

# 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

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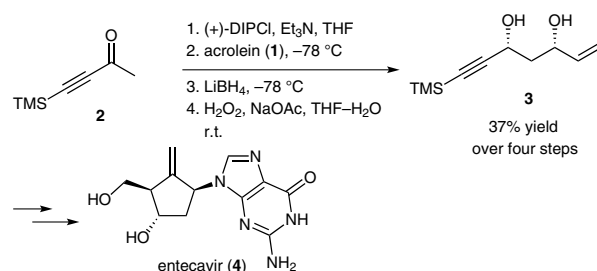
### Introduction

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>

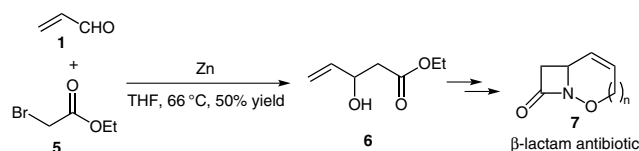
Diels–Alder reactions,<sup>2</sup> 1,3-dipolar cycloadditions,<sup>3</sup> and Morita–Baylis–Hillman (MBH) reactions.<sup>4</sup> Moreover, acrolein can be used for the synthesis of acrylic acid and acrylates which are widely used in the textile and resin industry.<sup>5</sup> In addition, it is a potential 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

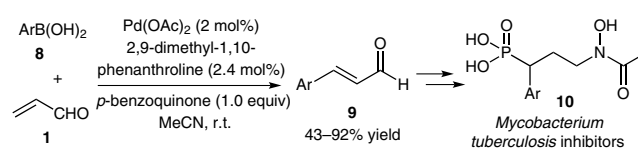
(A) The asymmetric aldol reaction of 4-trimethylsilyl-3-buten-2-one (**2**) with acrolein (**1**) provided aldol adduct **3**, which was further utilized for the synthesis of entecavir (**4**), one of the most frequently used antiviral agents against hepatitis virus (HBV).<sup>7</sup>



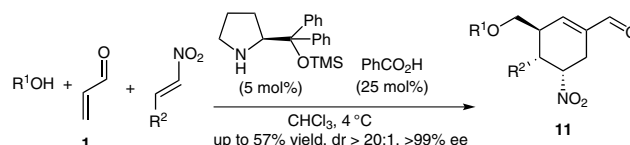
(B) A Reformatsky reaction between acrolein (**1**) and ethyl bromoacetate (**5**) afforded  $\beta$ -hydroxyethyl ester **6** which is an intermediate for the synthesis of  $\beta$ -lactam antibiotic **7**.<sup>8</sup>



(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>



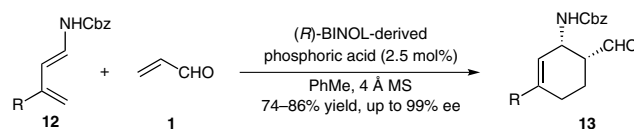
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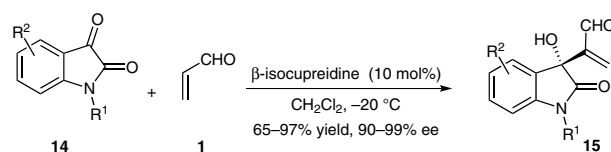
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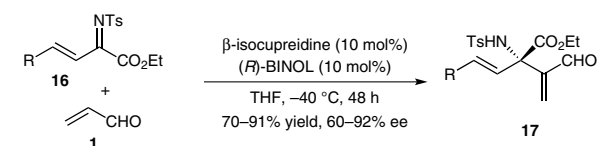
(E) The enantioselective Diels–Alder reaction of acrolein (**1**) with 1-*N*-acylamino-1,3-dienes (**12**) afforded cycloadducts **13** in good yields and enantioselectivities.<sup>11</sup>



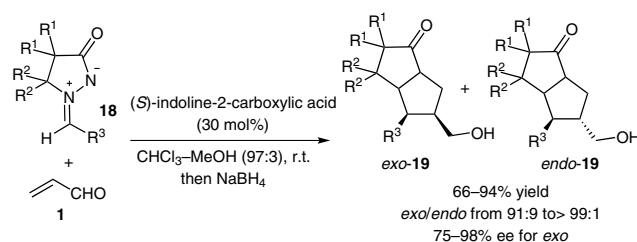
(F) Zhou and co-workers developed a highly enantioselective MBH reaction of isatins **14** and acrolein (**1**) to furnish enantioenriched 3-substituted 3-hydroxyoxindoles **15**.<sup>12a,b</sup> The first enantioselective MBH reaction of reactive aromatic aldehydes with acrolein was developed by the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