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“Advances in the Chemistry of Heteroorganic Compounds”

is dedicated to

Professor

Piotr Kiełbasiński

on the occasion of his 75th birthday

and

to honor his 53 years of scientific activity
at the Centre of Molecular and Macromolecular Studies
Polish Academy of Sciences

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Reaction of *ortho*-Quinone Methides with Amphiphilic Nucleophiles

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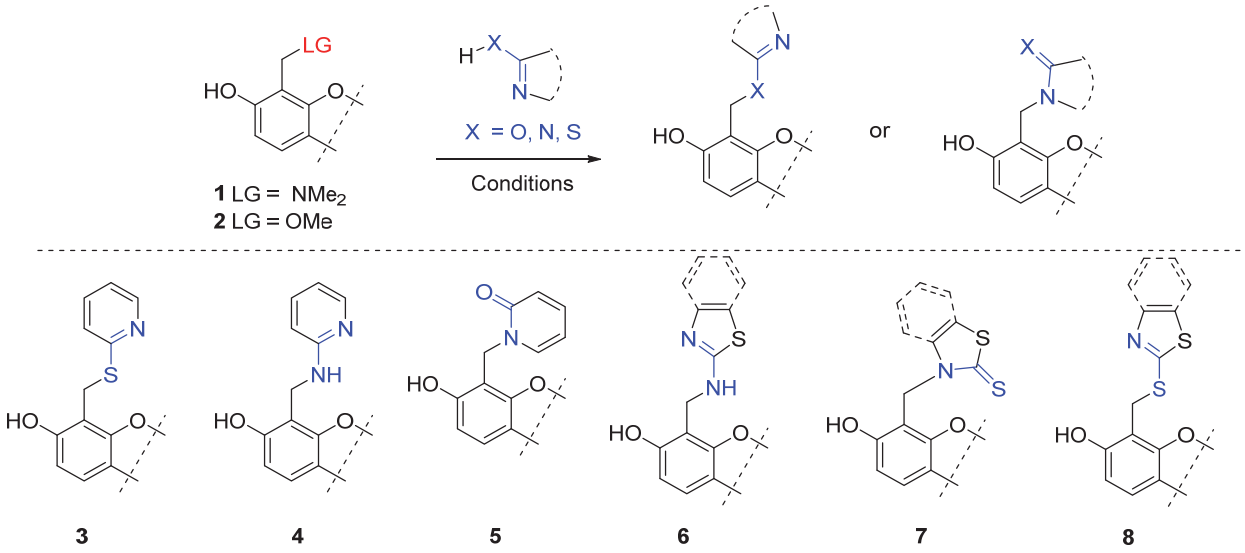
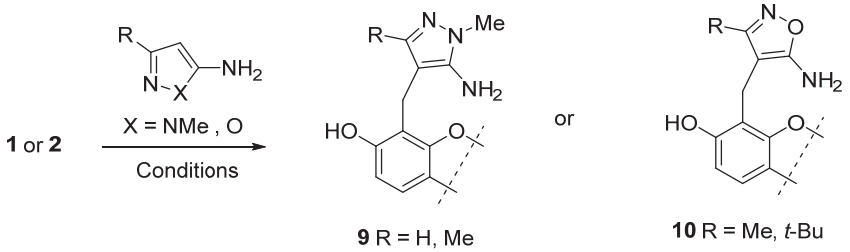
Nitrogen-based heterocyclic compounds have received a lot of attention in the last two decades, and they have contributed to the discovery of a lot of organic synthesis techniques and several applications in the biological/chemical sciences. Because of the ability of the N-atom to form hydrogen bonds with biological targets, nitrogen heterocycles comprising the pyrazole, imidazole, piperidine, etc. backbone are used as key components in many drugs [1]. In continuing our studies on flavonoid-like scaffolds as privileged structures in medicinal chemistry, we studied the reaction of isoflavonoid derivatives with amphiphilic nucleophiles with heterocyclic cores.



The direction of the reaction significantly depends on starting phenols **1** and **2**, nucleophiles, and reaction conditions. Thus, applying phenolic Mannich bases **1** led to the preferable formation of compounds **4-7** *via* thermal formation of *ortho*-quinone methides in aprotic solvents and subsequent Michael addition; only traces of compounds **1** and **8** were observed. However, these compounds were synthesized in the case of using methoxymethyl derivatives **2** in ethanol at reflux. Formation of compounds **5** did not depend on starting compounds **1** or **2**, in all cases applying aprotic solvents was required for the thermal generation of *ortho*-quinone methides.



In the case of the reaction of compounds **1** or **2** with 5-amino-1-methylpyrazoles or 5-aminoisoxazoles, only C-alkylation of these amines was observed. It should be mentioned that this reaction was successfully applied for the synthesis of chromone, coumarin, and aurone derivatives.

References

[1] R. J. Obaid et al., *Proc. Biochem.* **2022**, *120*, 250-259.