Issue 87 June 2024

The I.S.H.C. Bulletin

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Issue 87 June 2024

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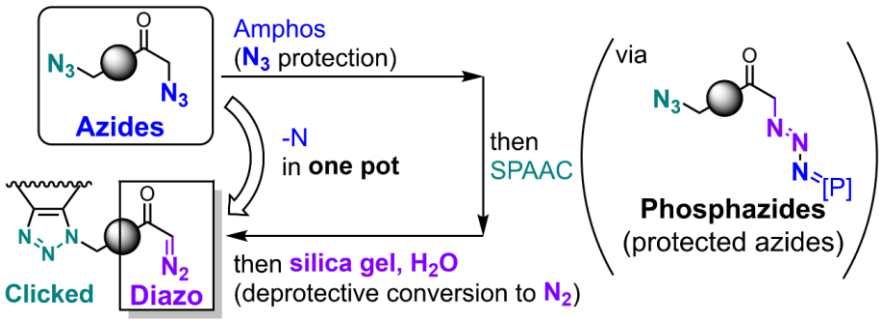
Amphos-Mediated Conversion of Alkyl Azides to Diazo Compounds and One-Pot Azide-Site Selective Transient Protection, Click Conjugation, and Deprotective Transformation

Hiroki Tanimoto*, Ryo Adachi, Kodai Tanisawa, and Takenori Tomohiro
Org. Lett. **2024**, *26(12)*, 2409–2413. DOI: 10.1021/acs.orglett.4c00566



A one-pot conversion of alkyl azides to diazo compounds is outlined. After the reaction of α-azidocarbonyl compounds with Amphos, treatment of the resulting phosphazides with silica gel in a wet solvent afforded α-diazo carbonyl products. Through the azido group protection property of Amphos, inter- and intramolecular azide-site selective reactions of azido group protection, click functionalization, and deprotection of the diazo group have been demonstrated in one pot.

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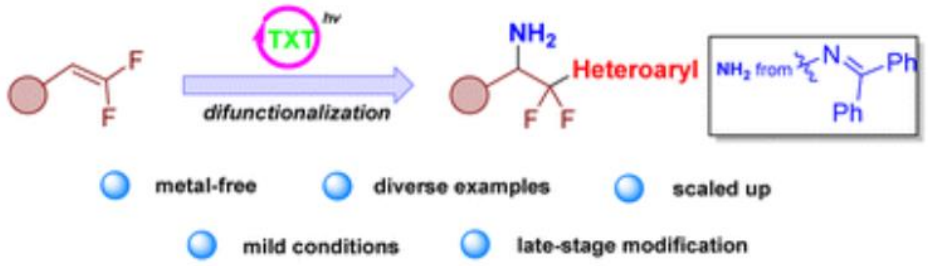
Difunctionalization of *gem*-Difluoroalkenes for Amination and Heteroarylation via Metal-Free Photocatalysis.

Yuanchen Zhong, Zhen Zhuang, Xiaofei Zhang, Bin Xu,* and Chunhao Yang.*

Chem. Commun. **2024**, *60, 4830–4833.* DOI: 10.1039/d4cc00528g

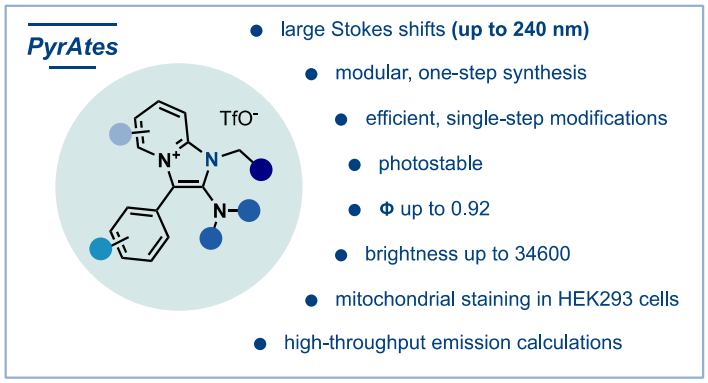


gem-Difluoroalkenes are widely used building blocks in fluorine chemistry. Herein, a metal-free photocatalytic amination and heteroarylation method of *gem*-difluoroalkenes with heteroaryl carboxylic acid oxime esters as substrates is reported. This environmentally benign reaction proceeds radical–radical cross-coupling by energy-transfer-mediated photocatalysis and can be used for rapid construction of heteroaryl difluoroethylamine scaffolds and late-stage modification of complex pharmaceutical structures.

PyrAtes: Modular Organic Salts with Large Stokes Shifts for Fluo-rescence Microscopy

Iakovos Saridakis, Margaux Riomet, Oliver J. V. Belleza, Guilhem Coussanes, Nadja K. Singer, Nina Kastner, Yi Xiao, Elliot Smith, Veronica Tona, Aurélien de la Torre, Eric F. Lopes, Pedro A. Sánchez-Murcia, Leticia González, Harald H. Sitte and Nuno Maulide*

Angew. Chem. Int. Ed. 2024, 63, e202318127; DOI: 10.1002/anie.202318127



The deployment of small-molecule fluorescent agents plays an ever-growing role in medicine and drug development. Herein, we complement the portfolio of powerful fluorophores, reporting the serendipitous discovery and development of a novel class with an imidazo[1,2-*a*]pyridinium triflate core, which we term *PyrAtes*. These fluorophores are synthesized in a single step from readily available materials (>60 examples) and display Stokes shifts as large as 240 nm, while also reaching NIR–I emissions at λ_{max} as long as 720 nm. Computational studies allow the development of a platform for the prediction of λ_{max} and λ_{Em}. Furthermore, we demonstrate the compatibility of these novel fluorophores with live cell imaging in HEK293 cells, suggesting PyrAtes as potent intracellular markers.

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Diversity of Heterocyclic Reactants in the Click Reaction

Frederick A. Luzzio

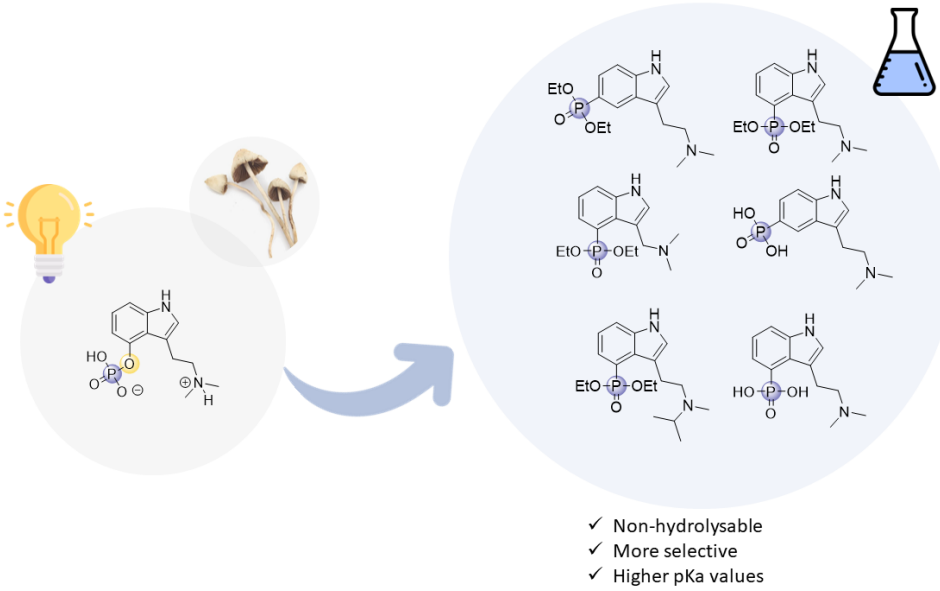
Advances in Heterocyclic Chemistry **2024**, Volume 143, Chapter 3; Pages 95-176 DOI:10.1016/bs.aihch.2023.11.002

Variants of the Huisgen 3 + 2 cycloaddition with respect to heterocyclic substitution on both the acetylenic and azide reacting components are presented. This chapter details applications of the click reaction to classes of heterocyclic reactants which bear either the acetylenic or azide reactive groups en route to the target triazoles. While the reaction coverage involves transformations whereby at least one reactant, either an acetylene or an azide, bears a heterocycle, its general focus includes the function of the product triazoles and forms the basis of the chapter outline and content. The synthetic methods and macrocycles sections involve new reactions, strategies or constricts. Other than the synthetic methods and macrocycles sections, the products of the click reactions are divided into classes which are categorized according to the role they play in catalysis, ligands, biological function or as probes, sensors or materials. In the sections which involve medicinal chemistry or drug development many of the reaction entries are general with selected examples describing biological activity for brevity.

Synthesis and bioactivity of psilocybin analogues containing a stable carbon–phosphorus bond

M. Vandevelde, A. Simoens, B. Vandekerckhove, C.V. Stevens

RSC Medicinal Chemistry, 2024, **15**, 998 – 1002



Psilocybin analogues have been synthesized comprising a non-hydrolysable P-C bond to evaluate the biological activity and the selectivity towards the 5-HT_{2A}R, the 5-HT_{2B}R and the TNAP receptor. No activity was observed towards the phosphatase, however all compounds showed good binding affinity for 5-HT_{2A}R and 5-HT_{2B}R and one compound showed a higher selectivity towards 5-HT_{2A}R than psilocin.

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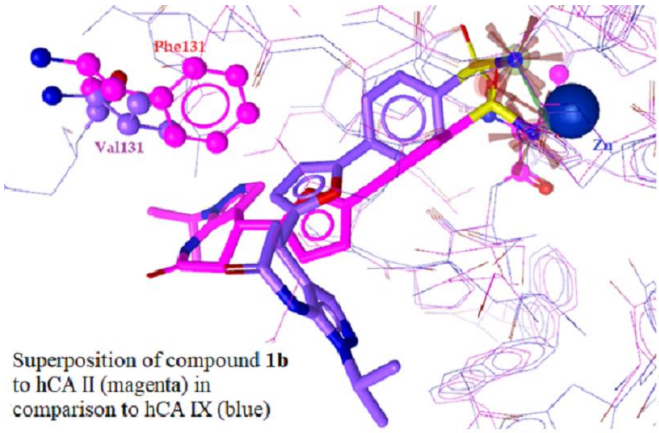
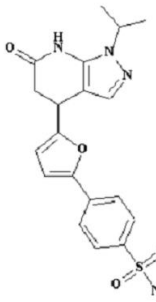
Substituted Furan Sulfonamides as Carbonic Anhydrase Inhibitors: Synthesis, Biological and In Silico Studies

Andrea Angeli[a,b], Victor Kartsev[c], Anthi Petrou[d], Boris Lichitsky[e], Andrey Komogortsev[e], Athina Geronikaki[d,*] and Claudiu T. Supuran[a,*]

Bioorganic Chemistry , **2023,**138,106621



Superposition of compound **1b** to hCA II (magenta) in comparison to hCA IX (blue)



Compound 1b

Ki (nM)

hCA I	hCA II	hCA IV	hCA IX
6.30	4.0	9.10	19.2

Fifteen novel furyl sulfonamides were designed, synthesized and evaluated against four human isoforms: hCA I, hCA II, hCA IV and hCA IX. Compounds appeared to be very active mostly against hCAI (8) and hCA IV (11) isoforms being more potent than reference drug acetazolamide (AAZ). It should be mentioned that four compounds were more active than AAZ against hCA IX isoform, with compound 12d to be selective against hCA I (SI 70), hCA II (SI 13.5) and hCA IV (SI 20). Furthermore, docking was performed for some of these compounds on all isoforms I order to understand the possible interactions with the active site. The most active compounds showed good bioavailability and drug likeness scores.