Coupling Reaction using N-tosylhydrazone as The Precursor of Diazo Compound



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1. Pd-catalyzed coupling reaction



2. Transition-metal free coupling reaction

Reaction of Diazo Compound



Pd-Carbenoid Catalyzed Reaction



Greenman, K. L.; Vranken, D. L. V. *Tetrahedron*, 2005, 61, 6438.

Disadvantage in Usage of Diazo Compound





1. Abelt, C. J.; Pleier, M. J. J. Am. Chem. Soc. 1989, 111, 1975.

Bamford-Stevens Reaction



Bamford, W. R.; Stevens, T. S. J. Chem. Soc. 1952, 4735.

In Situ Formation of Diazo Compound



Aggarwal, V. K.; Alonso, E.; Hynd, G.; Lydon, K. M.; Palmer, M. J.; Porcelloni, M.; Studley, J. R. *Angew. Chem. Int. Ed.* 2001, *40*, 1430.

Proposed Mechanism



Aggarwal, V. K.; Alonso, E.; Hynd, G.; Lydon, K. M.; Palmer, M. J.; Porcelloni, M.; Studley, J. R. *Angew. Chem. Int. Ed.* 2001, *40*, 1430.

Concept of Barluenga's Pd-Catalyzed Coupling

• In situ genaration of diazo compound



Barluenga's working hypothesis

N₂



Ph

Pd-Catalyzed Olefination of Tosylhydrazone



Barluenga, J.; Moriel, P.; Valdés, C.; Aznar, F. Angew. Chem. Int. Ed. 2007, 46, 5587.



One-Pot Procedure from Ketone



Barluenga, J.; Gamasa, M. T.; Moriel, P.; Aznar, F.; Valdés, C.; Chem. Eur. J. 2008, 14, 4792.

Short-Cut Synthsis of 4-Aryltetrahydropyidines





Application to α -Chiral Cyclic Ketone



Barluenga, J.; Escribano, M.; Aznar, F.; Valdés, C. Angew. Chem. Int. Ed. 2010, 49, 6856.

Proposed Explanation for Regioselectivity

Application to Tandem Pd-Catalyzed Reaction

Paraja, M.; Aguilar, C. P.; Valdes, C. Chem. Commun. 2015, 51, 16241.

Table of Contents

1. Pd-catalyzed coupling reaction

2. Transition-metal free coupling reaction

Reductive Coupling Reaction between Diazo Compound and Boronic Acid

Peng, C.; Zhang, W.; Yan, G.; Wang, J. Org. Lett. 2009, 11, 1667.

Reductive Coupling of Tosylhydrazone

Barluenga, J.; Gamasa, M. T.; Aznar, F.; Valdés, C.; Nat. Chem. 2009, 1, 494.

Proposed Reaction Mechaism

author said, X is not an intermediate but a transition state in the energy surface => path A is reasonable?

Plaza, M.; Aguilar, M. C. P.; Valdés, C. Chem. Eur. J. 2016, 22, 6253.

Proposed Explanation for Stereoselectivity

Scheme 7. DFT computational modelling of the reaction between 1-diazo-4methylcyclohexane I and 1-propenylboronic acid II at the M06-2X/6- $311 + + G^{**}/PCM(1,4-dioxane)$ level.

Plaza, M.; Aguilar, M. C. P.; Valdés, C. Chem. Eur. J. 2016, 22, 6253.

One-Pot Procedure from Ketone

Barluenga, J.; Gamasa, M. T.; Aznar, F.; Valdés, C.; Nat. Chem. 2009, 1, 494.

Nakagawa, S.; Bainbridge, K. A.; Butcher, K.; Ellis, D.; Klute, W.; Ryckmans, T. ChemMedChem 2012, 7, 233.

Application to Other Transformations

Barluenga, J.; Gamasa, M. T.; Aznar, F.; Valdés, C. Angew. Chem. Int. Ed. 2010, 49, 4993.

Munoz, A.-H. G.; Gamasa, M. T.; Aguilar, M. C.; Yanez, E. C.; Valdés, C. Eur. J. Org. Chem. 2012, 3925.

Yadav, A. K.; Srivastave, V. P.; Yadav, L. D. S. Chem. Commun. 2013, 49, 2154.

Short Summary and Perspective

Domino Carbocyclization

Plaza, M.; Valdés, C. J. Am. Chem. Soc. 2016, 138, 12061.

Proposed Mechanism

One-Pot Synthesis of Corresponding Alcohol

Plaza, M.; Valdés, C. J. Am. Chem. Soc. 2016, 138, 12061.

Summary

Asynchronous Concerted Mechanism

transition state

intermediate

Example of Protodeborylation

es = product ee / starting material ee

Nave, S.; Sonawane, R. P.; Elford, T. G.; Aggarwal, V. K. J. Am. Chem. Soc. 2010, 132, 17096.

Proposed Mechanism of Protodeborylation

Lozada, J.; Liu, Z.; Perrin, D. M. J. Org. Chem. 2014, 79, 5365.