

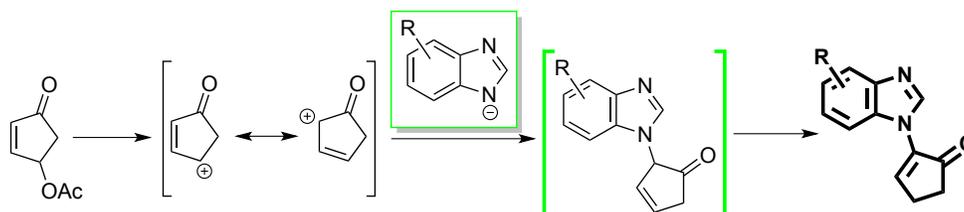
## The ISHC Bulletin

### Recent Publications of ISHC Members

Issue 25; November 2018

#### Synthesis of 2-Heterosubstituted Cyclopent-2-en-1-ones: A Preliminary Study of the Strategic Design of Antiviral Compounds

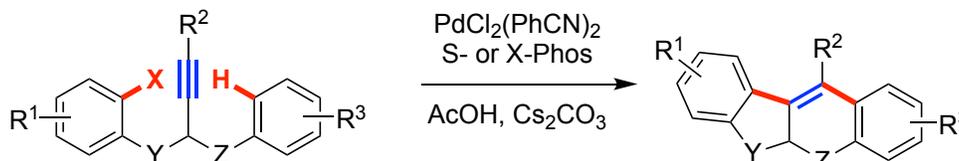
Karzan Khaleel Hameed, Ahmed Anwar Dezaye, Faiq Hamasaid Hussain, Teresa Basile, Misal Giuseppe Memeo, and Paolo Quadrelli  
*ARKIVOC* **2018**, part VII, 201–213. DOI: 10.24820/ark.5550190.p010.672



**Abstract:** A synthetic approach to heterosubstituted cyclopent-2-en-1-ones through a robust protocol that leads to single 2-substituted compounds is reported. In view of a strategic design of antiviral compounds, the methodology was applied to substituted benzimidazoles as neutral heterocyclic systems, as models for preliminary evaluation of their antiviral activities. By virtue of NMR investigations the synthesized compounds were structurally completely defined and the conformations were also located from DFT calculations. The preliminary biological tests revealed a general inactivity for most of the products with significant predictions for some bearing specific substituents. The results suggested possible structural changes apt to trigger the relative biological activities, to implement them in the new compounds.

#### *trans*-Carbocarbonation of Internal Alkynes through a Formal *anti*-Carbopalladation/C–H Activation Cascade

Andreas Reding, Peter G. Jones, and Daniel B. Werz  
*Angew. Chem. Int. Ed.* **2018**, 57, 10610–10614. DOI: 10.1002/anie.201805399



(X = Br, I)

- 27 examples, yields of up to 98%
- completely regioselective
- broad scope (including heterocycles)
- mechanistic investigations
- trapped intermediates

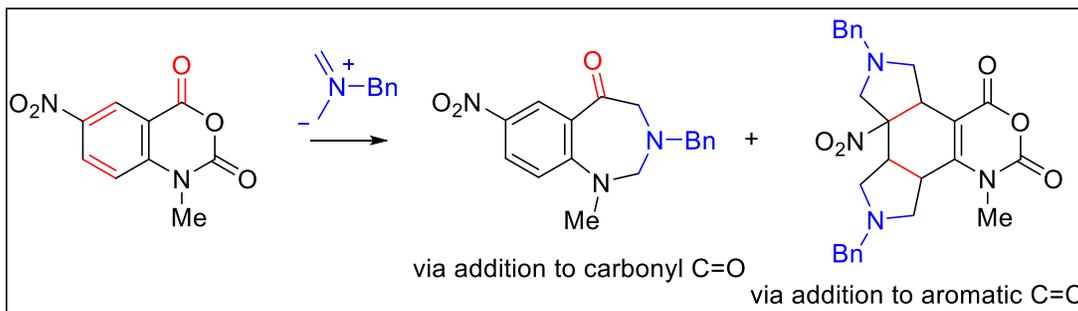
**Abstract:** An intramolecular Pd-catalyzed cascade reaction is presented that consists of a formal *anti*-carbopalladation of a C–C triple bond followed by C–H activation. As a result, oligocyclic ring systems with an embedded tetrasubstituted double bond are formed. The key to success in affording the *trans* geometry of the emerging double bond are alkyne units with residues that must not undergo  $\beta$ -hydride elimination (e.g., *t*-butyl or silyl groups). Silyl groups proved to be a perfect handle to further convert the tetrasubstituted alkenes. The evaluation of kinetic data with a deuterium-labeled compound and X-ray analyses of trapped intermediates provided additional insight into the catalytic cycle.

## Competitive 1,3-Dipolar Cycloaddition Reactions of an Azomethine Ylide with Aromatic and Carbonyl Groups of Nitro-Substituted Isatoic Anhydrides

Asha M. D'Souza, Daniel J. Rivinoja, Roger J. Mulder, Jonathan M. White, Adam G. Meyer, Christopher J. T. Hyland, and John H. Ryan

*Aust. J. Chem.* **2018**, *71*, 690–696.

DOI: 10.1071/CH18196



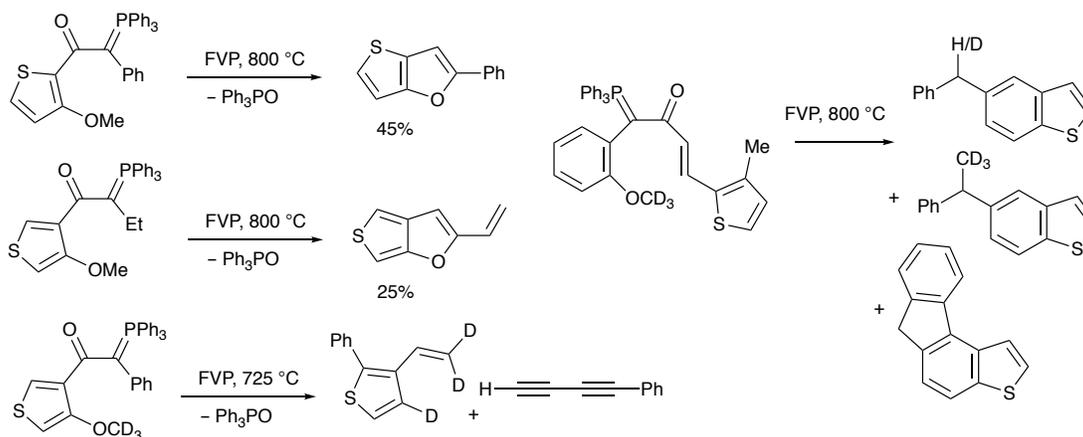
**Abstract:** An unexpected cycloaddition-dearomatisation process is reported. *N*-methyl-5-nitroisatoic anhydride underwent cycloaddition to both the isatoic anhydride C1-carbonyl group and to the nitro-substituted aromatic ring. The dearomative cycloaddition reactions result in the formation of novel tetracyclic products and opens up a new area of isatoic anhydride chemistry.

## Flash Vacuum Pyrolysis of oxo-Stabilised Phosphonium Ylides Containing Methoxythiophene and Methylthiophene Groups

R. Alan Aitken and Alasdair N. Garnett

*J. Anal. Appl. Pyrol.* **2018**, *135*, 369–378.

DOI: 10.1016/j.jaap.2018.08.013

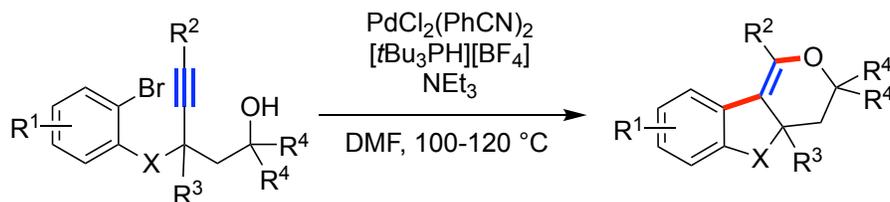


**Abstract:** Ten new oxo-stabilised phosphonium ylides containing substituted thiophene groups, as well as two deuterium-labelled analogues, are prepared and fully characterised. Upon flash vacuum pyrolysis at 800 °C, the simpler examples undergo extrusion of Ph<sub>3</sub>PO coupled with domino cyclisation to give thieno[3,2-*b*]furan and thieno[3,4-*b*]furan products but the corresponding approach to a thieno[2,3-*b*]furan fails. One ylide designed to give a thieno[3,4-*b*]furan instead gives phenylbutadiyne and 2-phenyl-3-vinylthiophene at 725 °C and the mechanism of this unusual process is elucidated by deuterium labelling. Attempts to access more complex heterocyclic products from extended methoxythienyl ylides failed. Two ylides bearing a 3-methyl-2-thienylacryloyl group gave 5-benzylbenzothiophene, 5-( $\alpha$ -methylbenzyl)benzothiophene and fluoreno[3,4-*b*]thiophene upon FVP at 800 °C and the mechanism was again elucidated by deuterium labelling.

## Intramolecular Pd-Catalyzed Formal *anti*-Carboalkoxylation of Alkynes: Access to Tetrasubstituted Enol Ethers

Theresa Schitter, Peter G. Jones, and Daniel B. Werz  
*Chem. Eur. J.* **2018**, *24*, 13446–13449.

DOI: 10.1002/chem.201803721



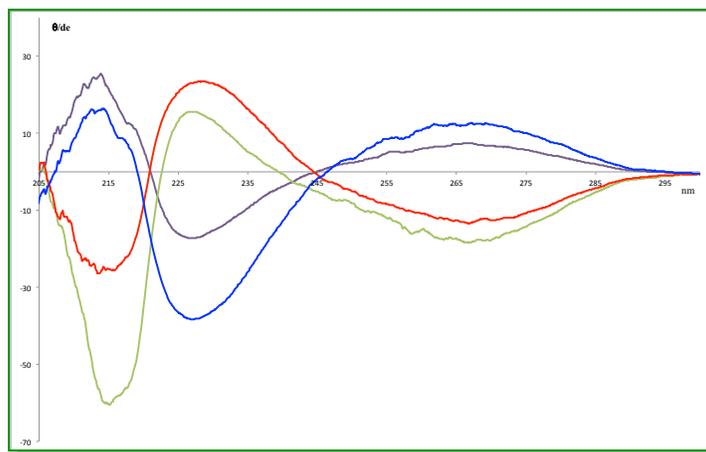
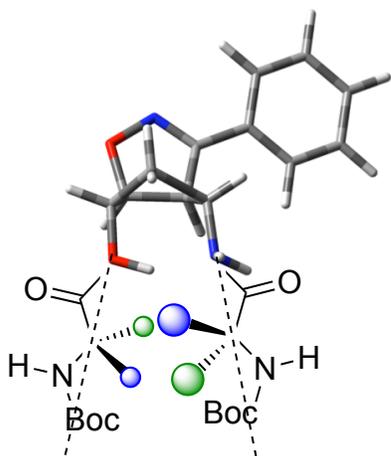
- 29 examples, yields of up to 99%
- 1°, 2°, 3° and aromatic hydroxy groups
- Broad scope
- Extended cascade by Tsuji–Trost-type reaction
- Follow-up chemistry

**Abstract:** An intramolecular Pd-catalyzed formal *anti*-carboalkoxylation reaction is presented that provides access to tetrasubstituted enol ethers. The key to success is a cascade consisting of a formal *anti*-carbopalladation of a carbon-carbon triple bond followed by a nucleophilic attack of a hydroxy group at the emerging vinyl organo-palladium species. The desired transformation proceeded smoothly with primary secondary, and tertiary alcohols, and even with phenols. Depending on the substitution pattern of the enol ethers, a further Tsuji–Trost type step may occur resulting in oligocyclic ketals.

## Cyclopenta[*d*]isoxazoline $\beta$ -Turn Mimics: Synthetic Approach, Turn Driving Force, Scope, and Limitations

Misal Giuseppe Memeo, Marco Bruschi, Luca Bergonzi, Giovanni Desimoni, Giuseppe Faita, and Paolo Quadrelli  
*ACS Omega* **2018**, *3*, 13551–13558.

DOI: 10.1021/acsomega.8b01670

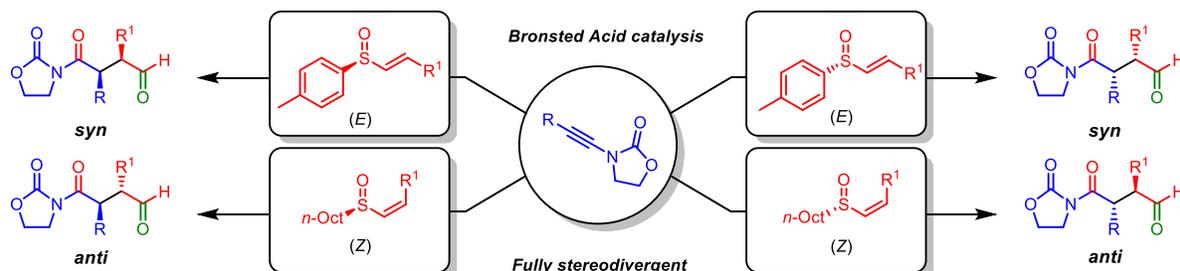


**Abstract:** Model  $\beta$ -turn inducers were prepared from constrained oxazanorbornene aminols. Taking advantage of the starting materials geometry, new diastereoisomeric compounds were synthesized, introducing different amino acidic residues. The products were spectroscopically characterized (VT and NMR titration). Temperature coefficients in dimethyl sulfoxide denote the existence of an intramolecular hydrogen bond. Chiroptical properties disclosed a  $\beta$ -turn arrangement of the synthesized compounds. The fused isoxazoline ring constraints the cyclopentane moiety, stabilizing a boat-like conformation that ensures the turn efficiency but limiting the accessibility to hindered amino acids.

## Stereodivergent Synthesis of 1,4-Dicarbonyls by Traceless Charge-Accelerated Sulfonium Rearrangement

Dainis Kaldre, Immo Klose, Nuno Maulide  
*Science* **2018**, *361*, 664–667.

DOI: 10.1126/science.aat5883.aat5883.aat5883



**Abstract:** A novel synthetic access to acyclic 1,4-dicarbonyl compounds has been developed. This process involves a charge-accelerated [3,3]-sigmatropic rearrangement combining ynamides and vinyl sulfoxides, the key reactants, which sets the chiral information around the newly formatted C–C bond. Depending on chirality on sulfur and double bond geometry of the vinyl sulfone partner, all four stereoisomers of the final 1,4-dicarbonyl product are accessible at will and with high diastereo- and enantioselectivities. This Brønsted acid-catalyzed reaction is tolerant of a wide range of other functionalities. When  $\beta,\beta$ -disubstituted vinyl sulfoxides are employed, all-carbon quaternary centers can be installed selectively.