

The ISHC Bulletin

Recent Publications of ISHC Members

Issue 16; October 2017

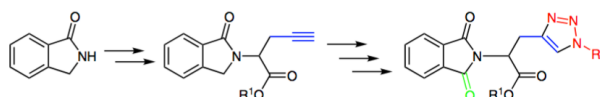
*Published as part of the *ISHC Conference Special Issue*

Unnatural Amino Acid Derivatives through Click Chemistry: Synthesis of Triazolylalanine Analogues

Pravin C. Patil and Frederick A. Luzzio

Synlett **2017**, 28, 1729–1732.*

DOI: 10.1055/s-0036-1588510



R¹ = *t*-Bu, R¹ = H, R² = alkyl, benzyl

Click conditions: R²-N₃/CuSO₄·5H₂O/Na ascorbate/THF-H₂O, yields, 67–95%, 7 examples.
Benzylic oxidation conditions: Oxone/KBr/MeCN-H₂O, yields, 72–91%, 7 examples.

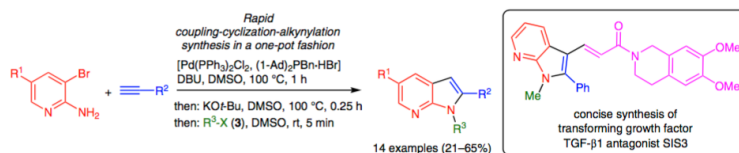
Abstract: A novel *tert*-butyl 2-(1-oxoisindolin-2-yl)acetate derivative is selectively alkylated with propargyl bromide in the presence of lithium hexamethyldisilazide. After removal of the *tert*-butyl protecting group, the resulting *N*-isindolinyl (ethynylalanine) derivative is reacted with a series of azides under 'click conditions'. The click reactions afford an array of *N*-isindolinyl-1,2,3-triazolylalanine derivatives as the free carboxylic acids. Following esterification, the *N*-isindolinone protecting group is then transformed into the more easily removable phthaloyl group by selective oxidation at the benzylic position.

One-Pot Coupling–Cyclization–Alkylation Synthesis of 1,2,5-Tribstituted 7-Azaindoles in a Consecutive Three-component Fashion

Timo Lessing and Thomas J. J. Müller

Synlett **2017**, 28, 1743–1747.*

DOI: 10.1055/s-0036-1590837



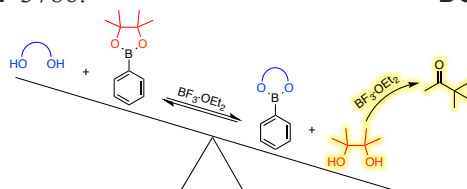
Abstract: 1,2,5-Trisubstituted 7-azaindoles are rapidly and efficiently prepared in a one-pot, copper-free alkylation–cyclization–alkylation sequence starting from unprotected 2-aminopyridyl halides in a consecutive three-component fashion. By extension to a consecutive four-component coupling–cyclization–iodination–alkylation synthesis of 3-iodo-1-methyl-2-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine, a concise synthesis of SIS3, a selective TGF-β1 and signaling inhibitor, was realized.

Boron Trifluoride Facilitated Transesterification of Dioxaborolananes

Chathuri J. Kombala, Dulamini I. Ekanayake, Dustin E. Gross

Tetrahedron Lett. **2017**, 58, 3782–3786.

DOI: 10.1016/j.tetlet.2017.08.052



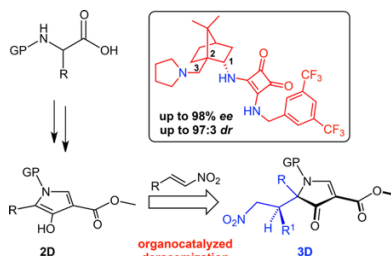
Abstract: The direct transesterification of dioxaborolananes (alkane-1,2-diol based boronate esters) was explored. Using BF₃·OEt₂, alkane-1,2-diol based mono- and bis-boronate esters (i.e., pinacol and ethylene glycol) have been converted quantitatively to either benzene-1,2-diol or alkane-1,3-diol based boronate esters. In the case of pinacol esters, esterification is facilitated by the accompanying pinacol rearrangement, thus shifting the reaction equilibrium.

Organocatalyzed Deracemization of Δ^2 -Pyrrolin-4-ones

Sebastijan Ričko, Anže Meden, Anže Ivančič, Andrej Perdih, Bogdan Štefane, Jurij Svete, and Uroš Grošelj

Adv. Synth. Catal. **2017**, *359*, 2288–2296.

DOI: 10.1002/adsc.201700539



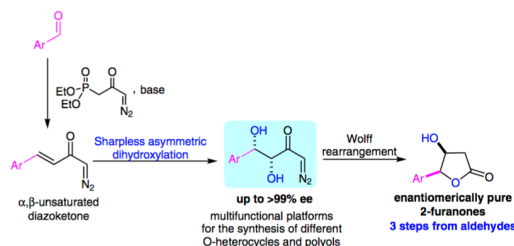
Abstract: Racemic pyrrolin-4-ones, accessible from α -amino acids, undergo asymmetric stereoselective organocatalyzed 1,4-additions to *trans*- β -nitrostyrenes (up to 98% ee; dr up to 97:3). From a series of typical organocatalysts, the best performance was achieved using (+)-camphor-1,3-diamine-derived bifunctional organocatalysts. A broad substrate scope and some follow-up modifications have been demonstrated.

Sharpless Asymmetric Dihydroxylation on α,β -Unsaturated Diazoketones: A New Entry for the Synthesis of Disubstituted Furanones

Alexánder G. Talero and Antonio C. B. Burtoloso

Synlett **2017**, *28*, 1748–1752.*

DOI: 10.1055/s-0036-1590977



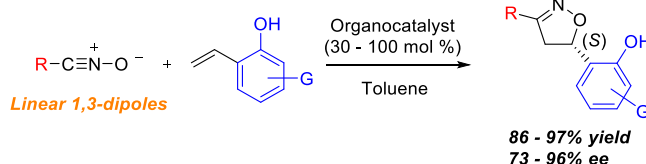
Abstract: The synthesis of enantiomerically pure 4,5-disubstituted 2-furanones is accomplished in three steps from aldehydes. The steps involve a highly enantioselective Sharpless asymmetric dihydroxylation of α,β -unsaturated diazoketones, followed by a photochemical Wolff rearrangement.

Amine-Urea-Mediated Asymmetric Cycloadditions between Nitrile Oxides and *o*-Hydroxystyrenes by Dual Activation

Hiroyuki Suga, Yohei Hashimoto, Yasunori Toda, Kazuaki Fukushima, Hiroyoshi Esaki, and Ayaka Kikuchi

Angew. Chem. Int. Ed. **2017**, *56*, 11936–11939.

DOI: 10.1002/anie.201705662



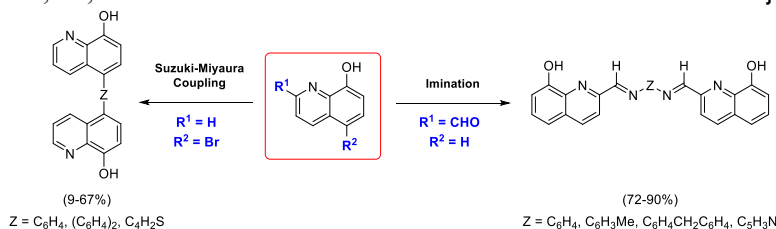
Abstract: The first example of asymmetric 1,3-dipolar cycloadditions between nitrile oxides and *o*-hydroxystyrenes, mediated by cinchona-alkaloid-based amine-ureas is reported. The method is based on a dual activation involving both LUMO and HOMO activations. In addition to the stoichiometric asymmetric induction, a catalytic amount of amine-urea enables the cycloadditions to proceed in an enantioselective manner. Computational studies strongly support the HOMO activation of *o*-hydroxystyrenes and LUMO activation of nitrile oxides by hydrogen-bonding interactions with the Brønsted acid/base bifunctional catalyst.

Synthesis of bis-8-Hydroxyquinolines *via* an Imination or a Suzuki–Miyaura Coupling Approach

Rob De Vreese, Koen Muylaert, Cedric Maton, Lise Dereu, Frederique Taillieu, Thomas Harth, Rik Van Deun, Henk Vrielinck, Christian V. Stevens, Matthias D’hooghe

Tetrahedron Lett. **2017**, *58*, 3803–3807.

DOI: 10.1016/j.tetlet.2017.08.039



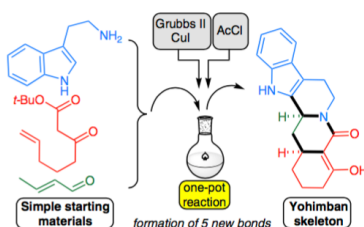
Abstract: Bis-8-hydroxyquinolines represent an important yet underexplored class of potential ligands for the preparation of various coordination polymers, which can be used in a plethora of applications. In this work, the synthesis of two types of bis-8-hydroxyquinolines, prepared *via* either an imination or a Suzuki-Miyaura coupling approach, as well as their analysis is discussed. Imination was pursued through the condensation of quinolinecarbaldehydes with diamines or aminoquinolines with dialdehydes, and the Suzuki-Miyaura coupling reactions were evaluated using a bromoquinoline substrate and diboronic acids.

A One-Pot Methodology for the Synthesis of the Yohimban Skeleton

Claudio Parra, Pablo Solis, Josep Bonjoch and Ben Bradshaw

Synlett **2017**, *28*, 1753–1757.*

DOI: 10.1055/s-0036-1589092



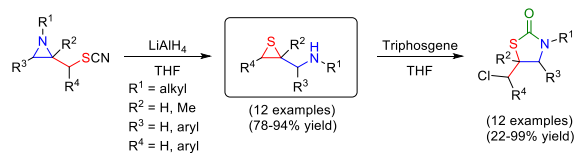
Abstract: A simple and straightforward assembly of the yohimban skeleton was achieved by condensation of an acyclic β -keto ester with tryptamine, followed by consecutive cross metathesis and tandem cyclization reactions, leading to the formation of three new rings. The whole process was readily carried out in the one-flask providing a rapid entry to the pentacyclic scaffold of yohimbine alkaloids.

LiAlH₄-Induced Thia-Aza-Payne Rearrangement of Functionalized 2-(Thiocyanatomethyl)aziridines into 2-(Aminomethyl)thiiranes as an Entry to 5-(Chloromethyl)thiazolidin-2-ones

Jeroen Dolfen, Kristof Van Hecke, and Matthias D’hooghe

Eur. J. Org. Chem. **2017**, 3229–3233.

DOI: 10.1002/ejoc.201700549



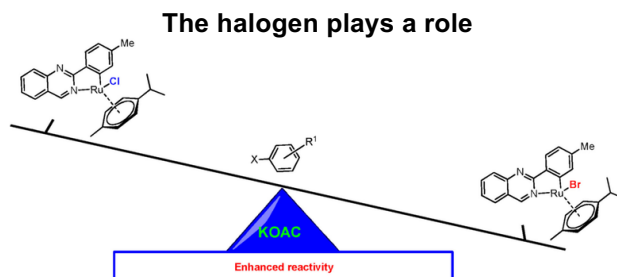
Abstract: Non-activated 2-(thiocyanatomethyl)aziridines with diverse substitution patterns were deployed as substrates to effect a LiAlH₄-promoted thia-aza-Payne rearrangement, providing access to functionalized 2-(aminomethyl)thiiranes in good to excellent yields (78-94%). The developed strategy is based on a hydride reduction of the thiocyanato moiety followed by intramolecular aziridine ring opening. Subsequent exposure of the obtained 2-(aminomethyl)episulfide intermediates to triphosgene resulted in the formation of 5-(chloromethyl)thiazolidin-2-ones.

Synthesis and Reactivity of 2-Arylquinazoline Halidoruthenacycles in Arylation Reactions

Petra Kuzman, Franc Požgan, Anton Meden, Jurij Svete and Bogdan Štefane

Chem. Cat. Chem. **2017**, *9*, 3380–3387.

DOI: 10.1002/cctc.201700494



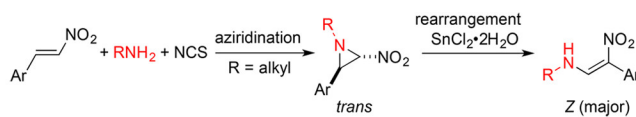
Abstract: The synthesis of a range of new cyclometallated organoruthenium(II) complexes through the *ortho*-C–H activation of the aryl group in 2-aryl-substituted quinazolines with $[\text{RuX}_2(p\text{-cymene})_2]$ is described. The beneficial effect of the carboxylate ligand on both the cyclometallation and the further arylation reaction step was demonstrated. Mechanistic studies reveal that bromide and iodide anions decelerate the arylation process by an in situ ligand exchange reaction. Additionally, a detailed NMR spectroscopy investigation was performed to explain some elementary steps in the arylation of 2-(aryl)quinazoline halidoruthenacycles.

Direct Aziridination of Nitroalkenes Affording *N*-Alkyl-*C*-nitroaziridines and the Subsequent Lewis Acid Mediated Isomerization to β -Nitroenamines

Feiyue Hao, Haruyasu Asahara and Nagatoshi Nishiwaki

Org. Lett. **2017**, *19*, 5442–5445.

DOI: 10.1021/acs.orglett.7b02724



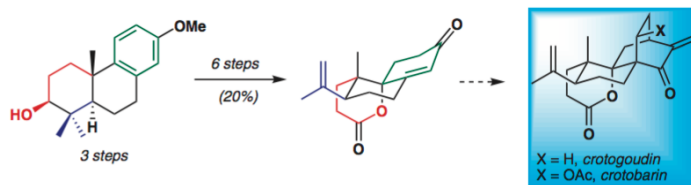
Abstract: A mild and highly diastereoselective one-pot synthesis of *trans*-*N*-alkyl-*C*-nitroaziridines was achieved by the treatment of nitroalkenes with aliphatic amines and *N*-chlorosuccinimide. Treatment of the obtained aziridines with a Lewis acid resulted in a facile ring opening reaction, accompanied by rearrangement and isomerization into functionalized (*Z*)- β -nitroenamines.

Efforts Toward a Synthesis of Crotogoudin and Crotoharin

Duy N. Mai, Dmitriy Uchenik, and Christopher D. Vanderwal

Synlett **2017**, *28*, 1758–1762.*

DOI: 10.1055/s-0036-1588560



Abstract: Two synthesis designs for the diterpenoid crotogoudin are discussed, and efforts to achieve each are described. First, a Cope rearrangement/intramolecular Diels–Alder cascade reaction was investigated. Second, a bioinspired sequence of cationic bicyclization and A-ring oxidative fragmentation set-up for a lactonization induced by a phenolic oxidation, ultimately providing a tricyclic intermediate that required only installation of the bridging ring of the salient bicyclo[2.2.2]octane system. This last endeavor was fraught with difficulty, but did lead to the development of conditions for cyclization of related keto-alkenes via manganese(III)-based radical chemistry.