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Pd and Cu catalysis in the formation of C(sp²)-N bonds for amines and polyamines modifications: comparison of the scope

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Homogeneous Pd(0)-catalyzed amination reactions can be successfully applied to the synthesis of N-aryl and N-heteroaryl substituted linear polyamines, nitrogen-containing macrocycles, macropolycycles and biologically active derivatives of adamantane-containing amines. The application of much cheaper copper catalysis also allows (hetero)arylation of amines and polyamines. The selectivity of the copper-mediated reactions dramatically depends on the nature of (poly)amines and (hetero)aryl halides and on the composition of the catalytic system.

1. Scope

Our investigations revealed that Pd(0)-catalyzed amination reactions of aryl and heteroaryl bromides can serve as a universal tool for the synthesis of N-aryl and N-heteroaryl substituted adamantane-containing amines differing by the spatial hindrances at the amino group, and what is of the special interest, can be equally used for the macrocyclization reactions leading to a great variety of N and O-containing macrocyclic and macropolycyclic compounds of various architectures with aryl and heteroaryl endocyclic spacers. The use of the catalysis by much cheaper copper complexes allowed the synthesis of N-aryl and N-heteroaryl substituted adamantane-containing amines, mono- and di(hetero)arylated diamines and polyamines. Our observations unveiled the dependence of the selectivity of Cu-catalyzed reactions on the nature of (poly)amines and (hetero)aryl halides and on the composition of the catalytic system.

2. Results and discussion

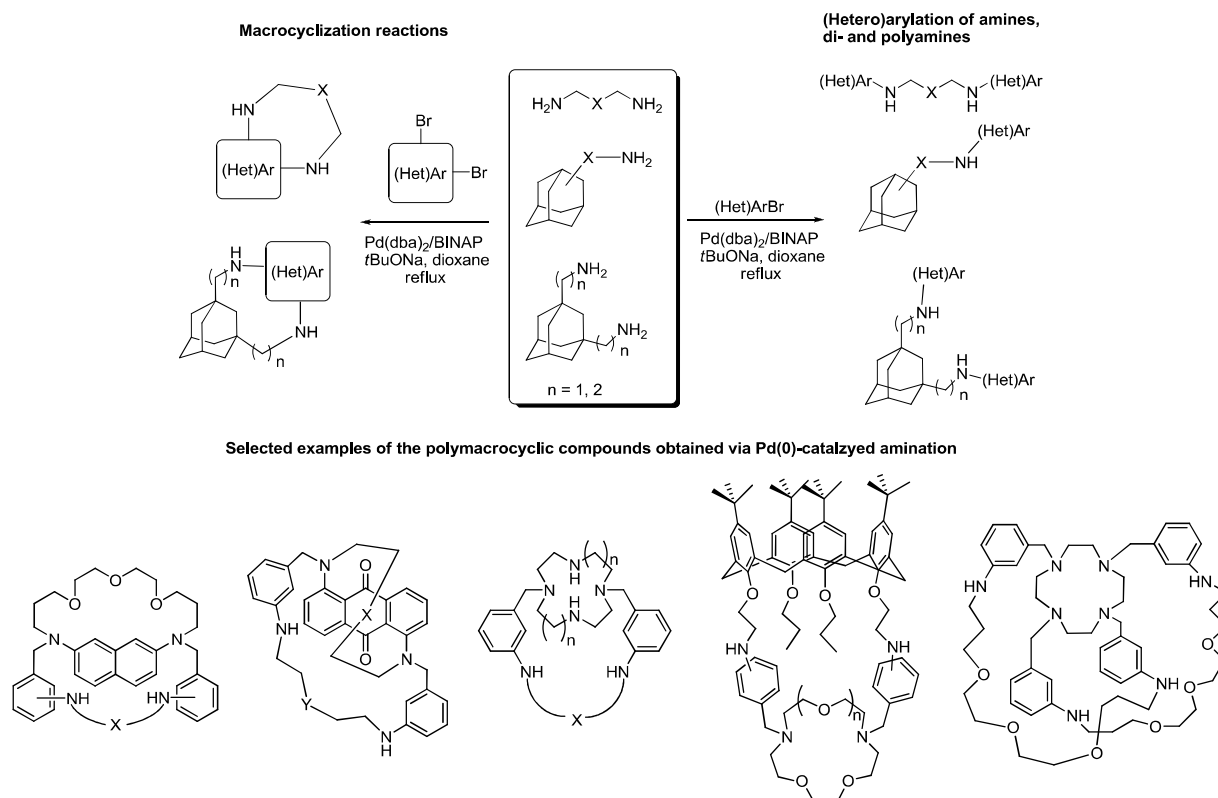
Pd(0)-catalyzed amination was shown to be fruitful in the modification of amines, diamines and polyamines with various aryl and heteroaryl substituents. Selective (hetero)arylation of primary amino groups in the presence of secondary amino groups was clearly demonstrated. Pd(dba)₂/BINAP (dba = dibenzylideneacetone, BINAP = 2,2'-bis(diphenylphosphino)-1,1'-binaphthalene) was found to be the most universal catalytic system for the majority of transformations. The main advantage of palladium catalysis is due to its ability to promote macrocyclization reactions between dibromo(hetero)arenes and linear di- and polyamines. Using this approach, hundreds of mono- and polymacrocyclic compounds were successfully obtained (Scheme 1). Among our latest achievements is the synthesis of valuable polyazapolyoxamacrocycles containing central quinoline¹ and 1,10-phenanthroline² moieties for fluorimetric detection of metal cations.

Catalysis by copper complexes were also successfully applied to the synthesis of mono- and di(hetero)aryl substituted diamines, polyamines and oxadiazines,^{3,4} as well as they were helpful in the synthesis of N-(hetero)aryl substituted adamantane-containing amines and diamines differing by the steric hindrances at primary amino groups (Scheme 2). Selectivity of the processes in the case of polyamines was somewhat lower than in Pd(0)-mediated amination reactions, but a proper choice of the copper source, ligand and solvent solved the problem affording high yields of the target products in the majority of cases. While the reactions with more active polyamines demanded the use of the systems with CuI and N,O-ligands, less active diamines and adamantane-containing amines were successfully converted using various sources of Cu(I) and O,O-ligands.

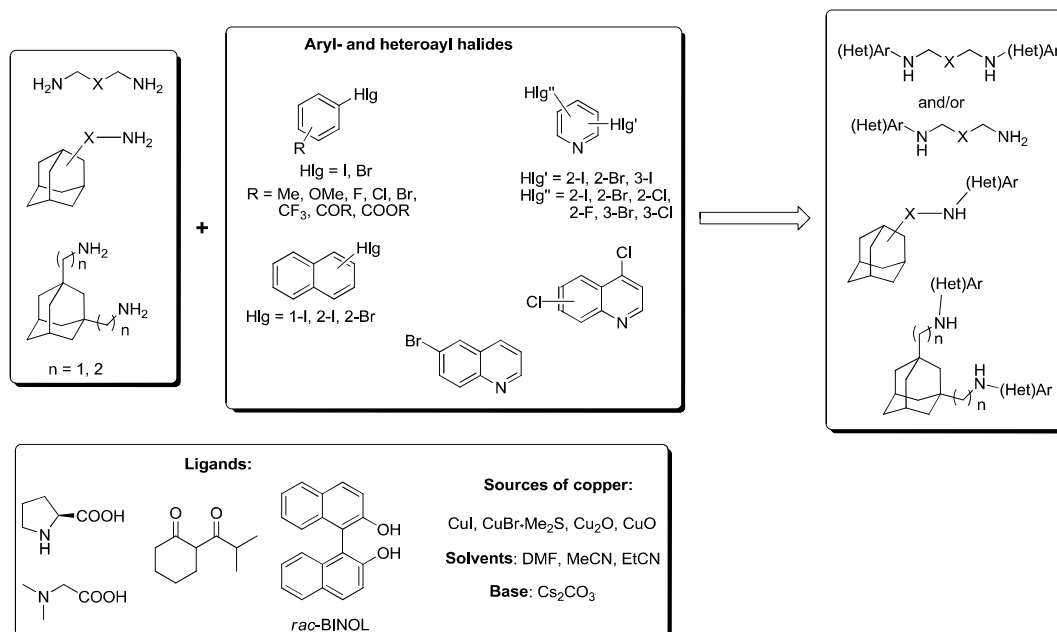
3. Conclusions

A cheaper copper catalysts was shown to be quite applicable in the majority of cases instead of more expensive Pd(0) catalysts except the synthesis of macrocyclic compounds as Cu(I)-catalyzed reactions

demanded much more concentrated solutions which hindered intramolecular cyclization and favored oligomers formation.



Scheme 1. Scope of Pd(0)-catalyzed amination reactions with polyamines and adamantane-containing amines.



Scheme 2. Scope of Cu(I)-catalyzed amination reactions with polyamines and adamantane-containing amines.

References

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