected on a Bruker D8 Venture kappa diffractometer equipped with a Photon II CPAD detector. An I μ s microfocus source provided the Mo K α radiation ($\lambda = 0.71073 \text{ \AA}$) that was monochromated with multilayer mirrors. The collection, cell refinement, and integration of intensity data was carried out with the APEX3 software.¹⁶ The absorption correction was performed by multi-scan methods using SADABS.¹⁷ The structure was solved with the dual space methods using SHELXT.¹⁸ The structure was refined with the full-matrix least-squares routine of SHELXL.¹⁹

2.3 Synthetic procedures. The procedure was adapted with a few modifications using previous reported protocols.^{13, 20}

2.3.1 Py-(BF₃)₂ (1). In an extremely dry Schlenk flask equipped with a septum and magnetic stir bar, BF₃-OEt₂ (2.13 g, 15 mmol) were added on pyrazine (0.25 g, 3.125 mmol) starting material suspension in CH₂Cl₂ cooled at 0°C in an ice bath under inert atmosphere. The precipitate, usually white, is generated after the BF₃-etherate addition. The mixture was left to slowly reach room temperature in a melting ice bath with stirring overnight. The product was dried under a vacuum for 24 h.

2.3.2 Q-(BF₃)₂ (2). In an extremely dry Schlenk flask equipped with a septum and magnetic stir bar, BF₃-OEt₂ (2.18 g, 15.38 mmol) were added on quinoxaline (0.5 g, 3.85 mmol) starting material suspension in Et₂O cooled at 0°C in an ice bath under inert atmosphere. The precipitate, usually white, is generated after the BF₃-etherate addition. The mixture was left to slowly reach room temperature in a melting ice bath with stirring overnight. The product was dried under a vacuum for 24 h.

2.3.3 Ph-(BF₃)₂ (3). In an extremely dry Schlenk flask equipped with a septum and magnetic stir bar, BF₃-OEt₂ (1.53 g, 10.8 mmol) were added on phenazine (0.5 g, 2.70 mmol) starting material suspension in CH₂Cl₂ cooled at 0°C in an ice bath under inert atmosphere. The precipitate, usually white, is generated after the BF₃-etherate addition. The mixture was left to slowly reach room temperature in a melting ice bath with stirring overnight. The product was dried under a vacuum for 24 h.

2.3.4 TMQ-(BF₃) (4). In an extremely dry Schlenk flask equipped with a septum and magnetic stir bar, BF₃-OEt₂ (1.65 g, 11.63 mmol) were added on quinoxaline (0.5 g, 2.90 mmol) starting material suspension in Et₂O cooled at 0°C in an ice bath under inert atmosphere. The precipitate, usually white, is generated after the BF₃-etherate addition. However, due to the methyl groups present in the structure, it was possible to obtain only one BF₃ coordinated to the structure. The mixture was

left to slowly reach room temperature in a melting ice bath with stirring overnight. The product was dried under a vacuum for 24 h.

2.3.5 *Dipy*-(BF₃)₂ (5). In an extremely dry Schlenk flask equipped with a septum and magnetic stir bar, BF₃-OEt₂ (1.81 g, 12.8 mmol) were added on 4,4'-dipyridil (0.5 g, 3.20 mmol) starting material suspension in CH₂Cl₂ cooled at 0°C in an ice bath under inert atmosphere. The mixture was left to slowly reach room temperature in a melting ice bath with stirring overnight.. The product was dried under a vacuum for 24 h.

2.4 Electrochemical measurements. All solution preparation and electrochemical measurements were performed inside an Ar-filled glovebox (MBraun Inc.). Electrochemical measurements were performed with a CH Instruments (Austin, TX) 7601 potentiostat. All the cyclic voltammetry experiments were performed with 3 mM Au macroelectrode (BASi). Ag and Pt wires were used as quasi-reference and counter electrodes, respectively.

3. Results and discussion

The N-Heterocyclic-BF₃ adducts synthesized (Figure 1) were structurally characterized by ¹H, ¹¹B, and ¹⁹F NMR (Figures S1 – S9). The principal shift that confirms the structures of ¹¹B and ¹⁹F NMR were summarized in table 1.

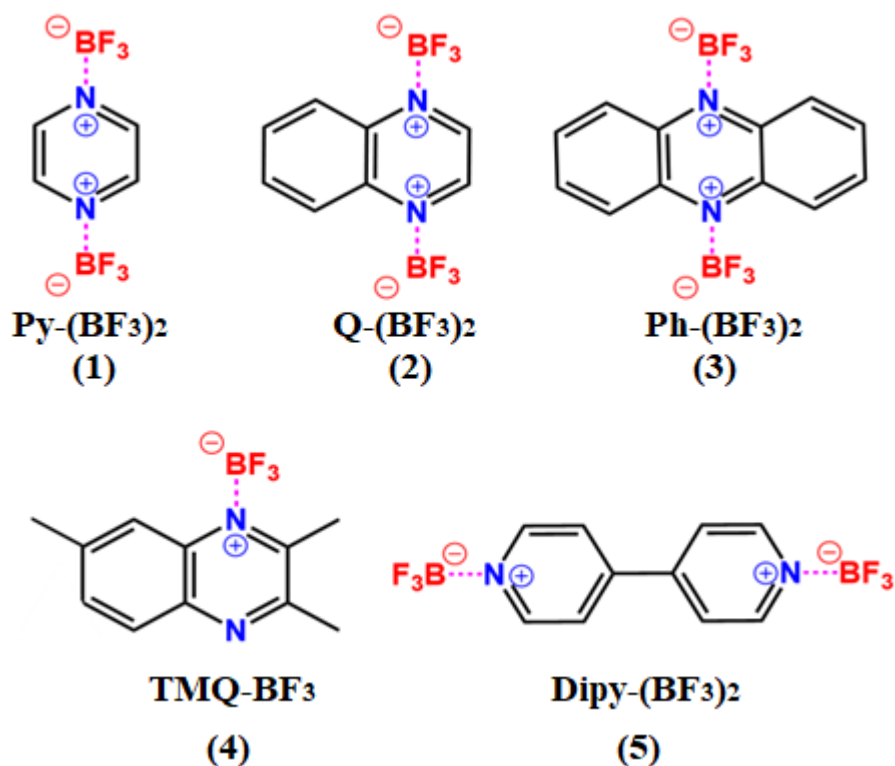


Figure 1. Depiction of the chemical structure of N-Heterocyclic-BF₃ adducts.

Table 1. Summary of ¹⁹F and ¹¹B NMR characterization

| Adduct | Solvent | ¹⁹ F NMR (δ ppm) | ¹¹ B NMR (δ ppm) |
|--------------------------------------|------------------------------------|-----------------------------|-----------------------------|
| Q-(BF ₃) ₂ | CD ₃ CN | -145.1 (s) | -0.12 |
| Py-(BF ₃) ₂ | CD ₃ CN | -151.1 (s) | 0.26 |
| Ph-(BF ₃) ₂ | CD ₃ CN | -151.5 (s) | -1.09 |
| Dipy-(BF ₃) ₂ | (CD ₃) ₂ CO | -151.7 (s) | -0.88 |
| TMQ-(BF ₃) | CD ₃ CN | -152.2 to -152.5 (m) | -1.22 |

All ¹⁹F NMR spectra were calibrated in the function of TBAPF₆.

BF₃ adducts were synthesized following and modified protocols previously reported^{13, 20, 21} with the addition of BF₃ etherate over suspension of the N-Heterocyclic molecules under

an inert atmosphere with ultra-dry CH_2Cl_2 or Et_2O . ^1H NMR showed a shift of precursor signals after reaction with BF_3 etherate. Molecules (1), (2), (3), and (5) kept the symmetry after the reaction, suggesting the addition of two BF_3 in each molecule. (4) does not show symmetry in the proton NMR signals due to the methyl group in position 6. Additionally, ^{19}F NMR data showed a multiplet signal between -149 to -151 ppm that reinforced the non-symmetry in the adduct. On the other hand, (1), (2), (3), and (5) adducts showed only a singlet fluorine NMR signal that corresponds to the equivalent fluorine on the two BF_3 in the adduct. ^{11}B NMR showed only singlet signals for all adducts. This fact suggests that the (1), (2), (3), and (5) adducts present two equivalent boron in the adduct structure, reinforcing the ^{19}F NMR results. However, the fact of observing only one boron signal for (4) adduct shows that it has only one boron atom coordinated to the TQM. This experiment is key to determining the number of BF_3 coordinated in the structure, due to not having an asymmetric structure, and that the ^{19}F NMR spectrum is not conclusive at determining the number of BF_3 molecules in the adduct. Several attempts were made to obtain the crystal structure of the BF_3 adducts within the glovebox. However, it was not possible to obtain single crystals with sufficient size to diffract. Additionally, the morphology observed in the microcrystals corresponds to amorphous systems, where it was possible to observe needles on needles. This is due to the rapid evaporation of the solvents used in the crystallization caused by the argon flow system inside the dry box.

3.3 N-Heterocycles- BF_3 adducts vs water

Due to the rapid evaporation of the solvents used in the crystallization caused by the fast argon flow system inside the dry box the solution was moved outside to ambient conditions. A yellow

solution containing the TMQ-(BF₃) adduct was slowly evaporated outside of the glovebox. Dark green needles were obtained after 2 weeks of slow evaporation which were suitable for X-ray diffraction (Figure 2). Surprisingly, the crystalline structure showed the presence of a BF₄⁻ molecule as a counterion, and the protonation of a nitrogen atom. Also, the structure shows a water molecule coordinated to the structure through a hydrogen bond between the oxygen in the water and the H that is protonating the nitrogen atom of the structure. Additionally, the bond distance observed between the oxygen atom and the protonated nitrogen atom (2.730(3) Å) is consistent with the distance required for the generation of a hydrogen bond.²² The packing of the crystal structure in the unit cell shows that the structure is mainly stabilized by π -stacking interactions (Figure S10) between the aromatic density. The calculated distance for π -stacking between least-squares planes is 3.270 Å. The centroid to centroid distance of the phenyl rings is 3.8324(4) Å. Additionally, the BF₄⁻ counterion is observed together with free water molecules occluded within the crystal structure. ¹⁹F NMR spectroscopy confirms the presence of BF₄⁻ in the solution containing the green materials dissolved in PC. Two peaks were observed at 151.45 and 155.27 ppm corresponding to ¹⁰BF₄⁻ and ¹¹BF₄⁻ respectively (Figure S11). Similar behavior was observed for (BF₃)₂-Phenazine adduct, but the refinement of the crystalline structure has an error greater than 10%. This molecule showed two different aromatic densities that not were identified. A picture of this structure was included in Figure S12. Additionally, cyclic voltammetry showed that the Q-BF₃ adduct is not stable to the environmental humidity. The voltametric peaks for Q-BF₃ reduction disappear after two weeks of exposure to air turning the adduct inactive to redox. This fact reinforced the reactivity observed for the N-Heterocycle-BF₃ adduct in the presence of water traces.

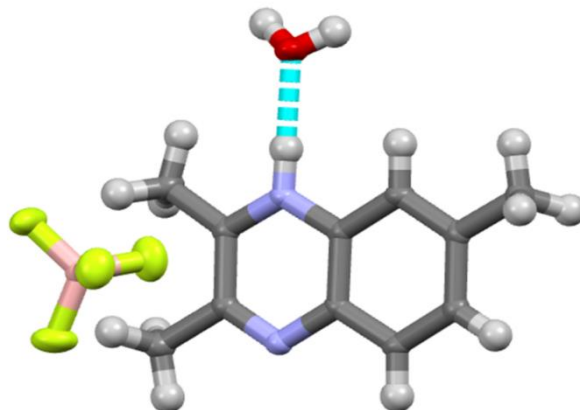


Figure 2. Molecular structure determined by X-ray analysis of $[\text{H}^+\text{N-TMQ}](\text{BF}_4)\cdot\text{H}_2\text{O}$. Ellipsoids at 50% level of probability.

3.4 Plausible mechanism for the generation of BF_4^- from BF_3 -adduct

The presence of water bonded to hydrogen in the protonated nitrogen, together with the presence of free water molecules, strongly suggests that water molecules are involved in the mechanism of BF_4^- generation from BF_3 present in the adduct. Based on Wamser's studies regarding the mechanism of HBF_4 formation, a possible BF_4^- counterion generation mechanism due to the presence of water from ambient humidity was proposed (Figure 5).

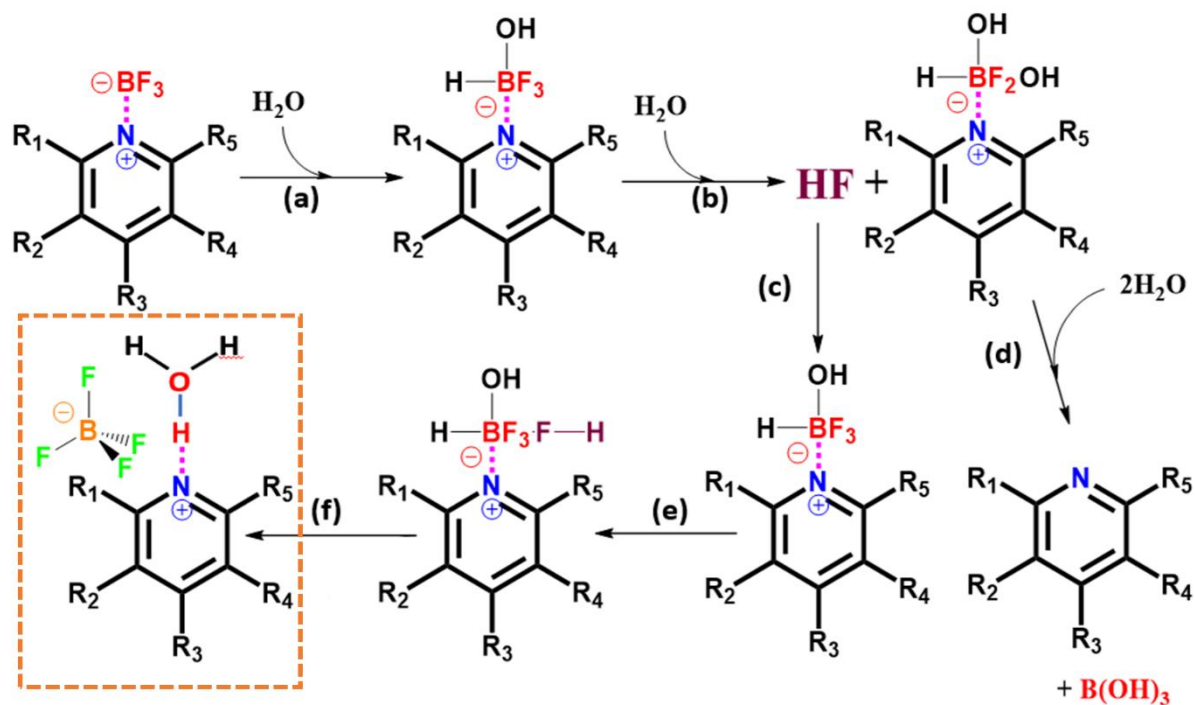


Figure 5. Plausible mechanism of BF_4^- generation from N-Heterocyclic- BF_3 adduct.

In the presence of a water molecule (**5a**), the BF_3 present in the adduct is hydrated, generating an $N\text{-(H)(OH)BF}_3$ structure. In turn, this can react with another water molecule (**5b**) to generate $N\text{-(H)(OH)BF}_2(\text{OH})$, and HF. The $N\text{-(H)(OH)BF}_2(\text{OH})$ structure with another water molecule (**5d**) can generate B(OH)_3 and the $N\text{-Heterocycle}$. Parallel HF generated as a product of (**5b**) can react with another BF_3 adduct (**5c**) to generate the intermediate species $N\text{-(H)(OH)BF}_3\text{-FH}$ (**5e**). Finally, pseudo-hydrofluoric acid protonates the nitrogen atom in the $N\text{-Heterocycle}$ while one water molecule is stabilized by hydrogen bonding to protonated nitrogen (**5f**), and BF_4^- ion is released. This reaction mechanism explains the generation of BF_4^- with traces of water. Obtaining crystalline structures required environmental humidity to activate the reaction. Additionally, electrochemistry measurements of $\text{Q-(BF}_3)_2$ outside of the globe box reinforced this finding. After two weeks

of exposure the adduct to environmental humidity, the redox character disappears (Figure S13). This fact suggests that the BF_3 in the redox adduct was transformed to BF_4^- , which is non-redox-active. Additionally, Figure S11 shown the presence of two peaks that correspond to BF_4^- anion.

4. Conclusion

In summary, we successfully synthesized three new BF_3 N-Heterocyclic adducts and replicate the synthesis of another two. The adducts were characterized by ^1H , ^{11}B , and ^{19}F NMR confirming the proposal structures and the number of BF_3 coordinated in the adduct. X-ray diffraction showed the formation of BF_4^- ion in the presence of traces of water. Additionally, the protonation of nitrogen atoms in the TMQ suggested that HF is formed in the mechanism of reaction with water of these adducts, as suggested by Wamser et al. for the reaction of BF_3 in water. The plausible mechanism proposed for the formation of BF_4^- from BF_3 -adducts is dependent on the water molecules present in the solution or those coming from the humidity of the air. In this sense, although quinoxaline, pyrazine, or pyridine adducts with BF_3 are presented as interesting study systems for redox reactions, it is very important to keep the *N*-heterocycles- BF_3 in totally anhydrous solutions. In addition, BF_3 adducts are extremely reactive, even at ambient humidity, generating exergonic reactions with the release of fuming HF.

Credit authorship contribution statement

Adolfo I. B. Romo synthesized the adduct, performed the characterization, and wrote the manuscript. Md Sazzad Hossain performed electrochemical measurements. Toby J. Woods

performed the X-ray diffractions. Joaquín Rodríguez-López wrote and edited the manuscript and secured funding for the project.

Declaration of competing interest

There are no conflicts to declare

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Supplementary materials

Supplementary materials contain NMR, crystallographic and electrochemical data.

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