

## The ISHC Bulletin

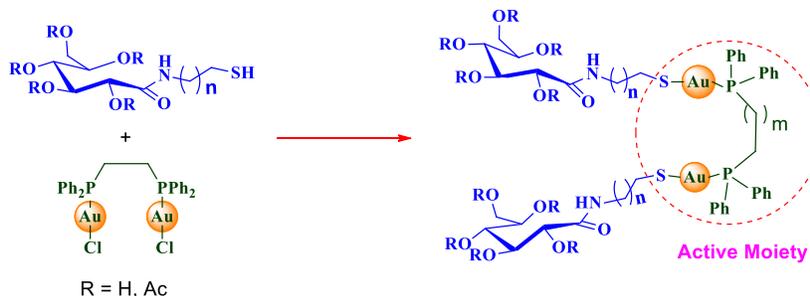
### Recent Publications of ISHC Members

Issue 17; November 2017

#### Synthesis, Characterization and Anticancer Evaluation of Phosphinogold(I) Thiocarbohydate Complexes

Christian K. Adokoh, James Darkwa, Henok H. Kinfe  
*Polyhedron* **2017**, *138*, 57–67.

DOI: 10.1016/j.poly.2017.09.010



**Binuclear glyco-gold(I) Complex -  
Tumor specificity = 980, IC<sub>50</sub> = 0.003 μM**

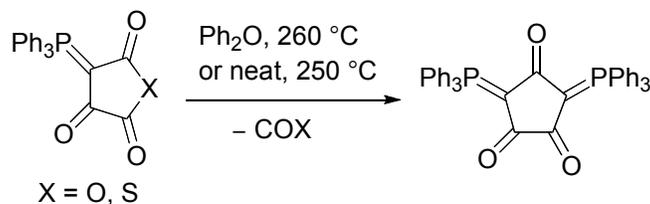
**Abstract:** Several novel thiocarbohydate phosphinogold(I) complexes were prepared *via* the reaction of *n*-gluconamidoalkyl thiol (**L1-L7**) {where **L1-L4** = *n*-gluconamidoalkyl thiol (*n* = 1-4), **L5-L7** = acetylated *n*-gluconamidoalkyl thiol (*n* = 1-3)} with the gold precursors [AuCl(PPh<sub>3</sub>)], [Au<sub>2</sub>Cl<sub>2</sub>(dppe)], [Au<sub>2</sub>Cl<sub>2</sub>(dppp)], and [Au<sub>2</sub>Cl<sub>2</sub>(dppb)] leading to the new gold(I) complexes [Au(**L1**)(PPh<sub>3</sub>)] (**1-4**), [Au(**L5**)(PPh<sub>3</sub>)] (**5-7**), [Au<sub>2</sub>(**L1**)<sub>2</sub>(dppe)] (**8-11**), [Au<sub>2</sub>(**L5**)<sub>2</sub>(dppx)] (**12-14**), [(Au<sub>2</sub>(**L6**)<sub>2</sub>(dppx)] (**15-17**), [Au<sub>2</sub>(**L7**)<sub>2</sub>(dppx)] (**18-20**), {where dppe = 1,2-bis(diphenylphosphino)ethane (*x* = e), dppp = 1,3-bis(diphenylphosphino)propane (*x* = p), and dppb = 1,4-bis(diphenylphosphino)butane (*x* = b)}. These gold complexes were characterized by a combination of NMR and infrared spectroscopy, microanalysis and mass spectrometry. Complexes **8**, **12**, **14-16** (IC<sub>50</sub> values between 0.003-1.8 μM) are all active against MCF7, HCT116 and PC3 cells. Complex **8** recorded the highest IC<sub>50</sub> value of 0.003 μM against PC3. Complex **14** was found to be selective toward both MCF7 and PC3 cells with TS of 142.1, while compounds **15** and **16** were highly selective toward PC3 cells with TS of 970.0 and 937.5, respectively.

#### New Reactions and Reactive Intermediates in the Pyrolysis of Cyclic Phosphonium Ylides

R. Alan Aitken, Vidar Bjørnstad, Tracy Massil, Jan Skramstad, and Robert J. Young

*Arkivoc* **2017**, part iii, 293–301.

DOI: 10.24820/ark.5550190.p010.208

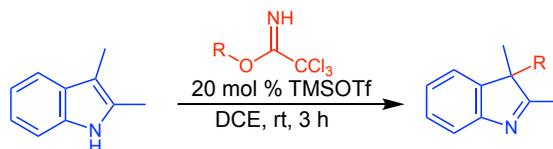


**Abstract:** Pyrolysis, either neat or in diphenyl ether solution, results in the conversion of both 4-triphenylphosphoranylidene-tetrahydrofuran-2,3,5-trione and 4-triphenylphosphoranylidene-tetrahydrothiophene-2,3,5-trione into 3,5-bis(triphenylphosphoranylidene)cyclopentane-1,2,4-trione. These reactions involve extrusion of CO<sub>2</sub> or COS to give 3-triphenylphosphoranylidene-cyclopropane-1,2-dione which further loses CO to give triphenylphosphoranylidene-ketene. The precise way in which these two reactive phosphorus compounds combine to give the observed product has been examined by chemical and isotopic labelling studies. Cyclotrimerization of triphenylphosphoranylidene-ketene upon thermolysis in diphenyl ether has also been observed for the first time. The erroneous literature interpretation of the <sup>13</sup>C NMR spectrum for triphenylphosphoranylidene-ketene is corrected.

## Synthesis of 3,3'-Disubstituted Indolenines Utilizing the Lewis-Acid Catalyzed Alkylation of 2,3-Disubstituted Indoles with Trichloroacetimidates

Arijit A. Adhikari, Léa Radal, and John D. Chisholm  
*Synlett* **2017**, 28, 2335–2339.

DOI: 10.1055/s-0036-1588491

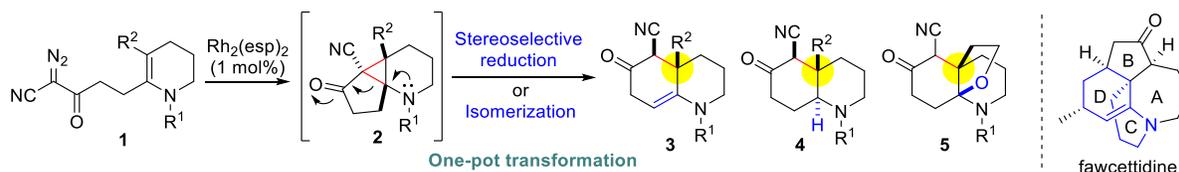


**Abstract:** Trichloroacetimidates function as effective electrophiles for the selective C3-alkylation of 2,3-disubstituted indoles to provide 3,3'-disubstituted indolenines. These indolenines are common synthetic intermediates that are often utilized in the synthesis of complex molecules. Effective reaction conditions utilizing Lewis acid catalysts have been determined, and the scope of the reaction with respect to indole and imidate reaction partner has been investigated. This chemistry provides an alternative to base promoted and transition metal catalyzed methods that are more commonly utilized to access similar indolenines.

## Synthesis of Octahydro- and Decahydroquinolines by a One-Pot Cascade Reaction of Tetrasubstituted Encarbamate

Tomohiro Kurose, Chihiro Tsukano, and Yoshiji Takemoto  
*Org. Lett.* **2017**, 19, 4762–4765.

DOI: 10.1021/acs.orglett.7b02122

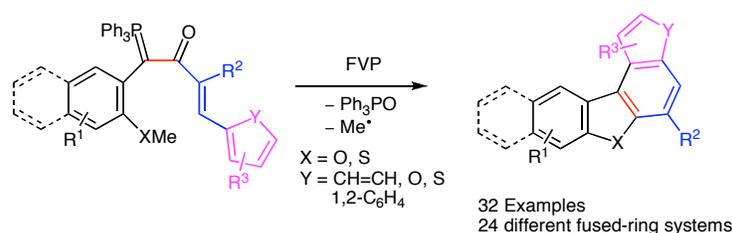


**Abstract:** A transition metal catalyzed-cyclopropanation followed by ring-opening was investigated for the synthesis of octahydroquinolines **3** and decahydroquinolines **4** having a quaternary carbon center at the angular position, which are core structures of the fawcettimine-type alkaloids (CD ring). A tandem reaction was also established for the synthesis of decahydroquinolines **4** and the tricyclic compound **5** through an iminium ion intermediate, readily produced by acidic treatment of cyclopropane **2**.

## Versatile Pyrolytic Synthesis of Fused Polycyclic Heteroaromatic Compounds

R. Alan Aitken and Alasdair N. Garnett  
*Synthesis* **2017**, 49, 4955–4977.

DOI: 10.1055/s-0036-1588586

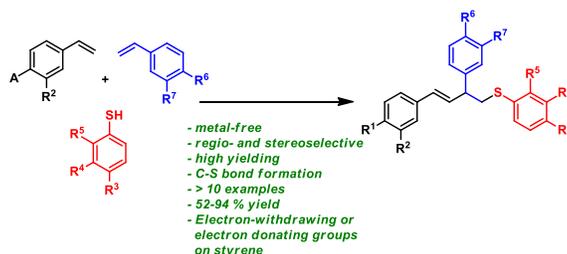


**Abstract:** Thirty-six new stabilised phosphonium ylides designed to undergo thermal loss of Ph<sub>3</sub>PO and radical domino cyclisation have been prepared and are generally found to undergo the desired reaction under flash vacuum pyrolysis conditions at 850 °C. A wide range of tetra- and pentacyclic fused-ring heterocycles, many previously unknown, are thus formed in moderate to high yield in a single step. By using suitably substituted starting materials, substituents such as CH<sub>3</sub> and Cl can be installed at various positions in the products. The method has also been demonstrated in a combinatorial mode to generate a small library of twelve fused-ring heterocycles in a single pyrolysis.

## Iodine- and $\text{PhI}(\text{OAc})_2$ -Mediated Multicomponent Synthesis of (*E*)-1,3-Diphenyl-1-butene Derivatives

Mokgethwa B. Marakalala and Henok H. Kinfe  
*Eur. J. Org. Chem.* **2017**, 3311–3317.

DOI: 10.1002/ejoc.201700199

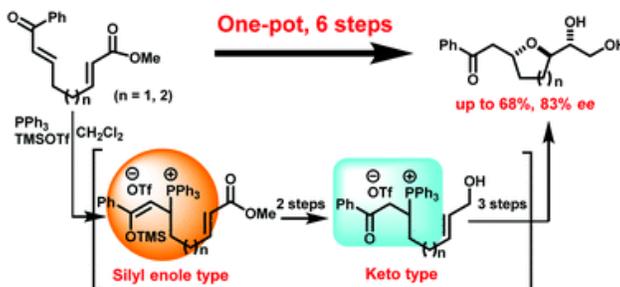


**Abstract:** Molecular iodine and diacetoxyiodobenzene promoted novel multicomponent methodology for the synthesis of (*E*)-1,3-diphenyl-1-butene derivatives is developed using styrene and thiophenol as substrates. The attractiveness of the protocol is its ability to introduce a sulfur heteroatom without a need for an extra reaction step. The scope and limitations of the protocol are investigated.

## Concise Synthesis of Oxacyclic Compounds Using Highly Discriminative Two-way Transformations of $\alpha,\beta$ -Unsaturated Esters in the Presence of Enones

Kenta Morita, Reiya Ohta, Hiroshi Aoyama, Kenzo Yahata, Mitsuhiro Arisawa and Hiromichi Fujioka  
*Chem. Commun.* **2017**, 53, 6605–6608.

DOI: 10.1039/C7CC03287K

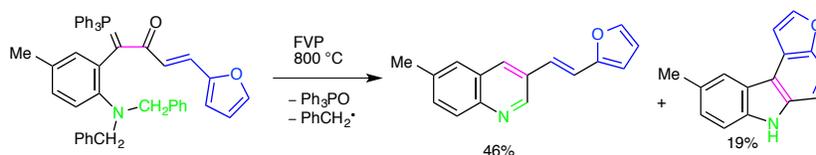


**Abstract:** Highly discriminative transformation of  $\alpha,\beta$ -unsaturated esters in the presence of enones using two types of phosphonium salts, and their application to the synthesis of oxacyclic compounds in six steps in one pot have been achieved.

## Gas-phase Domino Cyclization of Phosphonium Ylides Leading to the Total Synthesis of Eustifoline D

R. Alan Aitken and Lorna Murray  
*Tetrahedron Lett.* **2017**, 58, 4328–4332.

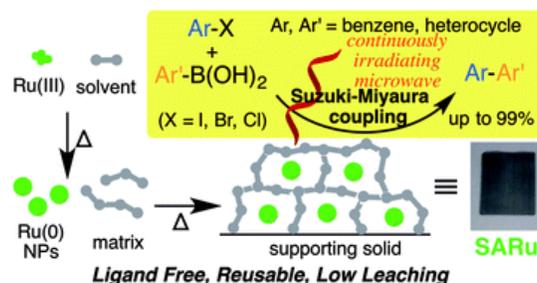
DOI: 10.1016/j.tetlet.2017.09.073



**Abstract:** Six stabilised phosphonium ylides bearing *ortho*-benzylaminophenyl and cinnamoyl (or a heterocyclic analogue) groups have been prepared and upon flash vacuum pyrolysis at 800 °C were found to undergo cascade cyclization processes to give mainly 3-styrylquinolines but also in some cases ring-fused carbazoles and other fused-ring heterocyclic products. By starting with an appropriate ring-methylated precursor the natural product Eustifoline D was obtained in 19% yield in the pyrolysis in addition to the 3-(2-furylethyl)quinoline (46%).

## Ligand-Free Suzuki–Miyaura Coupling Using Ruthenium(0) Nanoparticles and a Continuously Irradiating Microwave System

Toshiki Akiyama, Takahisa Taniguchi, Nozomi Saito, Ryohei Doi, Tetsuo Honma, Yusuke Tamenori, Yuuta Ohki, Naoyuki Takahashi, Hiromichi Fujioka, Yoshihiro Sato, Mitsuhiro Arisawa  
*Green Chem.* **2017**, *19*, 3357–3369. DOI: 10.1039/C7GC01166K

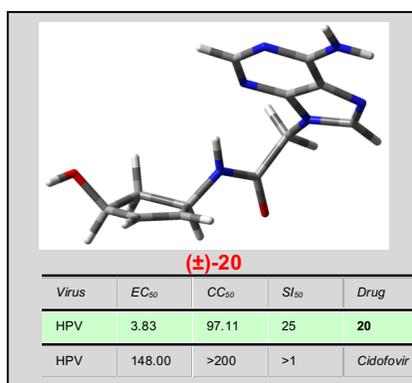


**Abstract:** We developed a conceptually and methodologically novel ruthenium(0) nanoparticle catalyst, sulfur-modified Au-supported ruthenium nanoparticles (SARu). SARu is easily prepared through a three-step procedure involving simultaneous in situ metal nanoparticle and nanospace organization. This unique method does not require any conventional preformed template to immobilize and stabilize metal nanoparticles. SARu is an ideal ruthenium catalyst for liquid-phase combinatorial synthesis because it repeatedly catalyzes ligand-free Suzuki–Miyaura coupling of aryl halides, including aryl chlorides, with arylboronic acids with low Ru leaching. Physical analysis of SARu showed that the active species in these reactions were ruthenium (0) nanoparticles with a size of 1–3 nm. Also, we developed a continuously irradiating microwave methodology, which can first time discriminate the heating effect and the microwave effect in microwave experiments.

## Pericyclic Reactions for Anti-HPV Antivirals: Unconventional Nucleoside Analogue Synthesis via Nitrosocarbonyl Chemistry

Dalya Al-Saad, Misal Giuseppe Memeo, and Paolo Quadrelli  
*ChemistrySelect*, **2017**, *2*, 10340–10346.

DOI: 10.1002/slct.201702059



**Abstract:** A new adenine derivative is prepared through the chemistry of nitrosocarbonyl intermediates. The synthesis relies upon the functionalization of adenine by inserting an ester moiety, to be transformed into the corresponding hydroxamic acid. The oxidation conducted in situ in the presence of cyclopentadiene afforded the hetero Diels–Alder cycloadduct, furtherly elaborated to give the target nucleoside analogue. This single product displayed a selective high activity against HPV. The EC<sub>50</sub> and EC<sub>90</sub> values are remarkably lower than the values collected for Cidofovir used as control drug. The EC<sub>50</sub> is 39 times lower while the CC<sub>50</sub> value is 97.11 μM.