Issue 66; April 2022

The ISHC Bulletin

Recent Publications of ISHC Members

Issue 66; April 2022

Synthesis of Benzo[4,5]thiazolo[2,3-*c*][1,2,4]triazole Derivatives *via* C–H Bond Functionalization of Disulfide Intermediates

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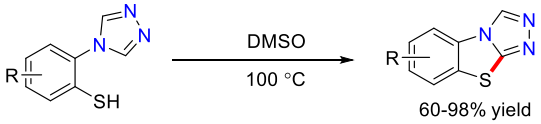
Molecules **2022**, *27*, 1464 (1–31). **DOI:** 10.3390/molecules27051464



Abstract: Many nitrogen- and sulfur-containing heterocyclic compounds exhibit biological activity. Among these heterocycles are benzo[4,5]thiazolo[2,3-*c*][1,2,4]triazoles for which two main synthetic approaches exist. Here we report a new synthetic protocol that allows the preparation of these tricyclic compounds via the oxidation of a mercaptophenyl moiety to its corresponding disulfide. Subsequent C–H bond functionalization is thought to enable an intramolecular ring closure, thus forming the desired benzo[4,5]thiazolo[2,3-*c*][1,2,4]triazole. This method combines a high functional group tolerance with short reaction times and good to excellent yields.

Asymmetric Direct/Stepwise Dearomatization Reactions Involving Hypervalent Iodine Reagents

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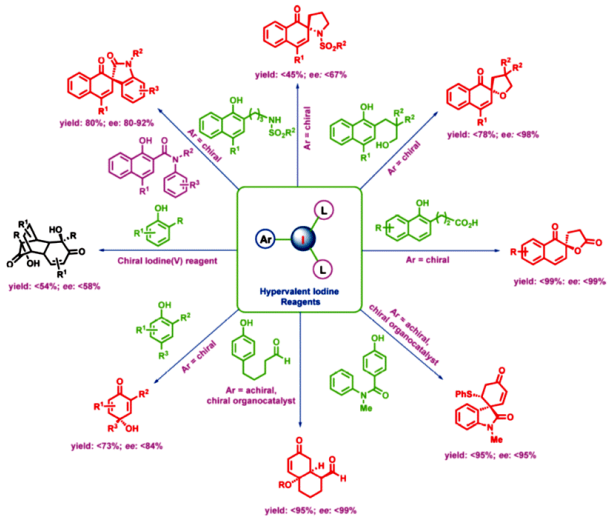
Chem Asian J. **2022**, *17*, e202101115 (1–20). **DOI:** 10.1002/asia.202101115



Abstract: A remarkable growth in hypervalent iodine-mediated oxidative transformations as stoichiometric reagents as well as catalysts have been well-documented due to their excellent properties, such as, mildness, easy handling, high selectivity, environmentally friendly nature, and high stability. This review aims at highlighting the asymmetric oxidative dearomatization reactions involving hypervalent iodine compounds. The present article summarizes asymmetric intra- and intermolecular dearomatization reactions using chiral hypervalent iodine reagents/catalysts as well as hypervalent iodine-mediated dearomatization reactions followed by desymmetrization.

Photoswitching of 5-Phenylazopyrimidines in Crystalline Powders and Thin Films

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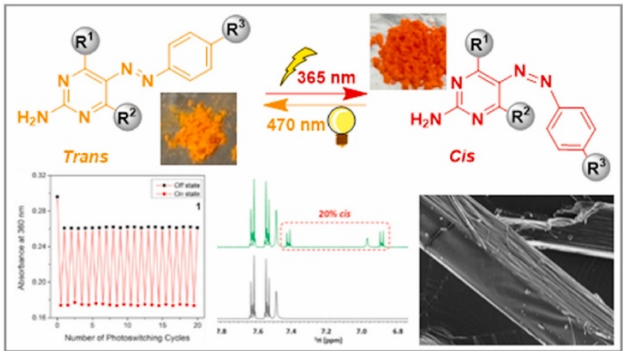
Dyes and Pigments **2022**, *199*, 110066 (1–9). **DOI:** 10.1016/j.dyepig.2021.110066

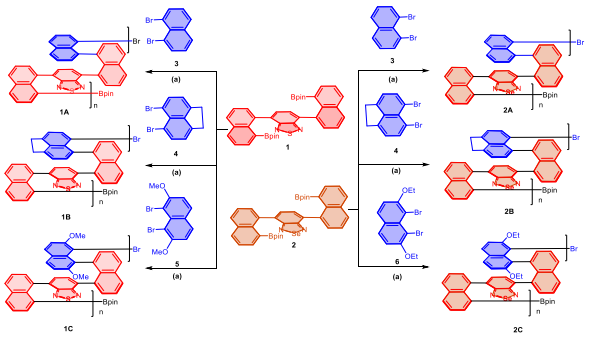


Abstract: Solid-state photoswitching enables the development of smart materials. However, the close packing of molecules and the lack of free volume in this state prevent sterically demanding structural changes induced by irradiation, thereby precluding the use of azobenzene photoswitches. Nevertheless, we report here the solid-state photoswitching of their derivatives, 5-phenylazopyrimidines, in crystalline powders and in amorphous thin layers. After identifying *trans-cis* photoisomerization by NMR spectroscopy, we demonstrated the applicability of 5-phenylazopyrimidines for future all-optical switching applications. For this purpose, we prepared thin films by spin-coating and confirmed their solid-state optical switching by optical transmission spectroscopy and their favorable surface topography by atomic force microscopy. Therefore, thin films of 5-phenylazopyrimidines are suitable for on-chip integration for emerging all-optical technologies.

Multilayer 3D Chiral Folding Polymers and Their Asymmetric Catalytic Assembly

Yao Tang, Shengzhou Jin, Sai Zhang, Guan-Zhao Wu, Jia-Yin Wang, Ting Xu, Yu Wang, Daniel Unruh, Kazimierz Surowiec, Yanzhang Ma, Shiren Wang, Courtney Katz, Hongjun Liang, Yunze Li, Weilong Cong, and Guigen Li* (guigenli@nju.edu.cn)

Research **2022**, 9847949 (1–8). **DOI:** 10.34133/2022/9847949



New multiple-layered *3D* polymers

Abstract: A novel class of polymers and oligomers of chiral folding chirality have been designed and synthesized, showing structurally compacted triple-column/multiple-layer frameworks. Both uniformed and differentiated aromatic chromophoric units were successfully constructed between naphthyl piers of this framework. Screening monomers, catalysts, and catalytic systems led to the success of asymmetric catalytic Suzuki-Miyaura poly-couplings. Enantio- and diastereochemistry were unambiguously determined by X-ray structural analysis and concurrently, by comparison with a similar asymmetric induction by the same catalyst in the asymmetric synthesis of a chiral three-layered product. The resulting chiral polymers exhibit intense fluorescence activity in a solid form and solution under specific wavelength irradiation.

Stereospecific α-(Hetero)arylation of Sulfoximines and Sulfonimidamides

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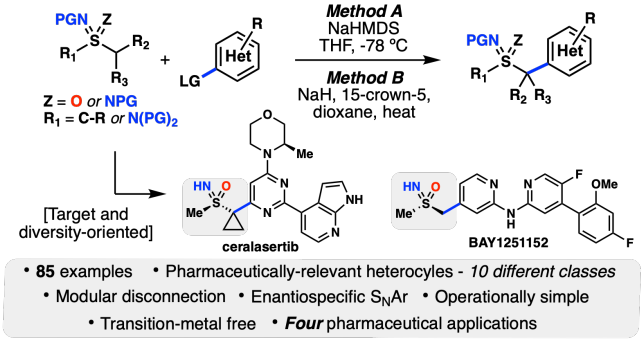
Nature Synthesis, **2022**, *1*, 170–179. **DOI:** 10.1038/s44160-021-00011-2

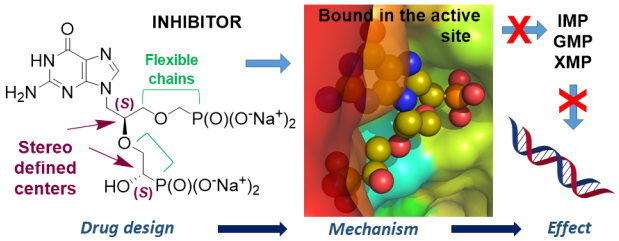


Abstract: The occurrence of sulfoximines and sulfonimidoyl groups in biologically active molecules within pharmaceuticals and agrochemicals has notably increased in the past decade. This increase has prompted a wave of discovery of methods to install the S(VI) functionality into complex organic molecules. Traditional synthetic methods to form α-substituted sulfonimidoyl motifs rely on S–C bond disconnections and typically require control of the stereogenic S-centre or late-stage modification at sulfur, and comprise multistep routes. Here, we report the development of a stereospecific, modular SNAr approach for the introduction of sulfonimidoyl functional groups into heterocyclic cores. This strategy has been demonstrated across 85 examples, in good to excellent yield, of complex and diverse heterocycles. Sulfoximines, sulfonimidamides and sulfondiimines are all compatible nucleophiles in the SNAr reaction and, hence, the methodology was applied to the synthesis of four sulfoximine-containing pharmaceuticals. Of these synthetic applications, most notably ceralasertib, an ATR inhibitor currently in clinical trials, was synthesized in an eight-step procedure on a gram scale.

Stereo-Defined Acyclic Nucleoside Phosphonates are Selective and Potent Inhibitors of Parasite 6-Oxopurine Phosphoriboxyltransferases

Tomáš Klejch, Dianne T. Keough, Gordon King, Eva Doleželová, Michal Česnek, Miloš Buděšínský, Alena Zíková, Zlatko Janeba,* Luke W. Guddat,* Dana Hocková (janeba@uochb.cas.cz or luke.guddat@uq.edu.au)

J. Med. Chem. **2022**, *65*, 4030–4057. **DOI:** 10.1021/acs.jmedchem.1c01881



Abstract: Pathogens such as *Plasmodium* and *Trypanosoma* spp. are unable to synthesize purine nucleobases. They rely on the salvage of these purines and their nucleosides from the host cell to synthesize the purine nucleotides required for DNA/RNA production. The key enzymes in this pathway are purine phosphoribosyltransferases (PRTs). Here, we synthesized sixteen novel acyclic nucleoside phosphonates, twelve with a chiral center at C-2′ and eight bearing a second chiral center at C-6′. Of these, bisphosphonate (*S,S*)-**48** is the most potent inhibitor of the *Plasmodium falciparum* and *P. vivax* 6-oxopurine PRTs and the most potent inhibitor of two *Trypanosoma brucei* (*Tbr)* 6-oxopurine PRTs yet discovered, with K_i values as low as 2 nM. Crystal structures of (*S,S*)-**48** in complex with human and *Tbr* 6-oxopurine PRTs show that the inhibitor binds to the enzymes in different conformations, providing an explanation for its potency and selectivity (*i.e.*, 35-fold in favour of the parasite enzymes).

Analgesic Opioid Ligand Discovery Based on Nonmorphinan Scaffolds Derived from Natural Sources

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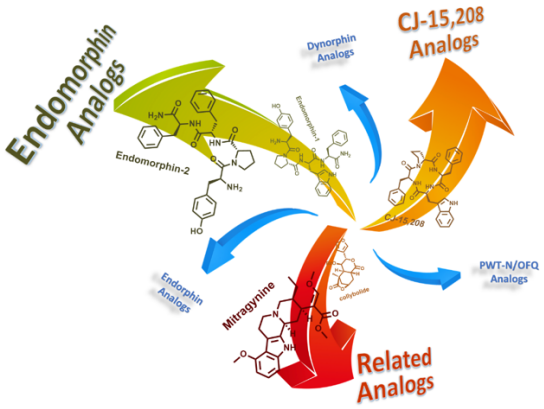
(maree.smith@uq.edu.au or c.williams3@uq.edu.au)

J. Med. Chem. **2022**, *65*, 1612–1661. **DOI:** 10.1021/acs.jmedchem.0c01915



Abstract: Prescription opioids are potent analgesics, especially drugs based on morphinan scaffolds, which are the mainstays in the FDA-recommended combination guidelines for treating moderate to severe pain and chronic cancer pain. Unfortunately, they have limited effectiveness in many areas (*e.g.,* treating neuropathic pain) and often come with serious adverse effects. In addition, due to the addictive nature of opioid based medications, opioid abuse has had a challenging impact on drug regulation. Meanwhile, overdose of prescription opioids is claiming lives at a staggering rate. Hence, reducing the addictiveness and adverse effects of opioids has been the "Holy Grail" for the development of novel and safer opioid analgesics. In this perspective, novel non-morphinan analgesic opioid ligands from natural sources are discussed in the context of background, chemical modification, and clinical (or experimental) status, together with prospects for opioids design and developments in the future.