

## The ISHC Bulletin

### Recent Publications of ISHC Members

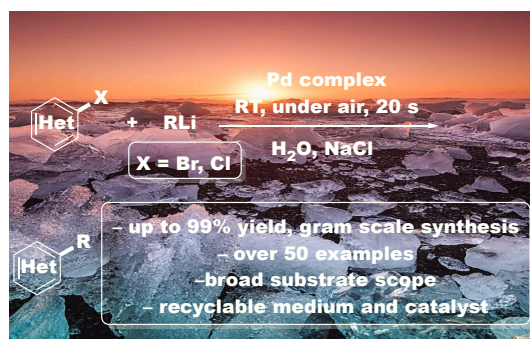
Issue 28; February 2019

#### Water and Sodium Chloride: Essential Ingredients for Robust and Fast Pd-Catalysed Cross-Coupling Reactions between Organolithium Reagents and (Hetero)aryl Halides

Guiseppa Dilauro, Andrea Francesca Quivelli, Paola Vitale, Vito Capriati,\* and Filippo Maria Perna ([vito.capriati@uniba.it](mailto:vito.capriati@uniba.it))

*Angew. Chem. Int. Ed.* **2019**, 58, 1799–1802.

DOI: 10.1002/anie.201812537



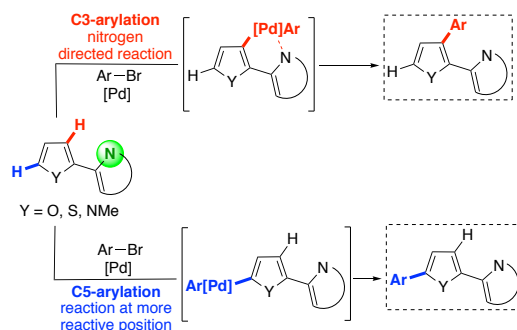
**Abstract:** Direct palladium-catalysed cross-couplings between organolithium reagents and (hetero)aryl halides (Br, Cl) proceed fast, cleanly and selectively at room temperature in air, with water as the only reaction medium and in the presence of NaCl as a cheap additive. Under optimised reaction conditions, a water-accelerated catalysis is responsible for furnishing C(sp<sup>3</sup>)-C(sp<sup>2</sup>), C(sp<sup>2</sup>)-C(sp<sup>2</sup>), and C(sp)-C(sp<sup>2</sup>) cross-coupled products, in competition with protonolysis, within a reaction time of 20 s, in yields of up to 99%, and in the absence of undesired dehalogenated/homocoupling side products even when challenging secondary organolithiums serve as the starting material. It is worth noting that the proposed protocol is scalable and the catalyst and water can easily and successfully be recycled up to 10 times, with an E-factor as low as 7.35.

#### The Influence of the Quinoline Moiety on Direct Pd-Catalyzed Arylation of Five-Membered Heterocycles

Bogdan Štefane, Uroš Grošelj, Jurij Svete, Franc Požgan, Drago Kočar, and Helena Brodnik Žugelj\* ([helena.brodnik@fkkt.uni-lj.si](mailto:helena.brodnik@fkkt.uni-lj.si))

*Eur. J. Org. Chem.* **2019**, 432–441.

DOI: 10.1002/ejoc.201800842

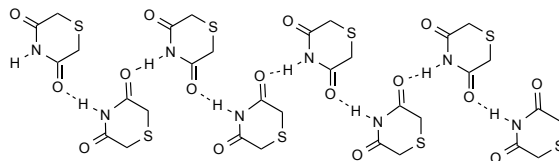


**Abstract:** Herein we report a study on the reactivity of C2-quinoline-substituted furan, thiophene and pyrrole derivatives in palladium-catalyzed direct C-H arylation. The regioselectivity of the reaction was strongly influenced by site position of the attached five-membered heterocycle thus giving rise to C3- and/or C5-arylated products. Furthermore, the Hammett correlation performed on 5-substituted-8-(furan-2-yl)quinolines indicates that a marginally positive charge is building up in the rate determining transition state and thus pointing towards the electrophilic metalation-deprotonation reaction mechanism.

## Tetrahydro-1,4-thiazine-3,5-dione

R. Alan Aitken,\* Alexandra M. Z. Slawin, and Pei-pei Yeh ([raa@st-and.ac.uk](mailto:raa@st-and.ac.uk))  
*Molbank* **2018**, 2018, M1036 (1–5).

**DOI:** 10.3390/M1036



X-ray structure

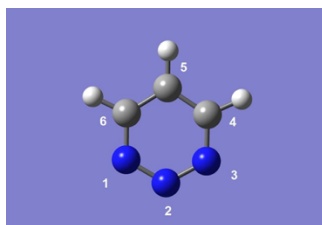
**Abstract:** The X-ray structure of the title compound contains eight molecules in the unit cell which form the basis of a herringbone arrangement of hydrogen bonded ribbons.

## The Rotational Spectrum and Derived Structure of 1,2,3-Triazine

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*J. Mol. Spectrosc.* **2019**, 355, 87–95.

**DOI:** 10.1016/j.jms.2018.11.012



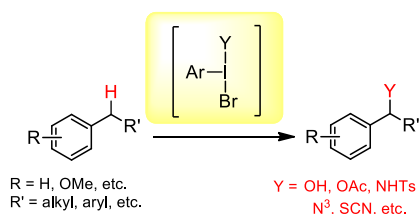
**Abstract:** The close similarity in patterns of bands in the microwave spectra of the isomeric 1,2,3- and 1,2,4-triazines has enabled assignment for the 1,2,3-isomer. Pure rotational transitions with J up to 65 were identified and fitted to a Watson-type Hamiltonian:  $A = 6334.1694(64)$ ,  $B = 6271.3135(64)$ ,  $C = 3151.2485(68)$ . A and B thus show near degeneracy. Coupled cluster calculations which include both singles, doubles and selected triple excitations (CCSD(T)), give very close agreement with the spectral data. The theoretical structure which includes estimates of the  $^{14}\text{N}$  quadrupole coupling, not determined in the spectrum, is described.

## Selective Carboxylation of Reactive Benzylic C–H Bonds by a Hypervalent Iodic(III)/Inorganic Bromide Oxidation System

Toshifumi Dohi, Shohei Ueda, Kosuke Iwasaki, Yusuke Tsunoda, Koji Morimoto, and Yasuyuki Kita\*  
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*Beilstein J. Org. Chem.* **2018**, 14, 1087–1094.

**DOI:** 10.3762/bjoc.14.94



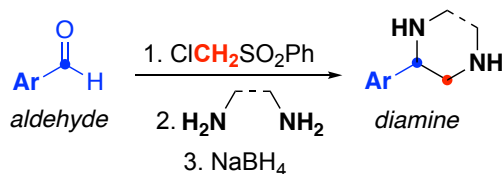
**Abstract:** The oxidation system comprised by phenyliodine(III) diacetate and iodosobenzene with inorganic bromide, *i.e.*, sodium bromide, in organic solvent was found to effect direct introduction of carboxylic acids into the benzylic secondary C-H bonds under mild conditions. The unique radical species, generated by the homolytic cleavage of labile I(III)-Br bond of *in situ* bromo-3-iodane, would initiate the benzylic carboxylations and show high sense of discrimination of the benzyl groups.

## Three-step Telescoped Synthesis of Monosubstituted Vicinal Diamines from Aldehydes

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*ACS Omega* **2019**, *4*, 2261–2267.

DOI: 10.1021/acsomega.8b03030



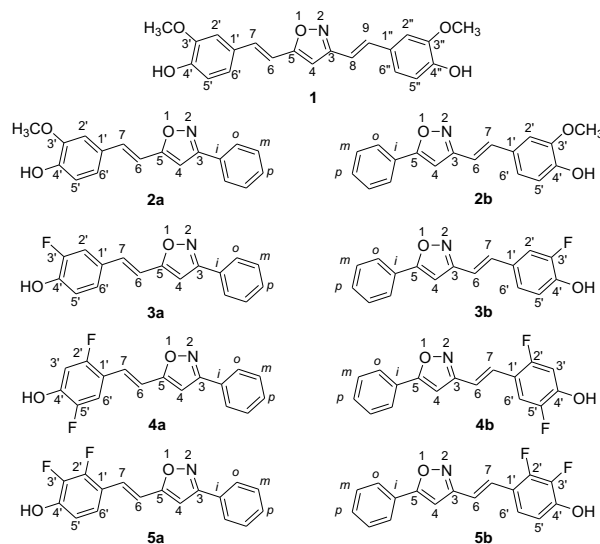
**Abstract:** Aldehydes are easily transformed into vicinal diamines and piperazines through a one-pot procedure including a Darzens reaction, treatment with an amine or diamine and then a reducing agent. Additionally, quinoxalines can be accessed by reaction with 1,2-benzenediamine under oxidative conditions. These transformations are simple methods for the preparation of synthetically interesting monosubstituted diamines, piperazines and quinoxalines.

## Synthesis, Structure and NMR Study of Fluorinated Isoxazoles Derived from Hemi-curcuminoids

Carla I. Nieto, M. Pilar Cornago, M. Pilar Cabildo, Dionisia Sanz, Rosa M. Claramunt,\* M. Carmen Torralba, and José Elguero ([rclaramunt@ccia.uned.es](mailto:rclaramunt@ccia.uned.es))

*J. Fluorine Chem.* **2019**, *219*, 39–49.

DOI: 10.1016/j.jfluchem.2018.12.012



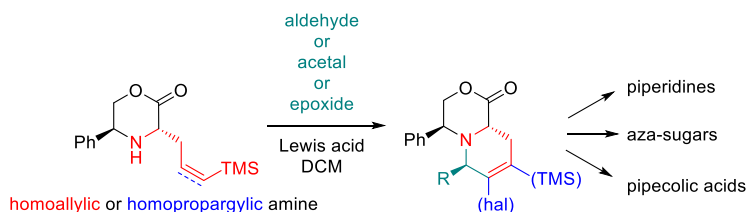
**Abstract:** The purpose of this work is to prepare a series of isoxazoles bearing phenyl and 4-hydroxy-styryl substituents at position 3 and 5; besides the phenyl group of the styryl residue bears one or two fluorine substituents. They were prepared to study their structure in the solid state and in solution by X-ray crystallography and solid-state NMR (SSNMR) for the solid state and NMR for the solution. The reaction of hydroxylamine with hemi-curcuminoid  $\beta$ -diketones affords two isomeric isoxazoles we have named series **a** (3-phenyl) and **b** (5-phenyl) that have been identified and characterized. Four pairs have been prepared that in three cases bear one or two fluorine atoms. Three X-ray structures have been determined **3a**, **3b** and **5b**; **3a** crystallizes without solvent, **3b** crystallizes with a water molecule hydrogen-bonded to a phenolic OH, finally **5b** crystallizes as a solvate with a methanol molecule hydrogen-bonded to the isoxazole N atom. This hydrogen bond results in larger differences between  $^{15}\text{N}$  chemical shifts in DMSO- $d_6$  solution and in the solid state. The splitting of some signals observed in Cross-Polarization Magic Angle Spinning (CPMAS)  $^{13}\text{C}$  NMR was assigned to  $^1J_{\text{CF}}$  dipolar couplings. The combined use of crystallography and SSNMR affords a complete characterization of isomeric isoxazoles, in particular the assignment of an isoxazole to **a** or to **b** series is not a trivial matter. In this work, we describe methods for the synthesis of isoxazoles bearing fluorine substituents that are promising structures for drug discovery.

## The Asymmetric Aza-silyl-Prins Reaction: Synthesis of Enantiopure Piperidines

Ramana R. Mittapalli, Sebastien J. J. Guesné, Robert J. Parker, Wim T. Klooster, Simon J. Coles, John Skidmore, and Adrian P. Dobbs\* ([a.dobbs@gre.ac.uk](mailto:a.dobbs@gre.ac.uk))

*Org. Lett.* **2019**, *21*, 350–355.

DOI: 10.1021/acs.orglett.8b03283



**Abstract:** The design and development of the first asymmetric aza-silyl-Prins reaction is reported, giving rise to valuable and diverse piperidines and pipercolic acid derivatives in both high yields and as single enantiomers. The creation of a novel chiral auxiliary-homoallylic amine for the aza-silyl-Prins reaction is essential to its success.

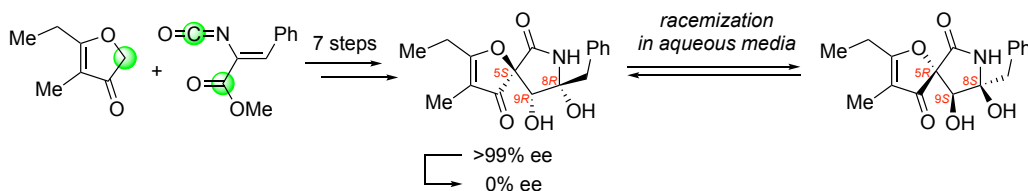
## Elucidation of Racemization Process of Azaspirene Skeleton in Neutral Aqueous Media

Shun Hirasawa, Ken Mukai, Shinnosuke Sakai, Shinnosuke Wakamori, Takahiro Hasegawa, Kazunori Souma, Nobuhiro Kanomata,\* Narihito Ogawa, Mamoru Aizawa, and Makoto Emoto\*

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*J. Org. Chem.* **2018**, *83*, 14457–14464.

DOI: 10.1021/acs.joc.8b02223



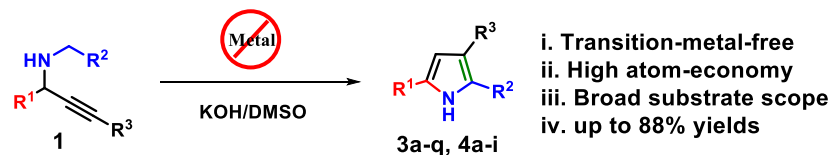
**Abstract:** Azaspirene and related congeners, which possess various biological activities, have a unique spirocyclic core structure. However, there are few studies on the chemical properties of (–)-azaspirene, despite the fact that it may provide important insights into unveiling the biosynthetic pathway. Here, we report a nine-step chemical synthesis of an azaspirene analogue with a new finding that the natural (–)-azaspirene skeleton easily racemizes in neutral aqueous media.

## Base-Mediated Direct Transformation of *N*-Propargylamines into 2,3,5-Trisubstituted 1*H*-Pyrroles

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*Org. Lett.* **2018**, *20*, 7182–7185.

DOI: 10.1021/acs.orglett.8b03112



$R^1$  = alkyl, aryl, (Het)aryl-,  $R^2$  = aryl, (Het)aryl-,  $R^3$  = alkyl, aryl, (Het)aryl-

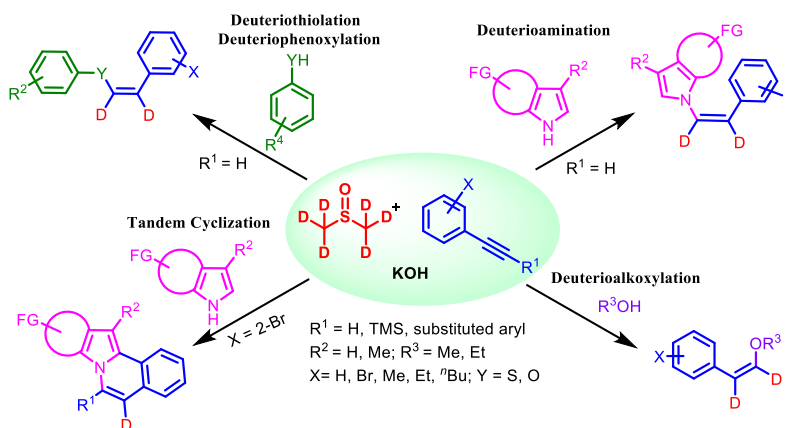
**Abstract:** An efficient and base-mediated intramolecular cyclization of *N*-propargylamines for the synthesis of structurally diversified pyrroles in high yield has been described. The developed methodology is broadly applicable and is tolerated by a variety of functional groups. Key intermediates of natural product discoipyrrole C as well as HMG-CoA-reductase inhibitor have been successfully synthesized using developed chemistry. The proposed mechanism was supported by control experiments.

## Base-Mediated Deuteration of Organic Molecules: A Mechanistic Insight

Monika Patel, Rakesh K. Saunthwal, and Akhilesh K. Verma\* ([averma@acbr.du.ac.in](mailto:averma@acbr.du.ac.in))

*ACS Omega* **2018**, 3, 10612–10623.

DOI: 10.1021/acsomega.8b01329



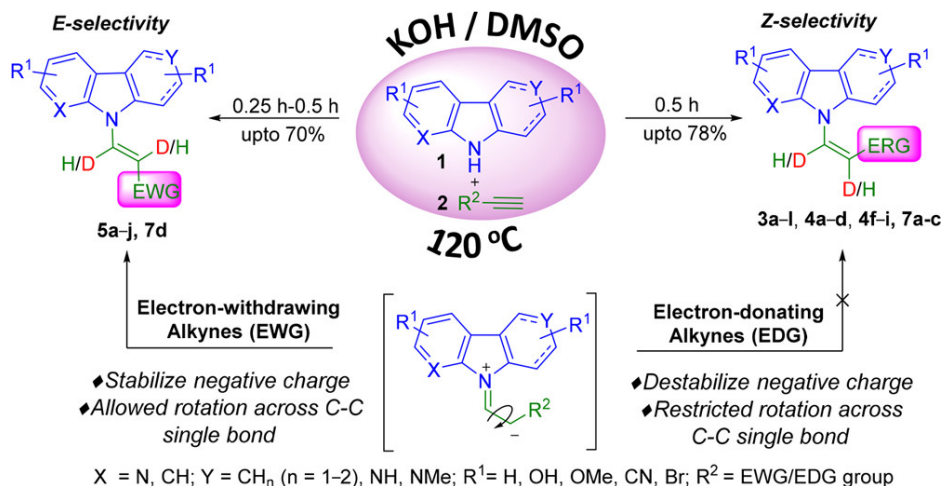
**Abstract:** A base-promoted step-economical and cost-effective strategy for introducing heavy isotopes into the organic molecules has been developed. The schemes involve the selective deuteration of various electronically distinct molecules that are formed due to deuterioamination, deuteriothiolation, deuteriophenoxylation, and deuterioalkoxylation as well as tandem cyclization using DMSO- $d_6$  as a deuterium source. The reaction involves a metal-, ligand-, and additive-free route and provides a high level of deuterium incorporation in the presence of DMSO- $d_6$  as an inflammable and ecological reagent. The reaction is well tolerated across the electronically varied substrates for the successful incorporation of deuterium into the product. The proposed mechanistic pathway for various transformations has been well supported by NMR studies.

## Substrate-Controlled Regio- and Stereoselective Synthesis of (*Z*)- and (*E*)-*N*-Styrylated Carbazoles, Aza-carbazoles, and $\gamma$ -Carbolines via Hydroamination of Alkynes

Vineeta Garg, Pradeep Kumar, and Akhilesh K. Verma\* ([averma@acbr.du.ac.in](mailto:averma@acbr.du.ac.in))

*J. Org. Chem.* **2018**, 83, 11686–11702.

DOI: 10.1021/acs.joc.8b01642



**Abstract:** We report herein the substrate-controlled regio- and stereoselective hydroamination of carbazoles, aza-carbazoles, and  $\gamma$ -carbolines with functionalized aromatic as well as aliphatic alkynes in a KOH/DMSO system in good yields. The electronic effect of the substrates governs the stereochemistry of the product. Electron-donating alkynes provided (*Z*)-stereoselective products, and electron-withdrawing alkynes provided (*E*)-stereoselective products. This approach also provides an easy route for the synthesis of mono- and bis-hydroaminated product. The deuterium-labeling studies were also conducted to support the mechanistic pathway.