POLISH NATIONAL AGENCY FOR ACADEMIC EXCHANGE

STER PROGRAMME

name of the unit:

DIVISION OF ORGANIC SYNTHESIS

Institute of Organic Chemistry, Lodz University of Technology

symbol:

I-32

https://chorg.p.lodz.pl/

head of the unit:	potential promoters:	contact person:
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scope of activities:

The main area of interest is stereoselective synthesis of organic compounds (including organophosphorus compounds) with potential cytotoxic activity and search for the structure-activity relationship (SAR). Our synthetic targets are usually compounds containing 2-alkylidene-1-oxoheterocyclic skeleton which are structurally related to a big group of natural a-alkylidene g- or d-lactones or lactams with well-recognized cytotoxic activity. In our research we often use, developed in our laboratory, Horner-Wadsworth-Emmons methodology for the introducing of alkylidene moiety onto the heterocyclic ring in regioselective manner. We also developed enantioselective synthesis of the target compounds by using phosphoryl groups containing menthyl or 1-phenylethylamino residues as chiral auxiliaries.

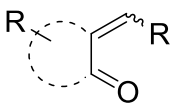
Obtained compounds are tested for their biological activity and in particular cytotoxic activity, in cooperation with Medical University of Lodz.

present activities:

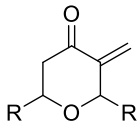
Currently we realize stereoselective synthesis of three libraries of 2-alkylidene-1-oxoheterocycles, with very promising cytotoxic activity. These are variously alkyl or aryl substituted 3-methylidenetetrahydropyran-4-ones, 3-methylidene-1-tosyl-2,3-dihydroquinolin-4(1*H*)-ones and 3-methylidene-1-tosyl-2,3-dihydro-1,8-naphthyridin-4(*1H*)-ones. In the final stage of the synthesis we utilize appropriate organophosphorus reagent for the Horner-Wadsworth-Emmons olefination of formaldehyde.

We also perform the synthesis of substituted in position 2, regioisomeric *N,O-anti* and *N,O-syn* 3-diethoxyphosphorylfuroquinoline-4,9-diones, which posses vey high cytotoxic activity. One of the obtained compounds with highest cytotoxic activity is being currently tested to established its mode of action.

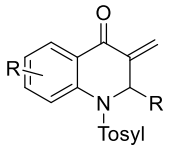
graphic material



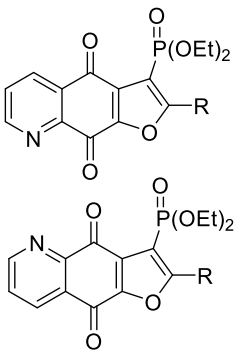
2-alkylidene-1-oxoheterocycles



3-methylidenedihydropyran-4-ones



3-methylidenedihydroquinolin-4-ones



N,O-syn and *N,O-anti* 3-diethoxy-phosphorylfuroquinoline-4,9-diones

The portfolio of research groups was created as part of the Programme "STER" – Internationalisation of doctoral schools" as part of the realization of the project "Curriculum for advanced doctoral education & taining – CADET Academy of Lodz University of Technology".

Future activities:

Enancjoselective synthesis of 3-methylidenetetrahydropyran-4-ones, 3-methylidene-1-tosyl-2,3-dihydroquinolin-4(1*H*)-ones and 3-methylidene-1-tosyl-2,3-dihydro-1,8-naphthyridin-4(*1H*)-ones using dimenthoxyphosphoryl group as chiral auxiliary.

publications/patents, awards, projects:

- Kędzia Jacek, Bartosik Tomasz, Drogosz Joanna, Janecka Anna, Krajewska Urszula, Janecki Tomasz „Synthesis and Cytotoxic Evaluation of 3-Methylidenechroman-4-ones" Molecules **2019**, *24*, 1868/1-1868/14.
- Bartosik Tomasz, Kędzia Jacek, Drogosz-Stachowicz Joanna, Janecka Anna, Krajewska Urszula, Mirowski Marek, Janecki Tomasz, „Synthesis of 2,2,6-Trisubstituted 5-Methylidenetetrahydropyran-4-ones with Anticancer Activity" Molecules **2020**, 25, 611
- Jakub Modranka, Joanna Drogosz-Stachowicz, Anna Pietrzak, Anna Janecka, Tomasz Janecki, "Synthesis and structure-activity relationship study of novel 3- diethoxyphosphorylfuroquinoline-4,9-diones with potent antitumor efficacy", European Journal of Medicinal Chemistry **2021**, 219, 113429.
- Tomasz Janecki, "Stereoselective Synthesis of Methylidenecoumarins and Methylideneuracils as Novel, Potent Anticancer Agents" The 17-th Annual Congress of International Drug Discovery Science & Technology, July 25-27, 2019, Kyoto, Japan, Lecture

Keywords:

organic synthesis, 2-alkylidene-1-oxoheterocycles, organophosphorus compounds, Horner-Wadsworth-Emmons reaction, cytotoxic activity, structure activity relationship

List of internship proposal in this research team:

List of attachments: