FKKT | UNIVERZA V LJUBLJANI
Fakulteta za kemijo in kemijsko tehnologijo

VABILO NA PREDAVANJE
V OKVIRU DOKTORSKEGA ŠTUDIJA
KEMIJSKE ZNANOSTI / INVITATION TO THE
LECTURE WITHIN DOCTORAL PROGRAMME IN
CHEMICAL SCIENCES

Prof. Dr. Marcin Sieńczyk

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z naslovom / title:

Phosphonic Inhibitors of Proteases: The Good, the Bad, and the Ugly

v sredo, 13. 5. 2026 ob 15. uri
v predavalnici 1 v 1. nadstropju Fakultete za kemijo in kemijsko tehnologijo, Večna pot 113 ***/***
on Wednesday, 13. 5. 2026 at 15.00
in lecture room 1, 1st floor at the Faculty of Chemistry and Chemical Technology, Večna pot 113

Vljudno vabljeni! / Kindly invited!

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Abstract:

Although 1-aminoalkylphosphonate diaryl esters have a history spanning nearly 50 years, they remain one of the premier classes of specific, irreversible, active-site-directed inhibitors. Their hallmark is an exquisite selectivity: they react exclusively with serine proteases while remaining completely inert toward other classes of proteolytic enzymes including cysteine, aspartyl, threonine or metalloproteases. Furthermore, their high chemical stability, combined with virtually limitless possibilities for structural modification, makes them an invaluable tool for studying serine proteases of diverse origins—human, bacterial, and viral—both in vitro and within living cells.

Historically, phosphonic activity-based probes (ABPs) were first designed and implemented to investigate proteases secreted by immune cells, including granzymes, elastase, and chymase. Subsequent research shifted focus toward developing inhibitors and probes targeting neutrophil serine proteases (NSPs), specifically proteinase 3, neutrophil elastase, cathepsin G, and NSP4. Since the structural diversification of phosphonates is constrained primarily by the researcher's imagination, numerous highly potent and selective compounds have been synthesized. These tools have proven essential in distinguishing between proteases with similar or overlapping substrate specificities. Beyond their traditional role as inhibitors, 1-aminoalkylphosphonates have demonstrated utility in the development of catalytic antibodies and, more recently, as functional components in PROTACs (Proteolysis Targeting Chimeras).

The presentation will explore the discovery, chemical evolution, and diverse applications of 1-aminoalkylphosphonates as protease inhibitors of different origin, while also addressing their limitations.