

# SYNLETT Spotlight 453

## Acrolein

Compiled by Long Chen



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

Long Chen was born in Dazhou, P. R. of China. After receiving his B.Sc. from Sichuan Normal University, he joined Prof. Jian Zhou's group as a Ph.D. student at East China Normal University, Shanghai. His research interests focus on the study of highly atom-economic reactions.

Shanghai Key Laboratory of Green Chemistry and Chemical Processes, East China Normal University, Shanghai 200062, P. R. of China

E-mail: harpshe11@foxmail.com

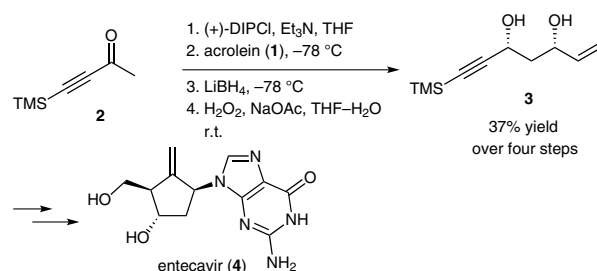
### Introduction

Acrolein, also called propylene aldehyde, 2-propenal, or allyl aldehyde, is considered the simplest  $\alpha,\beta$ -unsaturated aldehyde. It is a colorless liquid with a disagreeable, acrid smell. Because of its low boiling point and flammability, it evaporates quickly and burns easily. With two reactive functional groups, a C=C double bond and an aldehyde carbonyl, acrolein can readily participate in numerous types of transformations, including Michael additions,<sup>1</sup>

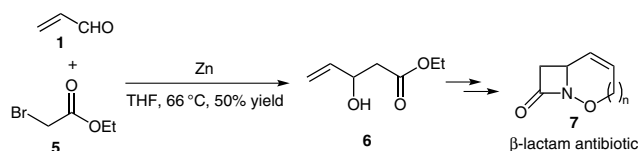
Diels–Alder reactions,<sup>2</sup> 1,3-dipolar cycloadditions,<sup>3</sup> and Morita–Baylis–Hillman (MBH) reactions.<sup>4</sup> Moreover, acrolein can be used for the synthesis of acrylic acid and acrylates which are widely used in the textile and resin industry.<sup>5</sup> In addition, it is a potential marker of various diseases, such as chronic renal failure, stroke, and cancer.<sup>6</sup> Acrolein is commercially available and can be industrially prepared by the oxidation of propene as well as by dehydration of glycerol.<sup>5</sup>

### Abstracts

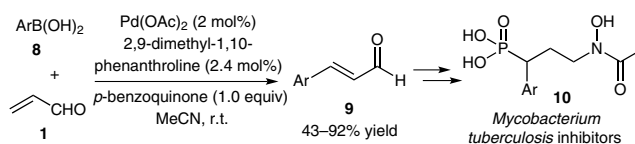
(A) The asymmetric aldol reaction of 4-trimethylsilyl-3-buten-2-one (**2**) with acrolein (**1**) provided aldol adduct **3**, which was further utilized for the synthesis of entecavir (**4**), one of the most frequently used antiviral agents against hepatitis virus (HBV).<sup>7</sup>



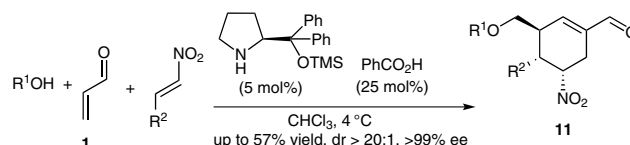
(B) A Reformatsky reaction between acrolein (**1**) and ethyl bromoacetate (**5**) afforded  $\beta$ -hydroxyethyl ester **6** which is an intermediate for the synthesis of  $\beta$ -lactam antibiotic **7**.<sup>8</sup>



(C) Oxidative palladium(II)-catalyzed Heck-type coupling reaction of arylboronic acids **8** and acrolein (**1**) provided cinnamaldehydes **9** which could further be used for the synthesis of  $\alpha$ -aryl substituted fosmidomycin analogues **10**, *Mycobacterium tuberculosis* inhibitors.<sup>9</sup>



(D) The oxa-Michael addition of alcohols to acrolein (**1**) in domino oxa-Michael–Michael–Michael–aldol condensation reactions provided optically pure, highly functionalized trisubstituted cyclohexene carbaldehydes **11**.<sup>10</sup>



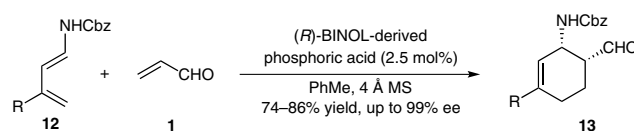
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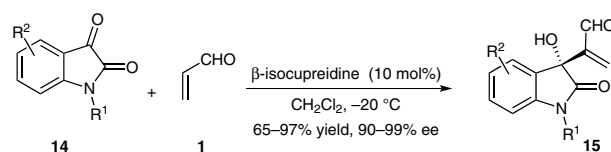
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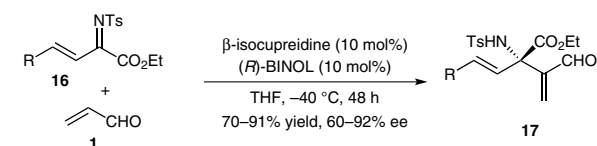
(E) The enantioselective Diels–Alder reaction of acrolein (**1**) with 1-*N*-acylamino-1,3-dienes (**12**) afforded cycloadducts **13** in good yields and enantioselectivities.<sup>11</sup>



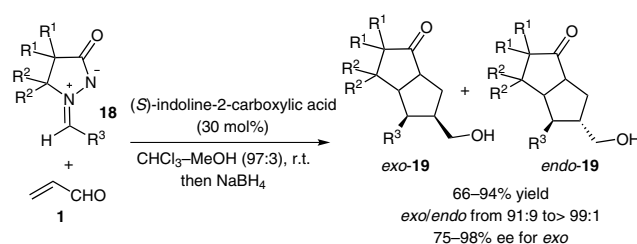
(F) Zhou and co-workers developed a highly enantioselective MBH reaction of isatins **14** and acrolein (**1**) to furnish enantioenriched 3-substituted 3-hydroxyoxindoles **15**.<sup>12a,b</sup> The first enantioselective MBH reaction of reactive aromatic aldehydes with acrolein was developed by the same group.<sup>12c</sup>



(G) Acrolein (**1**) could participate in the aza-MBH reaction with *N*-tosyl imines **16** derived from  $\beta,\gamma$ -unsaturated  $\alpha$ -ketoesters, affording the corresponding aza-MBH products **17** in high yields and enantioselectivities.<sup>13</sup>



(H) In the presence of (*S*)-indoline-2-carboxylic acid, the 1,3-dipolar cycloaddition of acrolein (**1**) and various *N,N'*-cyclic azomethine imines **18** provided cycloadducts **19** owning two contiguous stereocenters with high *exo*- and enantioselectivities.<sup>14</sup>



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