

## The ISHC Bulletin

### Recent Publications of ISHC Members

Issue 44; June/July 2020; PART I

#### Recent Progress in Nitro-Promoted Direct Functionalization of Pyridones and Quinolones

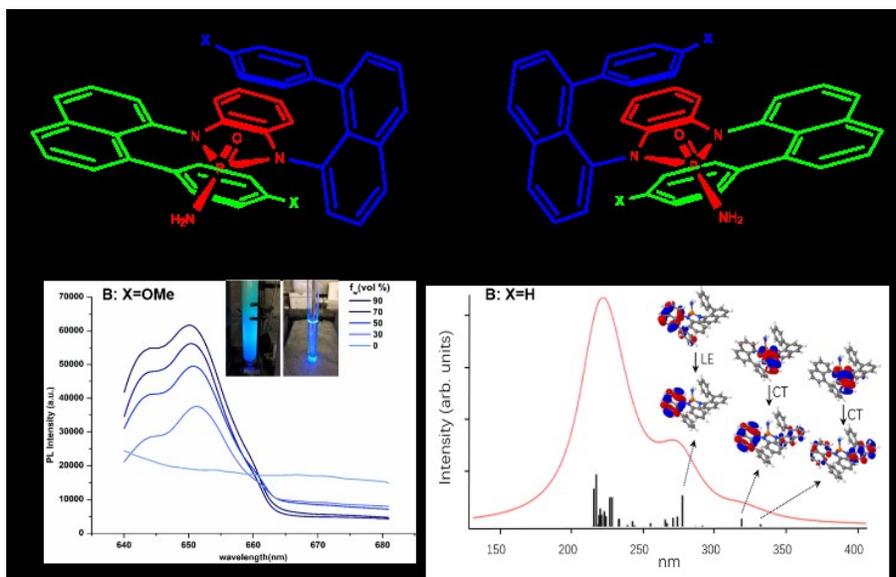
Feiyue Hao\* and Nagatoshi Nishiwaki\* ([haofeiye@tzc.edu.cn](mailto:haofeiye@tzc.edu.cn) or [nishiwaki.nagatoshi@kochi-tech.ac.jp](mailto:nishiwaki.nagatoshi@kochi-tech.ac.jp))  
*Molecules* **2020**, *25*, 673 (1–25). DOI: 10.3390/molecules25030673



**Abstract:** Nitro group is one of the most important functional groups in organic syntheses because its strongly electron-withdrawing ability activates the scaffold, facilitating the reaction with nucleophilic reagents or the Diels–Alder reaction. In this review, recent progress in the nitro-promoted direct functionalization of pyridones and quinolones is highlighted to complement previous reviews.

#### Multi-Layer 3D Chirality: New Synthesis, AIE and Computational Studies

Yangxue Liu, Guanzhao Wu, Zhen Yang, Hossein Rouh, Nandakumar Katakam, Sultan Ahmed, Daniel Unruh, Zhonghua Cui,\* Hans Lischka,\* and Guigen Li\* ([zcui@jlu.edu.cn](mailto:zcui@jlu.edu.cn) or [hans.lischka@univie.ac.at](mailto:hans.lischka@univie.ac.at) or [guigen.li@ttu.edu](mailto:guigen.li@ttu.edu))  
*Sci. China Chem.* **2020**, *63*, 692–698. DOI: 10.1007/s11426-019-9711-x



Multi-layer 3D molecules show AIE and computation of UV-vis

**Abstract:** New synthesis of multi-layer 3D chiral molecules has been developed under new conditions to give better outcomes as compared with the previous synthesis (<https://doi.org/10.34133/2019/6717104>). The aggregation-induced emission (AIE), UV irradiation/excitation, charge transfer (CT) and local excited (LE)  $\pi\pi^*$  transitions have been investigated on a representative individual enantiomer of *pseudo C*<sub>2</sub> asymmetry which was made possible by differentiating moieties on phosphorous on *N*-phosphonyl ring of chiral sandwich framework. In the meanwhile, a new tandem C-N/C-C coupling reaction was unexpectedly rendered providing a novel access to special benzo[*a*]carbazoles.

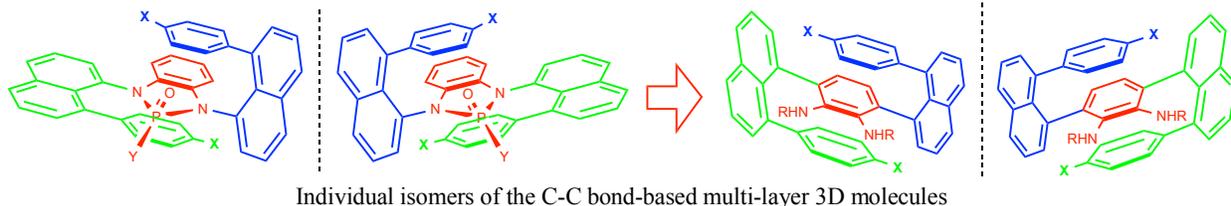
## Enantioselective Assembly of Multi-Layer 3D Chirality

Guanzhao Wu, Yangxue Liu, Zhen Yang, Tao Jiang, Nandakumar Katakam, Hossein Rouh, Liulei Ma, Yao Tang, Sultan Ahmed, Anis U. Rahman, Hongen Huang, Daniel Unruh, and Guigen Li\*

([guigen.li@ttu.edu](mailto:guigen.li@ttu.edu))

*Natl. Sci. Rev.* **2020**, *7*, 588–599.

DOI: 10.1093/nsr/nwz203



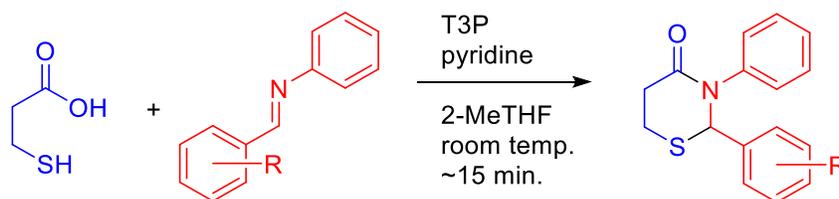
**Abstract:** The first enantioselective assembly of sandwich-shaped organo molecules has been achieved by conducting dual asymmetric Suzuki–Miyaura couplings and nine other reactions. This work also presents the first fully C-C anchored multi-layer 3D chirality with optically pure enantiomers, which are different from C-N bond-based version (<https://doi.org/10.34133/2019/6717104>). As confirmed by X-ray diffraction analysis that this chiral framework is featured by a unique  $C_2$ -symmetry in which a nearly parallel fashion consisting of three layers: top, middle and bottom aromatic rings. Unlike the documented planar or axial chirality, the present chirality shows its top and bottom layers restrict each other from free rotation, *i.e.*, this multi-layer 3D chirality would not exist if either top or bottom layer is removed. Nearly all multi-layered compounds showed strong luminescence of different colors under UV irradiation, and several randomly selected samples displayed aggregation-induced emission (AIE) properties. This work is believed to have broad impacts on chemical, medicinal and material sciences including optoelectronic materials in future.

## T3P-Promoted Synthesis of a Series of Novel 2-Aryl-3-phenyl-2,3,5,6-tetrahydro-4H-1,3-thiazin-4-ones

Lee J. Silverberg,\* Carlos Pacheco, Debashish Sahu, Tapas, Mal, Peter Scholl, Hany F. Sobhi, Heather G. Bradley, Omar A. Cardenas, Kyanna M. Gonzalez, Jasra M. Islam, Emily G. Kimmel, Winnie Li, Kristen C. Perhonitch, Jennifer T. Pothering, Michael E. Potts, Melissa E. Ramirez, Haley E. Reppert, Kelsey N. Shaffer ([ljs43@psu.edu](mailto:ljs43@psu.edu))

*Tetrahedron Lett.* **2020**, *61*, 151836 (1–4).

DOI: 10.1016/j.tetlet.2020.151836



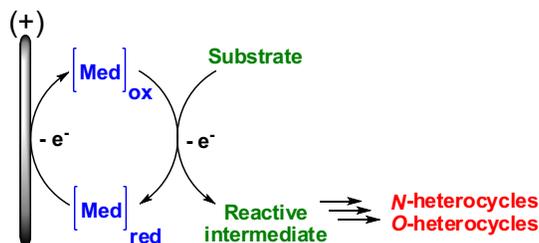
**Abstract:** A series of twelve novel 2-aryl-3-phenyl-2,3,5,6-tetrahydro-4H-1,3-thiazin-4-ones was prepared at room temperature by T3P-mediated cyclization of C-aryl-N-phenyl imines with 3-mercaptopropionic acid. The reaction can also be run as a 3-component reaction, forming the imine *in situ*. The reactions were operationally simple, rapid and gave yields as high as 75%. This provides ready access to C-aryl-N-phenyl compounds in this family, which have been generally difficult to prepare.

## Catalytic Electrosynthesis of *N,O*-Heterocycles – Recent Advances

Anna V. Listratova, Najoua Sbei, and Leonid G. Voskressenskiy\* ([voskresenskiy-lg@rudn.ru](mailto:voskresenskiy-lg@rudn.ru))

*Eur. J. Org. Chem.* **2020**, 2012–2027.

DOI: 10.1002/ejoc.201901635



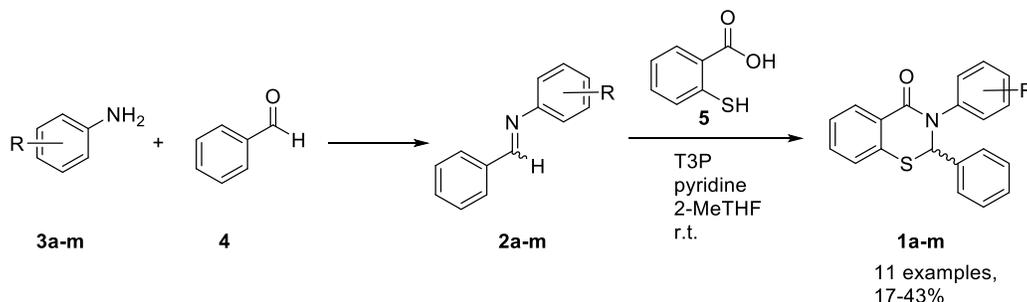
**Abstract:** Recognized as gentler and more environmentally friendly compared to conventional methods, catalytic electrochemical reactions are a powerful tool for constructing heterocycles. Of special interest is indirect electrolysis where the use of a redox mediator provides an additional means of reaction control, thus avoiding over-oxidation and facilitating improved selectivity. This minireview describes recent advances in catalytic electrochemical reactions for synthesizing *N,O*-heterocycles that appeared from 2018 until September 2019.

## T3P-Promoted Synthesis of a Series of Novel 3-Aryl-2-phenyl-2,3-dihydro-4*H*-1,3-benzothiazin-4-ones

Lee J. Silverberg,\* Carlos Pacheco, Debashish Sahu, Peter Scholl, Hany F. Sobhi, Joshua T. Bachert, Kaitlyn Bandholz, Ryan V. Bendinsky, Heather G. Bradley, Baylee K. Colburn, David J. Coyle, Jonathon R. Dahl, Megan Felty, Ryan F. Fox, Kyanna M. Gonzalez, Jasra M. Islam, Stacy E. Koperna, Quentin J. Moyer, Duncan J. Noble, Melissa E. Ramirez, Ziwei Yang ([ljs43@psu.edu](mailto:ljs43@psu.edu))

*J. Heterocyclic Chem.* **2020**, 57, 1797–1805.

DOI: 10.1002/jhet.3904



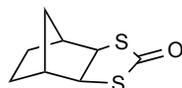
**Abstract:** A series of eleven novel 3-aryl-2-phenyl-2,3-dihydro-4*H*-1,3-benzothiazin-4-ones was prepared at room temperature by T3P-mediated cyclization of *N*-aryl-*C*-phenyl imines with thiosalicylic acid. This provides simple and ready access to *N*-aryl compounds in this family, which have been generally difficult to prepare.

## 3,5-Dithiatricyclo[5.2.1.0<sup>2,6</sup>]Decan-4-One

R. Alan Aitken,\* Neil S. Keddie and Alexandra M. Z. Slawin ([raa@st-and.ac.uk](mailto:raa@st-and.ac.uk))

*Molbank* **2020**, 2020, M1126 (1–4).

DOI: 10.3390/M1126



X-ray structure

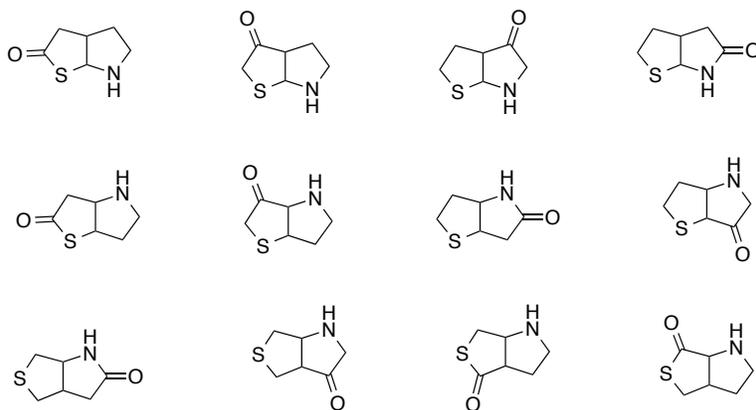
**Abstract:** The X-ray structure of the title compound has been determined and the structure shows an *exo*-configured planar dithiolanone ring. This is in contrast to the few previous dithiolanones to be characterised crystallographically, which are all twisted.

## The Chemistry of Thieno[*b*]pyrrolones, Dihydrothieno[*b*]pyrrolones, and Their Fused Derivatives

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*Adv. Heterocycl. Chem.* **2020**, *131*, 165–283.

DOI: 10.1016/bs.aihch.2019.11.001



**Abstract:** The chemistry of the known thieno[*b*]pyrrolones and dihydrothieno[*b*]pyrrolones as well as ring-fused analogs is reviewed up to the end of 2018 with 200 literature references. For each system, the properties, reactivity, synthesis, and applications are systematically covered. The compounds covered in this chapter contain two fused five-membered rings with a sulfur atom in one ring, a nitrogen atom which is adjacent to the ring junction in the other, and then, additionally, a single carbonyl group which can be in either ring. Depending on the relative arrangement of the heteroatoms and the carbonyl group, the fully unsaturated compounds can contain either three or two endocyclic double bonds and, consequently, the dihydro derivatives have either two or one. All these systems are included, together with cases where the thienopyrrolone forms part of a larger fused system.

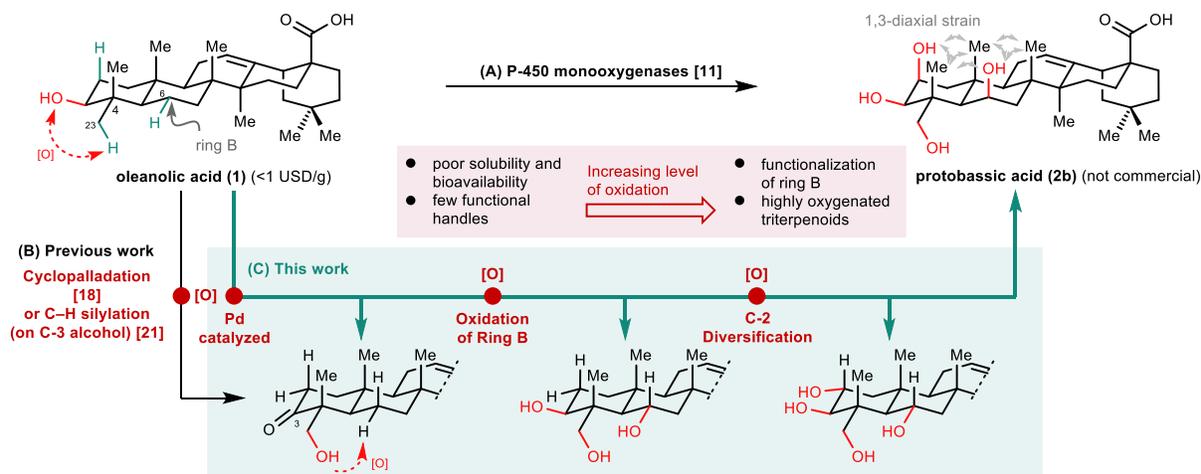
## Application of Relay C–H Oxidation Logic to Polyhydroxylated Oleanane Triterpenoids

Martin Berger, Christian Knittl-Frank, Sophie Bauer, Georg Winter, Nuno Maulide\*

([nuno.maulide@univie.ac.at](mailto:nuno.maulide@univie.ac.at))

*Chem* **2020**, *6*, 1183–1189.

DOI: 10.1016/j.chempr.2020.04.007



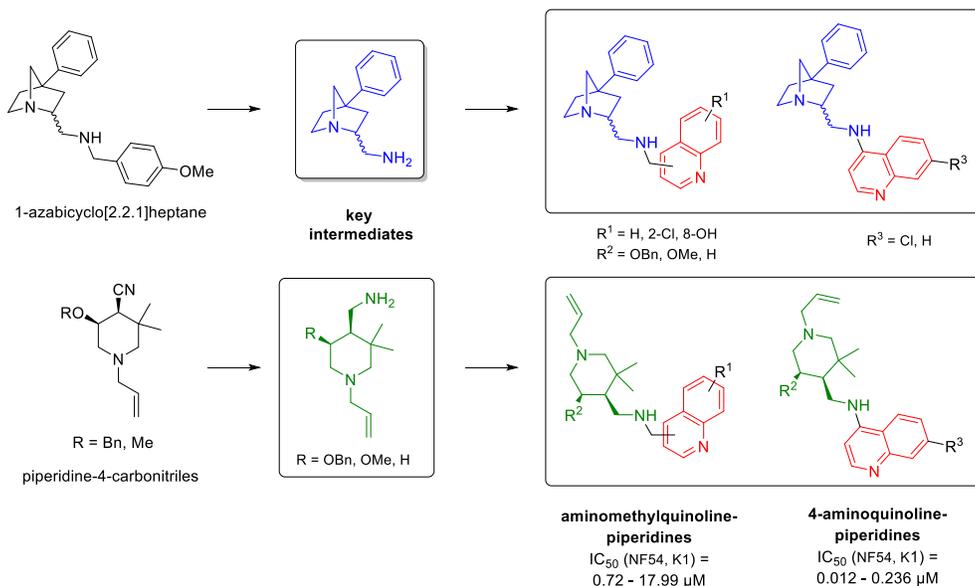
**Abstract:** Although biological applications of abundant feedstock triterpenoids such as oleanolic acid are limited because of poor solubility, synthetic access to higher hydroxylated metabolites is challenging. We use relay C–H oxidation logic to mimic the processes carried out in Nature by P450 monooxygenase enzymes. To this end, we use the C-23-OH as natural handle for a hydrogen-atom-transfer access to C-6, enabling the first syntheses of highly oxidized natural products as well as uncovering the anti-leukemic activity of a synthetic intermediate.

## Synthesis and Biological Evaluation of Novel Quinoline-Piperidine Scaffolds as Antiplasmodium Agents

Tim Van de Walle, Maya Boone, Julie Van Puyvelde, Jill Combrinck, Peter J. Smith, Kelly Chibale, Sven Mangelinckx, Matthias D'hooghe\* ([matthias.dhooghe@ugent.be](mailto:matthias.dhooghe@ugent.be))

*Eur. J. Med. Chem.* **2020**, *198*, 112330 (1–13).

DOI: 10.1016/j.ejmech.2020.112330



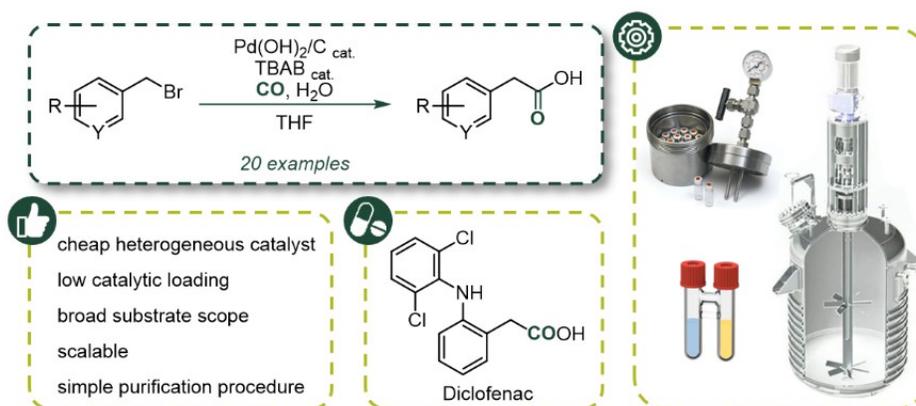
**Abstract:** The parasitic disease malaria puts almost half of the world's population at risk for infection and is responsible for more than 400,000 deaths each year. The first-line treatment, artemisinin-based combination therapies (ACT), is under pressure due to emerging resistance of *Plasmodium falciparum* in e.g. the Mekong delta. Therefore, the development of new antimalarial agents is crucial in order to amplify or replace the current treatments and to surpass the growing resistance. Chloroquine, the long-established antimalarial drug, still serves as role model for the design of novel quinoline analogues, which has resulted in numerous active derivatives against chloroquine-resistant *P. falciparum* strains over the past twenty years. In this work, a set of functionalized quinoline analogues, decorated with a modified piperidine-containing side chain, was produced. Both amino- and (aminomethyl)quinolines were synthesized, resulting in four different series of in total 18 novel quinoline-piperidine conjugates. Evaluation of their *in vitro* antiplasmodium activity against a CQ-sensitive (NF54) and a CQ-resistant (K1) strain of *P. falciparum* unveiled highly potent activities in the nanomolar range against both strains for five derivatives, all of them being 4-aminoquinolines. Moreover, no cytotoxicity was observed for all active compounds. Therefore, these five new aminoquinoline hit structures are of considerable value for antimalarial research and have the potency to be transformed into novel antimalarial agents upon further hit-to-lead optimization studies.

## Pd(OH)<sub>2</sub>/C, a Practical and Efficient Catalyst for the Carboxylation of Benzylic Bromides with Carbon Monoxide

Anne-Marie Wakuluk-Machado, Damien F. Dewez, Hajar Baguia, Miguel Imbratta, Pierre-Georges Echeverria,\* and Gwilherm Evano\* ([pierre-georges.echeverria@minakem.com](mailto:pierre-georges.echeverria@minakem.com) or [gwilherm.evano@ulb.be](mailto:gwilherm.evano@ulb.be))

*Org. Process Res. Dev.* **2020**, *24*, 713–723.

DOI: 10.1021/acs.oprd.9b00402



**Abstract:** A simple, efficient, cheap, and broadly applicable system for the carboxylation of benzylic bromides with carbon monoxide and water is reported. Upon simple reaction with only 2.5 wt % of Pearlman's catalyst and 10 mol % of tetrabutylammonium bromide in tetrahydrofuran at 110 °C for 4 h, a range of benzylic bromides can be smoothly converted to the corresponding arylacetic acids in good to excellent yields after simple extraction and acid–base wash. The reaction was found to be broadly applicable, scalable, and could be successfully extended to the use of *ex situ*-generated carbon monoxide and applied to the synthesis of the nonsteroidal anti-inflammatory drug diclofenac.