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Thiol-Free Procedure for the Synthesis of Thioethers

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Carbonic anhydrases (CA) that are zinc-containing enzymes play an important role in metabolic processes of bicarbonate and carbon dioxide. A vast majority of known CA inhibitors contain sulfonamide moiety as a Zn-binding group. Thiadiazole **1**, thiadiazoline **2** and thiophene **3** derivatives are among the most structurally studied heterocyclic sulfonamides. Among the thiadiazoline derivatives one should mention methazolamide **4**, which has been and still is used as antiglaucoma medication. Good inhibitory properties were also demonstrated for derivatives of thiophene-2-sulfonamide. Dorzolamide **5** and brinzolamide **6** are clinically used as antiglaucoma and antiepileptic agents and are effective CA inhibitors against a range of CA isoforms – CA II, CA IX, CA XII [1]. Expanding our research to new CA inhibitors we devoted our attention to derivatives of thiophene-2-sulfonamide thioethers **7** and sulfons **8**.

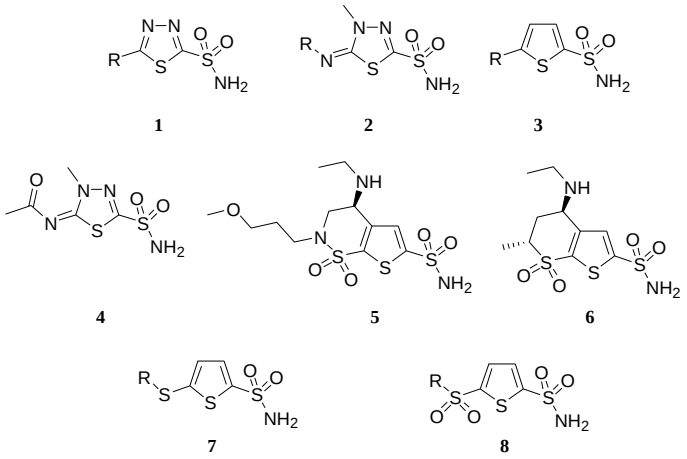
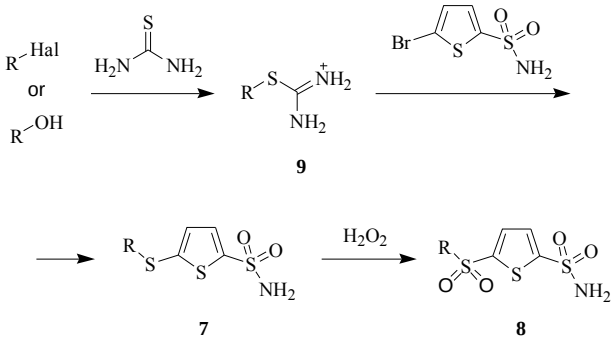


Figure 1. Heterocyclic sulfonamide derivatives

Herein, we report thiol-free procedure for the synthesis of thiophene-2-sulfonamide thioethers **7** based on derivatives of thiouronium salt **9**.



Scheme 1. Thiol-free procedure for the synthesis of thioethers

Supervisor: Dr.chem. R.Žalubovskis.

REFERENCES

[1] Alterio, V.; Di Fiore, A.; D'Ambrosio, K.; Supuran, C.T.; De Simone, G. *Chem. Rev.* **2012**, *112*, 4421–4468.