

SYNLETT Spotlight 473

Phenylacetylene

Compiled by Marcin Konrad Kowalski



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Marcin Konrad Kowalski was born in Opoczno, Poland, in 1989. He obtained his B.Sc. (2011) and M.Sc. (2013) in organic chemistry and synthesis from the University of Łódź, Poland. Currently, he is pursuing his Ph.D. in synthetic organic chemistry under the supervision of Professor Dr. Grzegorz Mlostoń at the same university. His research is focused on the synthesis of β -lactams and other heterocycles which are functionalized with fluoroalkyl groups.

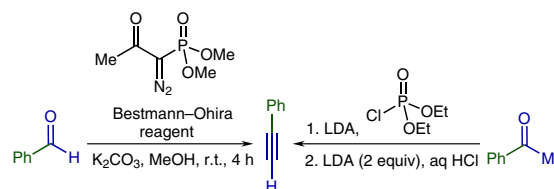
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Dedicated to Professor Dr. Grzegorz Mlostoń, Dr. Emilia Obijalska, and my family.

Introduction

Phenylacetylene (1-phenylethyne, 1-phenylacetylene) is a terminal alkyne which under standard conditions is a light yellow liquid with a characteristic odor. It can be conveniently prepared via the reaction of benzaldehyde with the Bestmann–Ohira reagent in the presence of a base at room temperature.^{1a} Other methods applied for its preparation consists in the treatment of acetophenone with lithium diisopropylamide (LDA) and diethyl chlorophosphate.^{1b} Phenylacetylene is widely applied as a versatile building block, for example in Kinugasa reactions, Diels–Alder re-

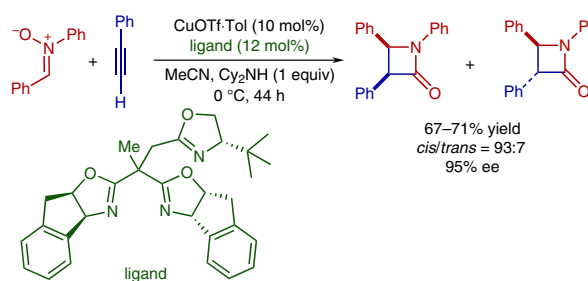
actions, 1,3-dipolar cycloaddition reactions, diverse transition-metal-supported coupling reactions, and in nucleophilic additions.



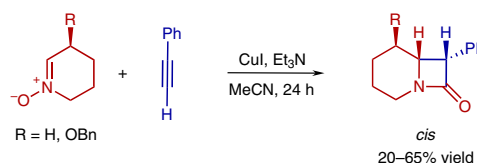
Scheme 1

Abstracts

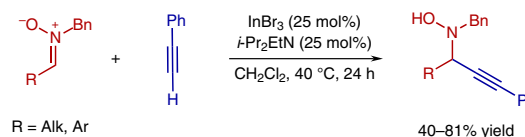
(A) Phenylacetylene is widely explored as a model acetylenic substrate in Kinugasa reactions. Saito et al. described an enantioselective version of this reaction which was performed in the presence of chiral oxazoline ligands.² The reported diastereo- and enantioselectivities were satisfactory, but chemical yields were rather low. In another paper, the applications of modified bis(oxazoline) ligands were reported, and in this case the desired β -lactams were obtained in high chemical yields. In addition, better diastereo- and enantioselectivities were observed.³



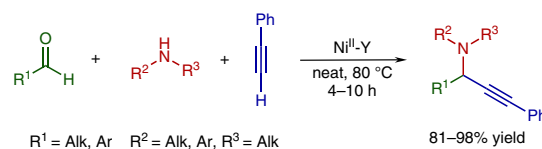
(B) Cyclic, achiral, and enantiopure nitrones were used in reactions with phenylacetylene under Kinugasa reaction conditions. In both cases only one diastereoisomer of the desired β -lactam was isolated in low to moderate yield.⁴



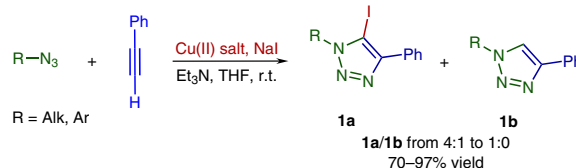
(C) Analogous reactions with diverse nitrones in the presence of catalytic amounts of indium tribromide (InBr_3) and a tertiary amine led to *N*-hydroxypropargyl amines in moderate to good yields.⁵



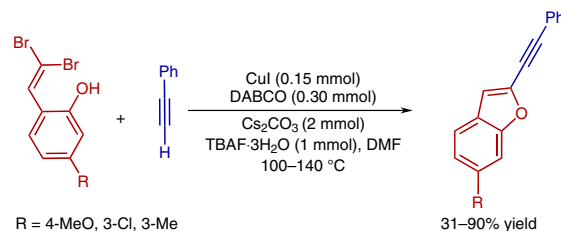
(D) In a three-component reaction, performed in the presence of a catalytic amount of Ni(II)-Y zeolite, phenylacetylene reacted with aldehydes and secondary amines yielding β -ynamines in high to excellent yields.⁶



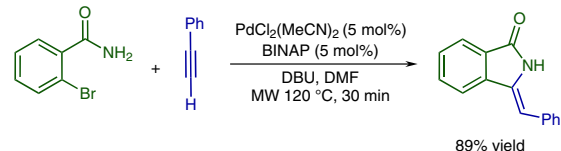
(E) 1,3-Dipolar cycloadditions of aryl- and alkylazides with phenylacetylene, carried out in the presence of copper(II) salts, sodium iodide, and a base, led to 5-iodo-1,2,3-triazoles formed as the main or exclusive products. However, the formation of 4-unsubstituted 1,2,3-triazoles as side-products was observed in reactions carried out in the presence of copper(II) chlorate(VII).⁷



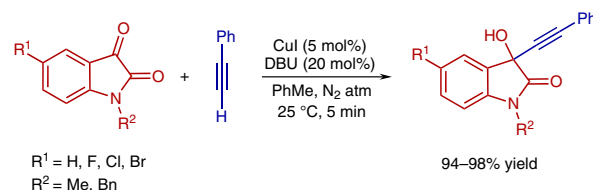
(F) Heterocyclization of *gem*-dibromovinylphenols followed by Sonogashira reaction of the initially formed 2-bromobenzofurane with phenylacetylene gave 2-phenylethynyl-substituted benzofurans in high yield.⁸ Upon optimizing the reaction conditions, copper(I) iodide, DABCO, and cesium carbonate were used in a one-pot procedure.



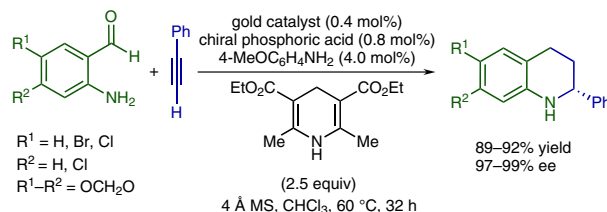
(G) In a microwave assisted, palladium-catalyzed tandem reaction, phenylacetylene and 2-bromobenzamide were used for the efficient preparation of isoindolinone derivatives.⁹



(H) The nucleophilic addition of phenylacetylene to isatin derivatives was achieved under copper-mediated C–H bond activation conditions.¹⁰



(I) 2-Substituted, optically active tetrahydroquinolines were obtained in high chemical yields and with high enantiomeric excess via the reaction of 2-aminobenzaldehydes with phenylacetylene under asymmetric cooperative triple catalysis.¹¹



References

- (1) (a) Möller, S.; Liepold, B.; Bestmann, H. J. *Synlett* **1996**, 521. (b) Negishi, E.; King, A. O.; Klima, W. L. *J. Org. Chem.* **1980**, *40*, 2526.
- (2) Saito, T.; Kikuchi, T.; Tanabe, H.; Yahiro, J.; Otani, T. *Tetrahedron Lett.* **2009**, *50*, 4969.
- (3) Chen, J.-H.; Liao, S.-H.; Sun, X.-L.; Shen, Q.; Tang, Y. *Tetrahedron* **2012**, *68*, 5042.
- (4) Grzeszczyk, B.; Poławska, K.; Shaker, S.; Stecko, Y.; Mames, M. A.; Woźnicka, M.; Chmielewski, M.; Furman, B. *Tetrahedron* **2012**, *68*, 10633.
- (5) Ji, D.-M.; Xu, M.-H. *Tetrahedron Lett.* **2009**, *50*, 2952.
- (6) Namitharan, K.; Pitchumani, K. *Eur. J. Org. Chem.* **2010**, 411.
- (7) Brotherton, W. S.; Clark, R. J.; Zhu, L. *J. Org. Chem.* **2012**, *77*, 6443.
- (8) Liu, J.; Zhang, N.; Yue, Y.; Wang, D.; Zhang, Y.; Zhang, X.; Zhuo, K. *RSC Adv.* **2013**, *3*, 3865.
- (9) Hellal, M.; Cuny, G. D. *Tetrahedron Lett.* **2011**, *52*, 5508.
- (10) Chouhan, M.; Senwar, K. R.; Kumar, K.; Sharma, R.; Nair, V. A. *Synthesis* **2014**, *46*, 195.
- (11) Patil, N. T.; Raut, V. S.; Tella, R. B. *Chem. Commun.* **2013**, 49, 570.