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Recent advances in the Pd-catalyzed chemical transformations of Baylis–Hillman adducts

Saravanan Gowrisankar, Hyun Seung Lee, Sung Hwan Kim, Ka Young Lee, Jae Nyoung Kim *

Department of Chemistry and Institute of Basic Science, Chonnam National University, Gwangju 500-757, Republic of Korea

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Contents

1. Introduction

The Baylis–Hillman reaction, which involves the coupling of activated vinylic systems with electrophiles under the catalytic influence of a tertiary amine, gives rise to adducts (Baylis–Hillman adducts) with a new stereocenter and has proven to be a very useful carbon–carbon bond-forming method in the synthesis of highly functionalized molecules.[1]

In 1963, Rauhut and Currier disclosed a patent describing a phosphine-catalyzed dimerization of activated alkenes.[2] This reaction involved a reversible phosphine conjugate addition to the

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* Corresponding author. Tel.: +82 62 530 3381; fax: +82 62 530 3389.
E-mail address: kimjn@chonnam.ac.kr (J.N. Kim).

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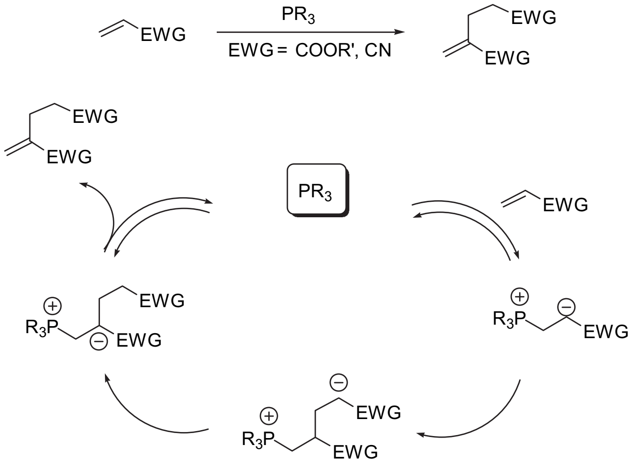
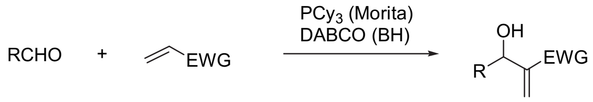
activated alkene, followed by a Michael reaction of the enolate with the second activated alkene. A prototropic shift followed by an elimination process forms the dimer and releases the phosphine.



The zwitterionic phosphonium Michael adducts can be trapped with other electrophiles such as aldehydes. The Rauhut–Currier dimerization of activated alkenes provided a clue to the advent of the finding of Morita.[3] The Morita–Baylis–Hillman reaction is an atom-economical coupling of an activated alkene and an aldehyde in the presence of a nucleophilic catalyst. The reaction was first discovered and reported by Morita and co-workers in 1968[3] and by Baylis and Hillman in 1972.[4] The nucleophilic catalyst employed by Morita was tricyclohexylphosphine, while Baylis and Hillman used tertiary amines such as DABCO. Activated alkenes include acrylic esters, acrylonitrile, vinyl ketones, phenyl vinyl sulfone, phenyl vinyl sulfonate, vinyl phosphonate, and acrolein.[1]



In 1983, Hoffmann and Rabe suggested the first arrow-pushing mechanism for the Baylis–Hillman reaction.[5] Later, Hill and Issacs reported a mechanism, which was accepted as the most probable mechanism for a long time.[6] Very recently, however, McQuade and co-workers suggested a new mechanism based on the reaction rate data collected in aprotic solvents.[7] They found that the rate-determining step is second order in aldehyde and first order in DABCO and acrylate. On the basis of these data, they have proposed a new mechanism involving a hemiacetal intermediate.

The Baylis–Hillman adducts have proved to be very useful multifunctional synthons for the preparation of many important cyclic and acyclic compounds.[1] There were, however, no outstanding investigations during almost two decades since the early 1970s after the initial finding of the Baylis–Hillman reaction. In the mid-1990s, the Basavaiah and Kim groups independently started extensive investigations with these useful Baylis–Hillman adducts. Later, many research groups reported further information and useful improvements in the Baylis–Hillman chemistry.[1] The number of published papers involving the Baylis–Hillman reaction has increased dramatically recently.

Palladium-catalyzed chemical transformations of modified Baylis–Hillman adducts started very recently, but have already provided many interesting results. We therefore believe that a compilation of such Pd-mediated chemical transformations of Baylis–Hillman adducts would be highly meaningful and timely.

This mini-review deals with almost all Pd-mediated syntheses involving the use of Baylis–Hillman adducts. The contents are subdivided into six sections, namely reactions involving the π-allylpalladium intermediate, synthesis of heterocyclic compounds, synthesis of carbocyclic compounds, synthesis of β-branched B–H adducts, Pd-catalyzed decarboxylative protonation and allylation, and some selected examples on the use of other transition-metal catalysts.

2. Use of π-allylpalladium intermediates

Palladium-catalyzed allylic substitution has been used in a wide variety of synthetically useful reactions involving the introduction of various oxygen and nitrogen nucleophiles. In addition, palladium-catalyzed cross-coupling reactions to form carbon–carbon bonds have been applied extensively in Baylis–Hillman chemistry. This section is divided into five subjects including the introduction of oxygen nucleophiles, introduction of nitrogen nucleophiles, cross-coupling reactions, synthesis of metal-containing Baylis–Hillman adducts, and miscellaneous reactions.

2.1. Introduction of *O*-nucleophiles

Introduction of phenols to the primary position of Baylis–Hillman acetates has been examined in the presence of a Pd(0) catalyst and/or KF/alumina.[8] In some cases, the use of one of these two reagents was sufficient to promote the OAc/OAr exchange, but, in general, faster reactions and higher yields were obtained when both reagents were used together.

Trost and co-workers used the carbonate of a Baylis–Hillman adduct for their synthesis of the key backbone of furaquinocins.[9] They introduced 2-iodoresorcinol at the secondary position of the