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Recent Publications of ISHC Members

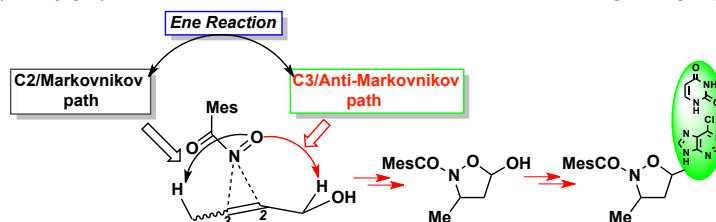
Issue 13; June 2017

***N,O*-Nucleosides from Ene Reaction of (Nitrosocarbonyl)mesitylene with Crotyl Alcohol: Selectivity, Scope, and Limitations**

Serena Carosso, Misal Guiseppa Memeo, Bruna Bovio, Elena Valletta, Beatrice Macchi, and Paolo Quadrelli

Synthesis **2017**, *49*, 1972–1982.

DOI: 10.1055/s-0036-1588695



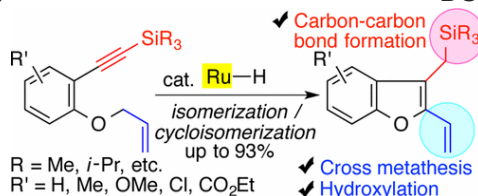
Abstract: Nitrosocarbonyl mesitylene intermediate undergoes Ene reaction with the crotyl alcohol affording two regioisomeric adducts in fair yields. The sterically demanding nitrosocarbonyl mesitylene slightly drifts the C2/Markovnikov orientation towards the C3/Anti-Markovnikov pathway affording the 5-hydroxy-isoxazolidine that serves as synthon for the preparation of *N,O*-nucleoside analogues through the Vorbrüggen protocol. The selectivity of the ene reaction is discussed in the light of C=C double bond polarization and steric effects. The structures of the *N,O*-nucleosides are attributed and discussed on the basis of spectroscopic observations and X-ray analysis.

Cycloisomerization between Aryl Enol Ether and Silylalkynes under Ruthenium Hydride Catalysis: Synthesis of 2,3-Disubstituted Benzofurans

Shohei Ohno, Kohei Takamoto, Hiromichi Fujioka, Mitsuhiro Arisawa

Org. Lett. **2017**, *19*, 2422–2425.

DOI: 10.1021/acs.orglett.7b00985



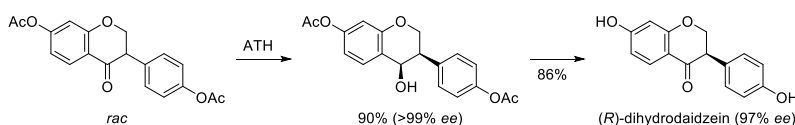
Abstract: Metal-catalyzed cycloisomerization reactions of 1,*n*-enynes have become conceptually and chemically attractive processes in the search for atom economy, which is a key subject of current research. However, metal-catalyzed cycloisomerization between aryl enol ether and silylalkynes has not been developed. The ruthenium hydride complex catalyzed cycloisomerization between aryl enol ether and silylalkynes is reported to give benzofurans having useful functional groups, vinyl and trimethylsilylmethyl, on the 2- and 3-positions, respectively.

Enantioselective Synthesis of Isoflavones by Catalytic Dynamic Kinetic Resolution

Tao Qin and Peter Metz

Org. Lett. **2017**, *19*, 2981–2984.

DOI: 10.1021/acs.orglett.7b01218



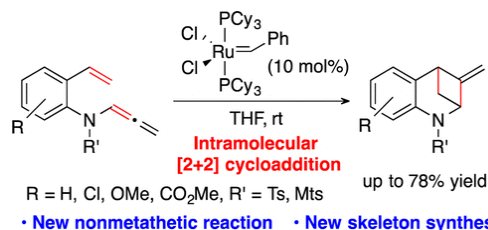
Abstract: A ruthenium-catalyzed asymmetric transfer hydrogenation of racemic isoflavanones with dynamic kinetic resolution yields virtually enantiopure isoflavanols as single diastereomers. Subsequent oxidation gives rise to isoflavanones in high enantiomeric purities.

Nonmetathesis Heterocycle Formation by Ruthenium-Catalyzed Intramolecular [2 + 2] Cycloaddition of Allenamide-enes to Azabicyclo[3.1.1]heptanes

Tomomi Nada, Yusuke Yoneshige, Yasuhiro Ii, Takashi Matsumoto, Hiromichi Fujioka, Satoshi Shuto, and Mitsuhiro Arisawa

ACS Catal. **2016**, *6*, 3168–3171.

DOI: 10.1021/acscatal.6b00628



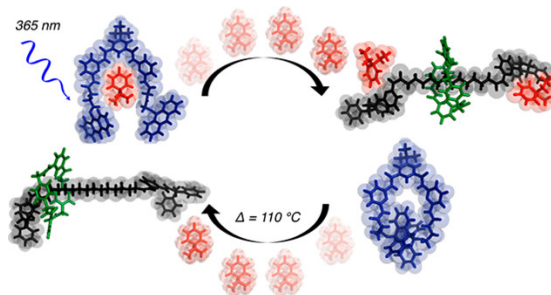
Abstract: We have developed a novel nonmetathesis reaction, namely, ruthenium-catalyzed intramolecular [2 + 2] cycloaddition of allenamide-enes, to give heterocycles (i.e., azabicyclo[3.1.1]heptanes). This is the first example of [2 + 2] cycloaddition using a ruthenium carbene catalyst. The reaction proceeds at room temperature, but not under thermal or radical conditions.

Remote Photoregulated Ring Gliding in a [2]Rotaxane via a Molecular Effector

Arnaud Tron, Isabelle Pianet, Alberto Martinez-Cuezva, James H. R. Tucker, Luca Pisciotanni, Mateo Alajarin, Jose Berna, and Nathan D. McClenaghan

Org. Lett. **2017**, *19*, 154–157.

DOI: 10.1021/acs.orglett.6b03457



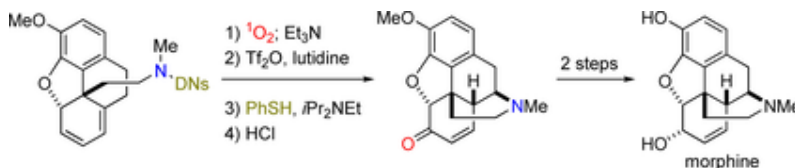
Abstract: A molecular barbiturate messenger, which is reversibly released/captured by a photoswitchable artificial molecular receptor, is shown to act as an effector to control ring gliding on a distant hydrogen-bonding [2]rotaxane. Thus, light-driven chemical communication governing the operation of a remote molecular machine is demonstrated using an information-rich neutral molecule.

Total Synthesis of (–)-Morphine

Hirotsu Umihara, Satoshi Yokoshima, Masayuki Inoue, and Tohru Fukuyama

Chem. Eur. J. **2017**, *23*, 6993–6995.

DOI: 10.1002/chem.201701438



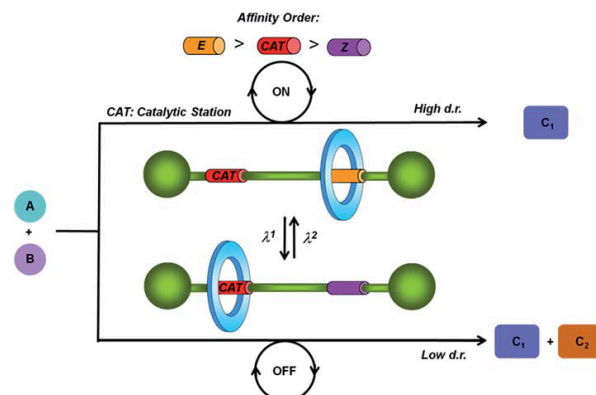
Abstract: Asymmetric total synthesis of (–)-morphine has been accomplished in 18 steps from commercially available 7-methoxy-2-tetralone. Our synthesis features a simple transformation from a readily prepared chiral intermediate, construction of the E-ring by acid-mediated cyclization, and singlet oxygen-mediated manipulation of the C-ring. Transformation of the final stage involves construction of the morphinan skeleton by means of 1,6-addition of *in situ* generated secondary amine.

Photoswitchable Interlocked Thiodiglycolamide as a Cocatalyst of a Chalcogeno-Baylis–Hillman Reaction

Alberto Martinez-Cuezva, Adrian Saura-Sanmartin, Tomas Nicolas-Garcia, Cristian Navarro, Raul-Angel Orenes, Mateo Alajarin, and Jose Berna

Chem. Sci. **2017**, *8*, 3775–3780.

DOI: 10.1039/C7SC00724H



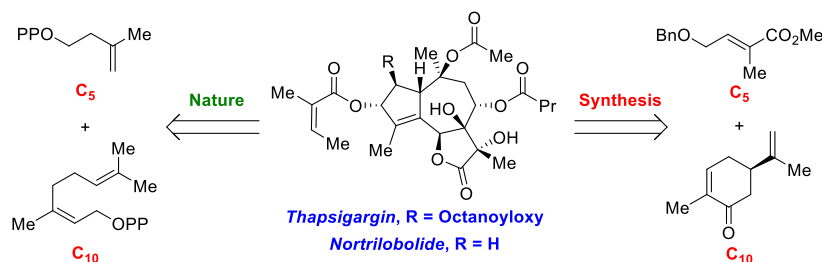
Abstract: En route to a photoswitchable interlocked catalyst we have proved the ability of thiodiglycolamide to act as a template in the formation of hydrogen-bonded [2]rotaxanes. X-ray diffraction studies reveal the shielding of the sulfide atom by the macrocycle. A series of molecular shuttles are described as having an isomerizable fumaramide and thiodiglycolamide binding sites for controlling the relative ring position at will. By employing these systems as photoregulated catalysts, the TiCl_4 -mediated chalcogeno-Morita–Baylis–Hillman reaction is tested. In the presence of the maleamide shuttle, in which the sulfide function is encapsulated by the macrocycle, a complete loss in control of the geometry of the produced aldol is observed. The E-aldol adduct is predominantly obtained when the photoisomerized fumaramide shuttle, in which the sulfide function is exposed, is used.

A Concise, Efficient and Scalable Total Synthesis of Thapsigargin and Nortrilobolide from (*R*)-(-)-Carvone

Dezhi Chen and P. Andrew Evans

J. Am. Chem. Soc. **2017**, *139*, 6046–6049.

DOI: 10.1021/jacs.7b01734

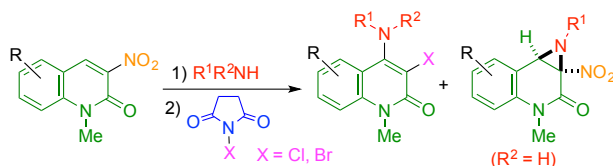


Abstract: A concise, efficient and scalable synthesis of thapsigargin and nortrilobolide from commercially available (*R*)-(-)-carvone was developed. Our synthetic strategy is inspired by nature's carbon–carbon bond formation sequence, which facilitates the construction of a highly functionalized sesquiterpene lactone skeleton in five steps *via* an enantioselective ketone alkylation and a diastereoselective pinacol cyclization. We envision that this strategy will permit the construction of other members of the family, structural analogs and provide a practical synthetic route to these important bioactive agents. In addition, we anticipate that the prodrug Mipsagargin, which is currently in late-stage clinical trials for the treatment of cancer, will also be accessible *via* this strategy. Hence, the limited availability from natural sources, coupled with an estimated demand of one metric ton per annum for the prodrug, provides a compelling mandate to develop practical total syntheses of these agents.

Direct Amino-Halogenation and Aziridination of the 2-Quinolone Framework by Sequential Treatment of 3-Nitro-2-Quinolone with Amine and *N*-Halosuccinimide

Feiyue Hao, Haruyasu Asahara, Nagatoshi Nishiwaki
Tetrahedron **2017**, *73*, 1255–1264.

DOI: 10.1016/j.tet.2017.01.028

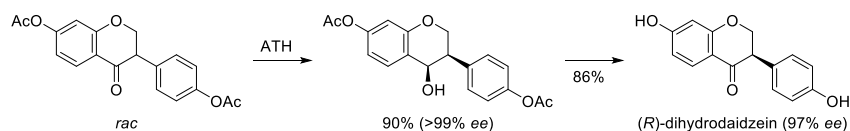


Abstract: The sequential treatment of 3-nitro-2-quinolones with amines and *N*-halosuccinimides under mild conditions facilitated the direct amino-halogenation and aziridination at the 4- and 3-positions of the 2-quinolone framework. The selectivity of the functionalization was influenced by the electronic properties of the substituents on the benzene moiety of the nitroquinolone. The electron-withdrawing nitro group promoted the amino-halogenation, and replacement of the nitro group with a halogen or hydrogen markedly increased the selectivity of the aziridination. Moreover, a succinimide group instead of an alkylamino group was introduced at the 4-position, affording the masked form of the 4-amino-3-chloro-2-quinolone derivative. Furthermore, the prepared bis-functionalized quinolones were subjected to Suzuki-Miyaura coupling reaction, ring opening, and hydrazinolysis to afford differently functionalized quinolones.

Enantioselective Synthesis of Isoflavanones by Catalytic Dynamic Kinetic Resolution

Tao Qin and Peter Metz
Org. Lett. **2017**, *19*, 2981–2984.

DOI: 10.1021/acs.orglett.7b01218

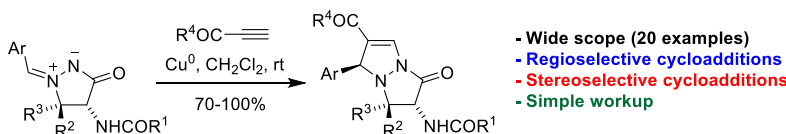


Abstract: A ruthenium-catalyzed asymmetric transfer hydrogenation of racemic isoflavanones with dynamic kinetic resolution yields virtually enantiopure isoflavanols as single diastereomers. Subsequent oxidation gives rise to isoflavanones in high enantiomeric purities.

Cu^0 -Catalysed 1,3-Dipolar Cycloadditions of α -Amino Acid Derived *N,N*-Cyclic Azomethine Imines to Ynones

Jona Mirnik, Eva Pušavec Kirar, Sebastijan Ričko, Uroš Grošelj, Amalija Golobič, Franc Požgan, Bogdan Štefane, Jurij Svete
Tetrahedron **2017**, *73*, 3329–3337.

DOI: 10.1016/j.tet.2017.04.050



Abstract: A series of 20 Cu^0 reactions between eight 4-acylamino substituted pyrazolidine-3-one-1-azomethine imines and four terminal ynones were performed using Cu^0 as catalyst. The corresponding fluorescent cycloadducts were obtained in very high yields upon simple workup. Thus, Cu -metal turned out to be a better catalyst than Cu^{I} in terms of yield and ease of isolation. Availability of azomethine imines, mild reaction conditions, and simple workup enable a "click" access to libraries of densely substituted 2,3-dihydro-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazol-1-ones. Reactivity of differently substituted dipoles was evaluated experimentally and by quantum chemical methods (DFT).