International Society
of Heterocyclic
Chemistry
ISHC

The ISHC Bulletin

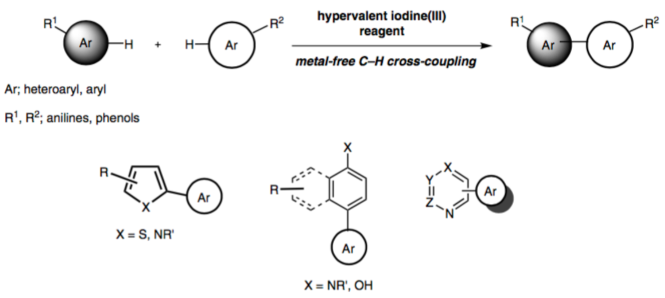
Recent Publications of ISHC Members

Issue 15; September 2017
*Published as part of the ***ISHC Conference Special Issue***

Metal-free Oxidative Cross-Coupling Reaction of Aromatic Compounds Containing Heteroatoms

Koji Morimoto, Toshifumi Dohi, and Yasuyuki Kita

Synlett **2017**, *28*, 1680–1694.* **DOI:** 10.1055/s-0036-1588455

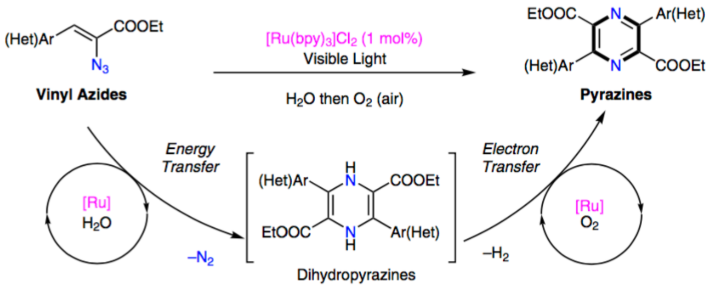


Abstract: The biaryl unit containing a heteroatom is a key structure in a large number of natural products and π-conjugated organic systems. The cross-couplings can provide powerful methods for the construction of biaryls and heterobiaryls; thus, the development of a new coupling method has been intensively studied by synthetic chemists. Therefore, the oxidative biaryl coupling reaction of arenes containing a heteroatom is a significantly attractive, convenient, and straightforward route to the synthesis of biaryls due to its operational simplicity avoiding the preparation of the corresponding halogenated and metallated arenes. In this report, recent progress in the field of metal-free oxidative cross-coupling reactions of aromatic compounds using hypervalent iodine(III) reagents, is presented.

Visible-Light-Mediated Synthesis of Pyrazines from Vinyl Azides Utilizing a Photocascade Process

Asik Hossain, Santosh K. Pagire, and Oliver Reiser

Synlett **2017**, *28*, 1707–1714.* **DOI:** 10.1055/s-0036-1590888

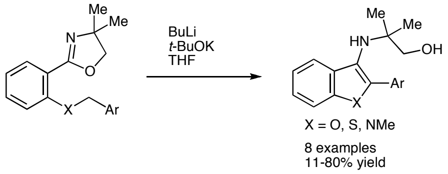


Abstract: A convenient method for the synthesis of substituted pyrazines from vinyl azides has been developed. This method is enabled by a dual-energy and electron-transfer strategy by visible-light photocatalysis. Initially, vinyl azides are activated by a triplet sensitization process from an excited ruthenium photocatalyst in the presence of water to form dihydropyrazines, followed by a single-electron-transfer (SET) process under oxygen (air) atmosphere that leads to the tetrasubstituted pyrazines in good to excellent yields.

Base-Induced Cyclisation of *ortho*-Substituted 2-Phenyloxazolines to Give 3-Aminobenzofurans and Related Heterocycles

R. Alan Aitken, Andrew D. Harper, Alexandra M. Z. Slawin

Synlett **2017**, *28*, 1738–1742.* **DOI:** 10.1055/s-0036-1588503

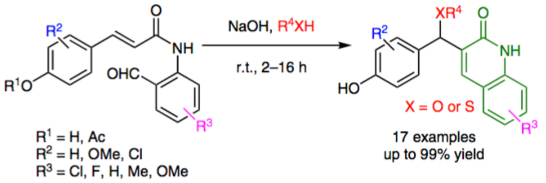


Abstract: Treatment of *ortho*-benzyloxyphenyloxazolines with butyllithium and potassium *t*-butoxide results in cyclisation with ring-opening of the oxazoline to give 2-aryl-3-aminobenzofurans. The reaction also occurs with the corresponding benzylthio- and benzylamino-compounds to give benzothiophenes and indoles, respectively. Use of an *ortho*-allyloxyphenyloxazoline gives the corresponding 2-vinylbenzofuran, while both α-methylbenzyloxy and benzylsulfonyl compounds form stable spirooxazolidine products. The X-ray structure of an aminobenzothiophene product has been determined.

Easy Access to Quinolin-2(1*H*)-ones via a One-Pot Tandem Oxa-Michael–Aldol Sequence

Lucie Jarrige, Jeremy Merad, Siwar Zaied, Florent Blanchard, Géraldine Masson

Synlett **2017**, *28*, 1724–1728.* **DOI:** 10.1055/s-0036-1588470

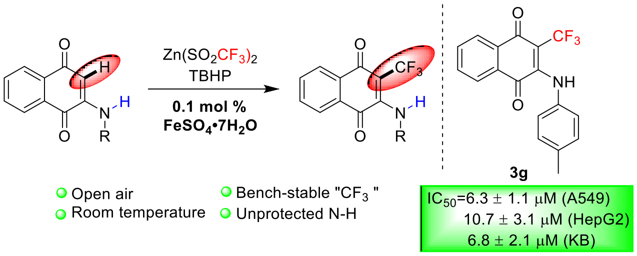


Abstract: An efficient strategy for the synthesis of a variety of quinolin-2(1*H*)-one derivatives has been developed. The reaction proceeded from cinnamide derivatives via a tandem reaction in the presence of NaOH to afford the corresponding 2- quinolin-2(1*H*)-one derivatives in good to excellent yields.

C–H Trifluoromethylation of 2-Substituted/Unsubstituted Aminonaphthoquinones at Room Temperature with Bench-Stable $(CF_3SO_2)_2Zn$: Synthesis and Antiproliferative Evaluation

Jing Li, Xiaofei Zhang, Haoyue Xiang, Linjiang Tong, Fang Feng, Hua Xie, Jian Ding, and Chunhao Yang

J. Org. Chem. **2017**, *82*, 6795–6800. **DOI:** 10.1021/acs.joc.7b00940

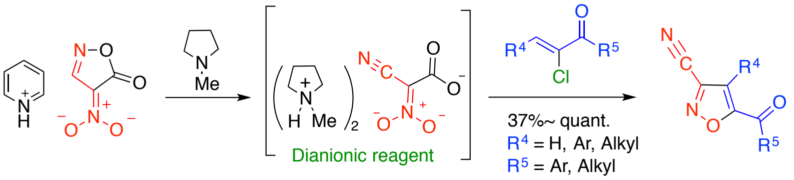


Abstract: A direct C-H trifluoromethylation of 2-amino-1,4-naphthoquinones analogues is described. This reaction proceeds under mild conditions at open atmosphere, providing a range of CF_3-containing naphthoquinones with good yield and functional group compatibility. All synthetic compounds were screened for antiproliferative activity against three human cancer cell lines. Notably, some of those trifluoromethyl analogs, such as **3a/3g/3j/3t**, showed good antiproliferative profile.

Synthesis of Functionalized 3-Cyanoisoxazoles Using a Dianionic Reagent

Kento Iwai, Haruyasu Asahara, and Nagatoshi Nishiwaki

J. Org. Chem. **2017**, *82*, 5409–5415. **DOI:** 10.1021/acs.joc.7b00811

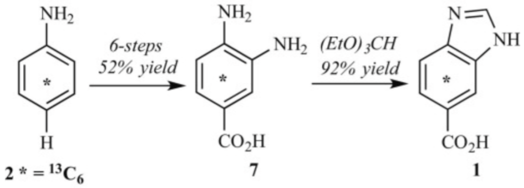


Abstract: A series of 5-acylated 3-cyanoisoxazoles wereefficiently synthesized by the Michael addition of dianioniccyano-aci-nitroacetate to α-chloro-α,β-unsaturated ketonesfollowed by intramolecular nucleophilic substitution of thenitronate ion intermediate. In this process, the dianionicreagent serves as the safe synthetic equivalent of the explosivenitroacetonitrile. The 3-cyano group is sufficiently reactive toward ethanolysis and 1,3-dipolar cycloaddition with an azide to afford ethyl ester and tetrazole, respectively. A pyridine ring between the 5-acyl and the 4-aryl group was also constructed. This led to the formation of the isoxazolo[5,4-*c*]quinoline derivative.

Synthesis of [$^{13}C_6$]3,4-Diaminobenzoic Acid as a Precursor for Stable Isotope Labeled Benzimidazoles

Matthew G. Donahue, Nicholas G. Jentsch, Casey R. Simons

Tetrahedron Lett. **2017**, *58*, 1692–1694. **DOI:** 10.1016/j.tetlet.2017.03.045

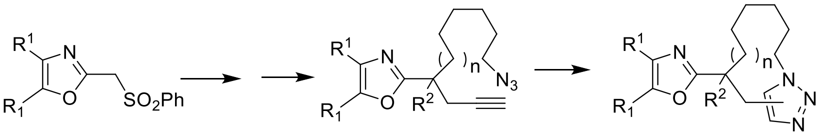


Abstract: The synthesis of [$^{13}C_6$]3,4-diaminobenzoic acid from commercially available [$^{13}C_6$]aniline is described in six steps. Salient features of this route include the preparation of a differentially protected 3,4-diaminobenzonitrile, hydrogen gas free aromatic nitro group reduction with ammonium formate and facile benzimidazole ring closure of the *ortho*-arylenediamine with triethylorthoformate. This stable-labeled 3,4-diaminobenzoic acid is an ideal [M+6]isotopomer to synthesize complex benzimidazole fragments for mass spectrometry internal assays.

The Intramolecular Click Reaction Using 'Carbocontiguous' Precursors

Pravin C. Patil and Frederick A. Luzzio

Tetrahedron **2017**, *73*, 4206–4213. **DOI:** 10.1016/j.tet.2016.11.016



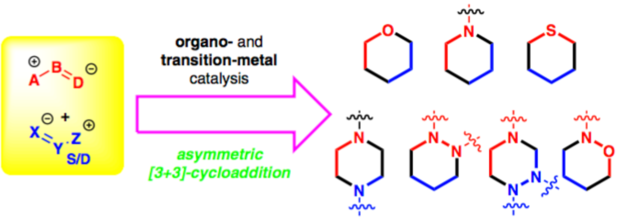
R^1= phenyl, R^2= phenylsulfonyl, n = 1,2,3,4

Abstract: The synthesis and utilization of all carbon-chain 'carbocontiguous' azidoalkynyl precursors for an intramolecular click reaction is described. The substrates contain both azidoalkyl and ethynylmethyl groups which are conjoined by a 2-(phenylsulfonylmethyl)-4,5-diphenyloxazole lynchpin and are suitably disposed for ring closure. On promotion by copper salts, a number of cyclic click products having the 1,4-disubstituted *endo*-fused triazole component and the 4,5-diphenyloxazole component are obtained. In one case, removal of the phenylsulfonylmethyl group from the substrate prior to cyclization gave the 1,5-disubstituted *exo*-fused triazole. The utilization of $CuSO_4$/sodium ascorbate system appears to be the optimal conditions for closure/cyclization and afforded the cyclized products in yields of 84–95%.

Asymmetric [3+3] Cycloaddition for Heterocycle Synthesis

Yongming Deng, Qing-Qing Cheng, and Michael P. Doyle

Synlett **2017**, *28*, 1695–1706.* **DOI:** 10.1055/s-0036-1588453

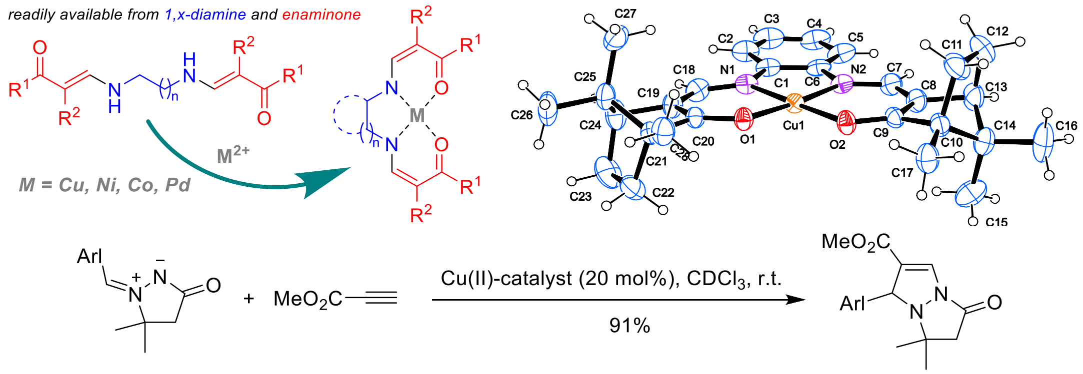


Abstract: Asymmetric syntheses of six-membered ring heterocycles are important research targets not only in synthetic organic chemistry but also in pharmaceuticals. The [3+3]-cycloaddition methodology is a complementary strategy to [4+2] cycloaddition for the synthesis of heterocyclic compounds. Recent progress in [3+3]-cycloaddition processes provide powerful asymmetric methodologies for the construction of six-membered ring heterocycles with one to three heteroatoms in the ring. In this account, synthetic efforts during the past five years toward the synthesis of enantioenriched six-membered ring heterocycles through asymmetric [3+3] cycloaddition are reported. Asymmetric organocatalysis uses chiral amines, thioureas, phosphoric acids, or NHC catalysis to achieve high enantiocontrol. Transition-metal catalysts used as chiral Lewis acids to activate a dipolar species is an alternative approach. The most recent advance, chiral transition-metal-catalyzed reactions of enoldiazo compounds, has contributed toward the versatile and highly selective synthesis of six-membered heterocyclic compounds.

Combinatorial Synthesis of Acacen-Type Ligands and Their Coordination Compounds

Urša Tomažin, Uroš Grošelj, Marta Počkaj, Franc Požgan, Bogdan Štefane, and Jurij Svete

ACS Comb. Sci. **2017**, *19*, 386–396. **DOI:** 10.1002/acscombsci.7b00027



Abstract: A highly modular synthetic method for the preparation of acacen-type ligands and their coordination compounds was developed. A series of 46 acacen-type ligands were synthesized by a combinatorial acid-catalyzed transamination between six primary diamines and eight enaminones. The bis-enaminone products were used as tetradentate ligands for coordination of copper(II), nickel(II), cobalt(II), and palladium(II). Dependence of the preferred *E*- or *Z*-configuration of the enaminone ligand on the α-substituent of the enaminone moiety in solution was determined by NMR and confirmed by X-ray diffraction. The copper(II) complexes were tested for their suitability as catalysts in 3 + 2 cycloaddition of azomethine imine to methyl propiolate.