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ELECTROCHEMICAL ASYMMETRIC SYNTHESIS OF (+)-*N*-ACETYLCOLCHINOL

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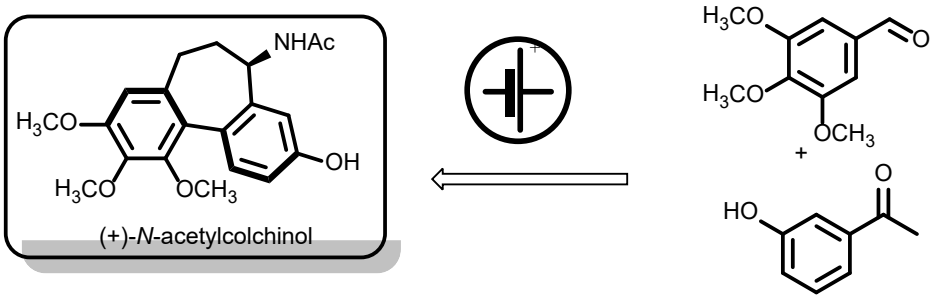
Abstract. Colchicine is a well-known pseudo-alkaloid that has been widely used to treat gout, immune-mediated diseases, and psoriatic arthritis.[1] It was shown to inhibit leukocyte-endothelial cells and T-cells by binding to intracellular tubulin monomers, which prevents their polymerization.[2] Thus, colchicine has the potential to impair the process of antigen recognition and may inhibit cancer cell growth, but it proved to be toxic to normal cells. More recently, based on its anti-inflammatory properties, colchicine was investigated as a potential treatment for COVID-19 with some positive effects reported.[3] *N*-Acetylcolchinol is a known tubulin polymerisation inhibitor.



- ***Racemic: 4 steps, 41% yield. Asymmetric: 7 steps, 33% yield***
- ***All redox steps, except for asymmetric reduction, carried out electrochemically***

A short synthesis of *N*-acetylcolchinol using a greener and step-economical pathway is reported where all the redox reactions, except for the asymmetric reduction, were carried out electrochemically, replacing protocols that employ transition metals or toxic reagents. In a 4-step racemic sequence, chemoselective reduction of chalcone and intramolecular oxidative arene-arene coupling were performed in an electrochemical cell giving the target *N*-acetylcolchinol with an overall 41% yield. In a 7-step asymmetric variant, electrochemistry was also employed for the deprotection of *p*-methoxyphenyl amine. [4]

References

1. Shekelle P.G., Newberry S.J., FitzGerald J.D., Motala A., O'Hanlon C.E., Tariq A., Okunogbe A., Han D., Shanman R. Management of Gout: A Systematic Review in Support of an American College of Physicians Clinical Practice Guideline // Ann. Intern. Med. 2017. № 1. C. 37-51.

2. Taraboletti G., Micheletti G., Dossi R., Borsotti P., Martinelli M., Fiordaliso F., Ryan A.J., Giavazzi R. Potential antagonism of tubulin-binding anticancer agents in combination therapies // Clin. Cancer Res. 2005. № 7. C. 2720-6.

3. Reyes A.Z., Hu K.A., Teperman J., Wampler Muskardin T.L., Tardif J.-C., Shah B., Pillinger M.H. Anti-inflammatory therapy for COVID-19 infection: the case for colchicine // Ann. Rheum. Dis. 2021. № 5. C. 550.

4. Du Y., Lunga A., Rubtsov A.E., Malkov A.V. Short electrochemical asymmetric synthesis of (+)-N-acetylcolchinol // Green Chemistry. 2022.

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