VIETNAM NATIONAL UNIVERSITY - HCMC
HO CHI MINH CITY UNIVERSITY OF TECHNOLOGY

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INFORMATION OF THE THESIS

Thesis title: Direct functionalization of C-H bonds in pyrrolo[1,2-*a*]quinoxaline derivatives

Major: Chemical Engineering Major Code : 9520301

PhD. Candidate: Ca Thi Thuy

Supervisors: 1. Dr. Nguyen Thanh Tung

2. Prof. Dr. Phan Thanh Son Nam

Training Institution: Ho Chi Minh City University of Technology, VNU – HCMC

Major contributions of the thesis

Compounds containing the pyrrolo[1,2-*a*]quinoxaline framework have many important applications in various fields, such as pharmaceutical, dye, materials, and organic chemistry. Methods for synthesizing pyrrolo[1,2-*a*]quinoxalines have been developed over the past decade. Notably, the functionalization of C_1-H bonds in pyrrolo[1,2-*a*]quinoxalines into valuable bonds, such as C_1-S, C_1-N, C_1-halogen, and C_1-C bonds, have been rapidly reported in recent years. Among these bonds, we were particularly interested in the C_1-S and C_1-C bonds because they had not been widely explored. Therefore, this thesis aimed to research and develop methods for directly converting the C_1-H bonds of pyrrolo[1,2-*a*]quinoxalines into C_1-S and C_1-C bonds. For each reaction investigated, the reaction products were extracted with ethyl acetate, then separated from the organic mixture by column chromatography, and the isolation yields were calculated. Then, the chemical structures of the products were determined by spectroscopic methods. There were four specific methods as follows:

First, the direct C_1-H sulfenylation of pyrrolo[1,2-*a*]quinoxalines with different sulfenyl sources, such as di(hetero)aryl disulfides or arylsulfonyl hydrazides. With di(hetero)aryl disulfide reagents, the copper-catalyzed direct C_1-H sulfenylation of 4-phenylpyrrolo[1,2-*a*]quinoxaline with diphenyl disulfide was successfully conducted under the investigated conditions with a yield of 73%. These reaction conditions were also compatible with an array of pyrrolo[1,2-*a*]quinoxaline substrates and di(hetero)aryl disulfide reagents, giving products with good yields. This method was first published for the direct C_1-H sulfenylation of pyrrolo[1,2-*a*]quinoxalines, and 21 new compounds were successfully synthesized with

yields from 18% to 76%. Meanwhile, with sulfonyl hydrazide reagents, the reaction yield between 4-phenylpyrrolo[1,2-*a*]quinoxaline and *p*-toluenesulfonyl hydrazide in the presence of iodine reached 80% in the studied conditions. The reaction scope was expanded with substrates and reagents bearing different substituents. There were 21 compounds successfully synthesized with yields from 22% to 80%, of which 2 were known in the sulfenylation method with diaryl disulfide, and the remaining 19 were new compounds. Using the sulfur sources as arylsulfonyl hydrazides, the substituent groups at the C_1 positions of pyrrolo[1,2-*a*]quinoxalines would be more diverse because arylsulfonyl hydrazides were easily synthesized from abundant arylsulfonyl chloride. In general, these methods were simple, easy to perform, and effective.

Second, the sulfonylation of 1-iodopyrrolo[1,2-*a*]quinoxaline derivatives with sodium (hetero)arylsulfinate salts under mild conditions requiring only DMSO solvent at 100 ^oC in just 15 minutes. The reaction between 1-iodo-4-phenylpyrrolo[1,2-*a*]quinoxaline and sodium phenylsulfinate produced the **C1** sulfone compound with a high yield of 90%. Many (hetero)arylsulfinate substrates and nucleophiles were also successfully investigated, especially heterocyclic nucleophiles such as 2-thiophenylsulfinate. There were 19 compounds successfully synthesized with yields from 43% to 90%, including 9 new substances and 10 reported ones in the sulfonylation reaction of Le's group. The sulfonylation method of pyrrolo[1,2-*a*]quinoxalinyl iodides occurred *via* nucleophilic substitution mechanism in simple reaction conditions, without transition metals or other additives, and improved the disadvantages of Le's method.

Third, the direct morpholinomethylation method of the C_1-H bonds in pyrrolo[1,2-*a*]quinoxalines with a carbon source for methylation from morpholine. This transformation also took place under simple and easy-to-perform conditions, including PIFA oxidant and CuI promoter in DMSO solvent at 120 ^oC for 24 hours. The morpholinomethylation of 4-phenylpyrrolo[1,2-*a*]quinoxaline produced compound **D1** with a yield of 48% in the studied conditions. Substrates bearing substituents including methyl, methoxy, or heterocycles such as pyridine, thiophene, and furan were investigated to expand the reaction scope. This was a new method for the direct morpholinomethylation of the C_1-H bonds in pyrrolo[1,2-*a*]quinoxalines and a total of 11 new compounds were successfully synthesized with yields from 25% to 71%. These compounds also contained the morpholine core with important biological activities.

Fourth, the method of direct formylation of C_1-H bonds in pyrrolo[1,2-*a*]quinoxalines with DMSO as a carbon source. This formylation occurred in mild conditions, including CuI and TFA at 120 ^oC for 22 hours. The formylated product of 4-phenylpyrrolo[1,2-*a*]quinoxaline was obtained in a yield of 40% in the studied conditions. Some other substrates were also used for this transformation and gave average yields. A total of 7 substances were synthesized with the highest yield of 48%, of which 6 were new substances, and 1 substance was published in Guillon's research. This method was simple, easy to perform, and less toxic than Guillon's method.

Scientific supervisors **PhD. Candidate**

Dr. Nguyen Thanh Tung **Prof. Dr. Phan Thanh Son Nam** **Ca Thi Thuy**