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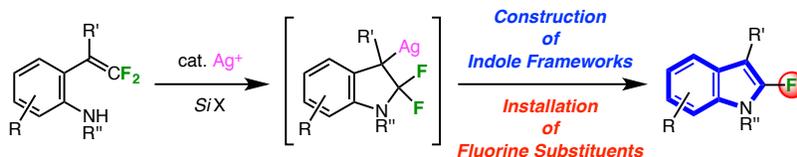
***Special Issue of The Journal of Organic Chemistry dedicated to Heterocyclic Chemistry:** The International Society of Heterocyclic Chemistry and *The Journal of Organic Chemistry* have co-sponsored the publication of a special issue of *JOC* devoted to heterocyclic chemistry. *JOC* Issue #21 was published on November 4, 2016. We thank the American Chemical Society, and in particular, the entire *JOC* staff, for their efforts toward the success of this project. The full *JOC* Special Issue can be found at: <http://pubs.acs.org/toc/joceph/81/21> Contributions to the special issue that are also highlighted in The ISHC Bulletin are indicated with a red asterisk.

Silver-catalyzed Vinylic C–F Bond Activation: Synthesis of 2-Fluoroindoles from β,β -Difluoro-*o*-sulfonamidostyrenes

Takeshi Fujita, Yota Watabe, Shigeyuki Yamashita, Hiroyuki Tanabe, Tomoya Nojima, and Junji Ichikawa

Chem. Lett. **2016**, *45*, 964–966. (Editor's Choice)

DOI: 10.1246/cl.160427



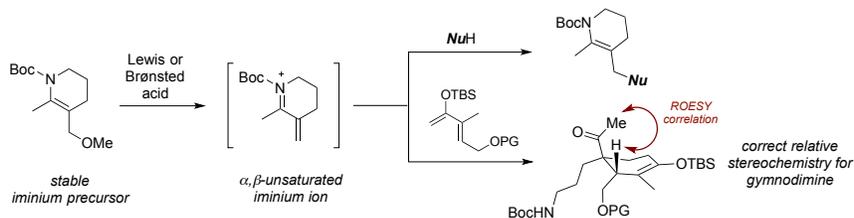
Abstract: We accomplished a silver-catalyzed 2-fluoroindole synthesis via electrophilic 5-*endo-trig* cyclization followed by β -fluorine elimination starting from β,β -difluoro-*o*-sulfonamidostyrenes. On treatment with a silver(I) catalyst and *N,O*-bis(trimethylsilyl)acetamide (BSA) in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP), difluorosulfonamidostyrenes underwent the 5-*endo-trig* cyclization to afford 2-fluoroindoles. This protocol enabled simultaneous construction of indole frameworks and regioselective installation of fluorine substituents.

Cyclic Encarbamates as Precursors of α,β -Unsaturated Iminium Ions: Reactivity and Synthesis of 6,6-Spirocyclic Ring Systems

Zhanwei Wang, Niels Krogsgaard-Larsen, Benjamin Daniels, Daniel. P. Furkert, and Margaret A. Brimble

J. Org. Chem. **2016**, *81*, 10366–10375. *

DOI: 10.1021/acs.joc.6b01343



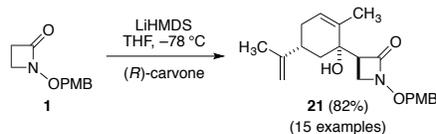
Abstract: The scalable synthesis of cyclic encarbamates and their use as convenient precursors of α,β -unsaturated *N*-acyl iminium ions is reported. The newly developed route overcomes synthetic and reactivity difficulties in previously reported methods, is readily scaled up and proceeds through stable intermediates suitable for long-term storage if required. Preliminary investigations probing the reactivity of cyclic α,β -unsaturated *N*-acyl iminium ions as dienophiles in Diels-Alder reactions and electrophilic alkylating agents are described. In the presence of Lewis and Brønsted acids, iminium precursor **22a** underwent efficient Diels-Alder cycloaddition with a range of simple and complex dienes, culminating in the synthesis of 6,6-spirocyclic ring systems possessing the same relative stereochemistry as the spirocyclic imine present in the marine natural product gymnodimine **1**.

Studies of Azetid-2-one as a Reactive Enolate Synthon of β -Alanine for Condensations with Aldehydes and Ketones

David R. Williams, Andrew F. Donnell, David C. Kammler, Sarah A. Ward, and Levin Taylor, IV

J. Org. Chem. **2016**, *81*, 10463–10475.*

DOI: 10.1021/acs.joc.6b01585



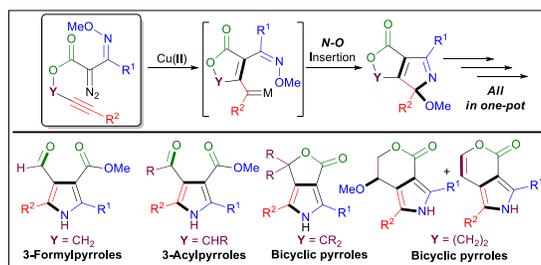
Abstract: Studies describe formation of the lithium enolate of *N*-(4-methoxybenzyloxy)azetid-2-one (**1**) and characterization of representative aldol reactions with aldehydes and ketones. Diastereoselectivity features the production of *anti*-aldol adducts from α,β -unsaturated ketones and α -branched aliphatic aldehydes. The stereoselectivity is rationalized via closed, six-membered transition-state arrangements leading to the formation of Felkin–Anh and anti-Felkin products. Examples illustrate the direct incorporation of monocyclic β -lactams into a variety of molecular architectures. The utility of **1** as an enolate synthon of homoglycine (β -alanine) is illustrated by the efficient synthesis of novel β -amino acid derivatives, including complex 4-hydroxy-2-pyridinones.

Chemodivergent Synthesis of Multi-substituted/Fused Pyrroles via Copper-catalyzed Carbene Cascade Reaction of Propargyl α -Iminodiazoacetates

Cheng Zhang, Sailan Chang, Lihua Qiu, and Xinfang Xu

Chem. Commun. **2016**, *52*, 12470–12473.

DOI: 10.1039/c6cc06864b



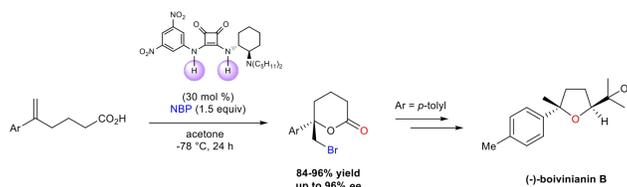
Abstract: A novel cascade reaction of alkynyl-tethered α -iminodiazoacetates has been developed, which provides a general access to both multi-substituted and fused pyrroles in high yields with a broad substrate scope. The γ -imino carbene is proposed as the key intermediate in this divergent reaction and followed by unrepresented transformations.

Enantioselective Organocatalyzed Bromolactonizations: Applications in Natural Product Synthesis

Marius Aursnes, Jørn E. Tungen, and Trond V. Hansen

J. Org. Chem. **2016**, *81*, 8287–8295

DOI: 10.1021/acs.joc.6b01375

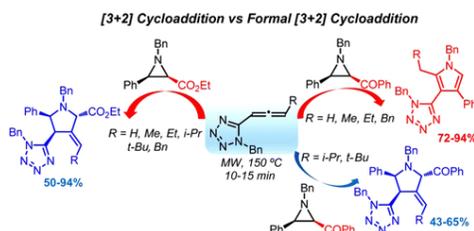


Abstract: Asymmetric bromolactonization reactions of δ -unsaturated carboxylic acids have been investigated in the presence of 10 chiral squaramide hydrogen-bonding organocatalysts. The best catalyst enabled the cyclization of several 5-arylhex-5-enoic acids into the corresponding bromolactones with up to 96% ee and in high to excellent chemical yields. The reported catalysts are prepared in a straightforward manner in two steps from dimethyl squarate. The utility of the developed protocol was demonstrated in highly enantioselective syntheses of the sesquiterpenoids (–)-gossoronol and (–)-boivinianin B. Both natural products were obtained in $\geq 99\%$ enantiomeric excess.

(1*H*-Tetrazol-5-yl)-Allenes: Building Blocks for Tetrazolyl Heterocycles

Ana L. Cardoso, Marta S. C. Henriques, José A. Paixão, Teresa M. V. D. Pinho e Melo
J. Org. Chem. **2016**, *81*, 9028–9036.

DOI: 10.1021/acs.joc.6b01679

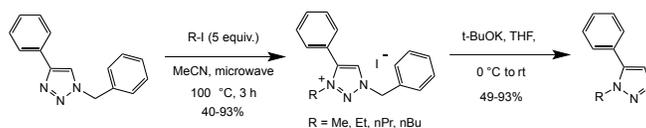


Abstract: (1*H*-Tetrazol-5-yl)-allenenes have been prepared for the first time and their reactivity towards aziridines explored. Reaction of a (1-benzyl-1*H*-tetrazol-5-yl)-phosphonium chloride and acyl chlorides in presence of triethylamine afforded the target allenenes via Wittig reaction of the *in situ* generated phosphorous ylide and ketenes. 1-(1-Benzyl-1*H*-tetrazol-5-yl)propa-1,2-diene and 3-methyl-, 3-ethyl- and 3-benzyl derivatives undergo microwave-induced formal [3+2] cycloaddition with *cis*-*N*-benzyl-2-benzoyl-3-phenylaziridine, through C-N bond cleavage, to give selectively tetrasubstituted pyrroles. In contrast, with (1*H*-tetrazol-5-yl)-allenenes bearing bulkier substituents at C-3, such as *i*-propyl or a *tert*-butyl, 4-methylenepyrrolidines were obtained exclusively via [3+2] cycloaddition of the *in situ* generated azomethine ylide. The latter allenenes also gave 4-methylenepyrrolidines on reacting with *cis*-2-benzoyl-*N*-cyclohexyl-3-phenylaziridine whereas with the other allenenes pyrroles were obtained as major products together with the formation of 4-methylenepyrrolidines. All the studied (1*H*-tetrazol-5-yl)-allenenes reacted with *N*-benzyl-*cis*-3-phenylaziridine-2-carboxylate to give the corresponding 4-methylenepyrrolidines exclusively.

Ruthenium-Free Preparation of 1,5-Disubstituted Triazoles by Alkylative Debenzylation of 1,4-Disubstituted Triazoles

Philip C. Bulman Page, G. Richard Stephenson, James Harvey, Alexandra M. Z. Slawin
Synlett **2016**, *27*, 2500–2504.

DOI: 10.1055/s-0035-1562603

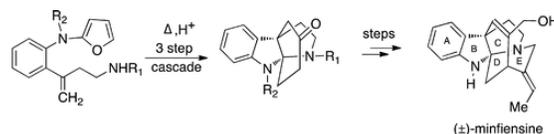


Abstract: A method that cleanly converts the 1,4-disubstituted 1,2,3-triazole products of the copper-catalysed ‘click’ dipolar cycloaddition reaction of benzyl azide with terminal alkynes into 1,5-disubstituted triazoles is described. Selective N-alkylation of 1,4-disubstituted 1,2,3-triazoles under microwave irradiation is followed by debenzylation of the resulting 1,3,4-trisubstituted triazolium cations by treatment with potassium *tert*-butoxide.

IMDAF Cascade Approach toward the Synthesis of the Alkaloid (±)-Minfiensine

Carolyn A. Leverett, Gang Li, Stefan France, and Albert Padwa
J. Org. Chem. **2016**, *81*, 10193–10203. *

DOI: 10.1021/acs.joc.6b00771

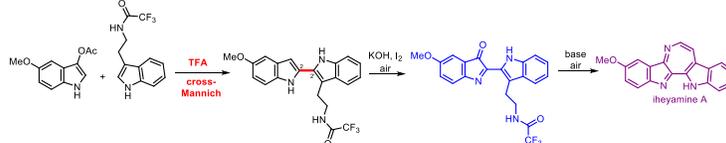


Abstract: The total synthesis of the *Strychnos* alkaloid (±)-minfiensine was achieved via an intramolecular amidofuran Diels–Alder cycloaddition/rearrangement followed by an iminium ion/cyclization cascade sequence. This domino process provides for a rapid access to the unique 1,2,3,4-tetrahydro-9a,4a-iminoethanocarbazole core structure found in the alkaloid minfiensine (**2**). In this paper, the full account of our synthetic study is described, highlighting the successful application of the cascade sequence to form the A/B/C/D rings of (±)-minfiensine (**2**) in high yield. A palladium-catalyzed enolate coupling reaction was then used to furnish the final E ring and complete the total synthesis of (±)-minfiensine (**2**).

Synthesis of the Azepinobisindole Alkaloid Iheyamine A Enabled by a Cross-Mannich Reaction

Ashley C. Lindsay, Ivanhoe K. H. Leung, and Jonathan Sperry
Org. Lett. **2016**, *18*, 5404–5407.

DOI: 10.1021/acs.orglett.6b02798

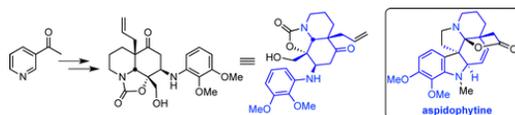


Abstract: The total synthesis of the azepinobisindole alkaloid iheyamine A is described. The successful strategy hinged on an intermolecular cross-Mannich reaction between 5-methoxy-3-acetoxyindole and a protected tryptamine to access an unsymmetrical 2,2'-bisindole, which was subsequently converted into iheyamine A via a deep-blue 3-indolone intermediate. VT ¹H NMR infers that iheyamine A exists as a mixture of tautomers that undergo intermediate chemical exchange on the NMR timescale. The intermolecular cross-Mannich reaction described herein is a viable alternative to metal-catalyzed cross-coupling strategies commonly employed to access 2,2'-bisindoles.

Studies Directed toward the Synthesis of Aspidophytine: Construction of Its Perhydroquinoline Core

Yunus E. Türkmen, Michel Gravel, and Viresh H. Rwal
J. Org. Chem. **2016**, *81*, 10454–10462. *

DOI: 10.1021/acs.joc.6b01574

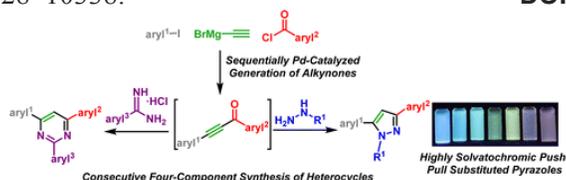


Abstract: We have developed an efficient route for the synthesis of the perhydroquinoline core of the indole alkaloid aspidophytine (2), starting from commercially available and inexpensive 3-acetylpyridine. This densely functionalized perhydroquinoline core displays four contiguous stereocenters including an all-carbon quaternary center. The synthetic sequence features a highly effective Diels–Alder reaction using a carbamate-substituted siloxy diene accompanied by a spontaneous intramolecular substitution of the newly formed 3°-alkyl bromide with a carbamate group. The installation of the electron-rich aniline moiety was accomplished via a TBSOTf-mediated intramolecular aza-Michael reaction, and the relative stereochemistry of the aza-Michael product (30) was confirmed by X-ray crystallographic analysis. Among the useful transformations that were developed through this study is a highly enantioselective Diels–Alder reaction of a versatile cyclic carbamate siloxy diene.

One-Pot Coupling–Coupling–Cyclocondensation Synthesis of Fluorescent Pyrazoles

Alissa C. Götzinger, Florian A. Theßeling, Corinna Hoppe, and Thomas J. J. Müller
J. Org. Chem. **2016**, *81*, 10328–10338. *

DOI: 10.1021/acs.joc.6b01326



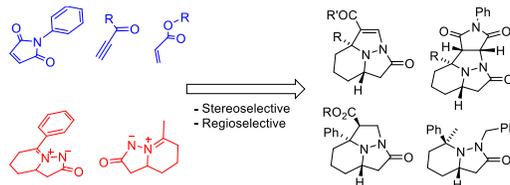
Abstract: Consecutive four-component coupling–coupling–cyclocondensation syntheses of pyrazoles and pyrimidines were developed by taking advantage of the provisional, sequentially Pd-catalyzed one-pot generation of alkyne from aryl iodides, ethynylmagnesium bromide, and acid chlorides. This one-pot methodology allows the concise, diversity-oriented generation of a set of donor-, acceptor-, and donor–acceptor-substituted pyrazoles, which are interesting fluorophores. Most distinctly, donor–acceptor pyrazoles display remarkably red-shifted emission maxima and pronounced positive solvochromicity, spanning an overall range from 363 nm (cyclohexane) to 595 nm (acetonitrile). DFT and TD-DFT calculations elucidate the electronic structure and the photophysical behavior. Upon photonic excitation, considerable charge-transfer character becomes apparent, which rationalizes the origin of huge Stokes shifts and solvochromic behavior.

Synthesis of 3D-Rich Heterocycles: Hexahydropyrazolo[1,5-*a*]pyridin-2(1*H*)-ones and Octahydro-2*H*-2a,2a¹-diazacyclopenta[*cd*]inden-2-ones.

Eva Pusavec Kirar, Miha Drev, Jona Mirnik, Uroš Groselj, Amalija Golobic, Georg Dahmann, Franc Pozgan, Bogdan Štefane, and Jurij Svete

J. Org. Chem. **2016**, *81*, 8920–8933.

DOI: 10.1021/acs.joc.6b01608



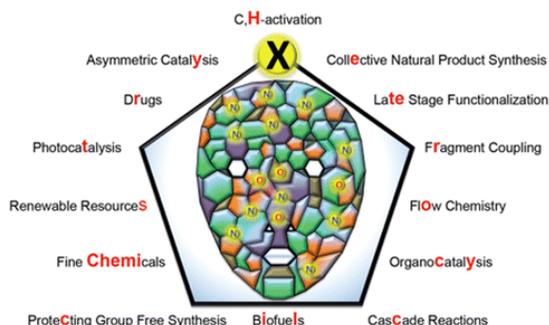
Abstract: Two cyclic azomethine imines, 7-methyl- and 7-phenyl-2-oxo- Δ^7 -hexahydropyrazolo[1,5-*a*]pyridin-8-ium-1-ide were prepared in seven steps from the respective commercially available δ -keto acids. The addition of Grignard reagents followed by *N*-alkylation at position 1 afforded the 1,7,7-trisubstituted hexahydropyrazolo[1,5-*a*]pyridin-2(1*H*)-ones, whereas 1,3-dipolar cycloadditions of these dipoles to typical acetylenic and olefinic dipolarophiles gave 4a-substituted 2a,2a¹-diazacyclopenta[*cd*]indene derivatives, as the first representatives of a novel heterocyclic system. Regio- and stereoselectivity as well as the mechanism of these [3+2]-cycloadditions were evaluated using computational and experimental methods. The data obtained were in agreement with the polar concerted cycloaddition mechanism *via* the energetically favorable *syn/endo*-transition states.

The Modern Face of Synthetic Heterocyclic Chemistry

Chiara Cabrele and Oliver Reiser

J. Org. Chem. **2016**, *81*, 10109–10125.*

DOI: 10.1021/acs.joc.6b02034



Abstract: The synthesis of heterocycles is arguably one of the oldest and at the same time one of the youngest disciplines of organic chemistry. Groundbreaking principles to form heterocycles, mainly by condensation reactions, were recognized in the beginning of the 19th century, and many of the classical reactions discovered at that time are still of great value today. In the 21st century, the wealth of synthetic methodology toward heterocycles is overwhelming, and catalysis, in particular, as one of the cornerstones of green and sustainable chemistry has contributed in a major way to these developments. This perspective tries the impossible by discussing some recent advances in the construction of heterocycles, focusing on catalytic methodology. We are aware that we do not come close to giving adequate credit to the great creativity of chemists in the field.

*Special Issue dedicated to Heterocyclic Chemistry