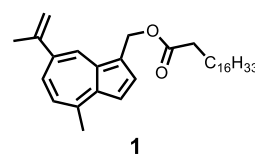


## Total synthesis of pigments with azulene skeleton in an edible blue mushroom

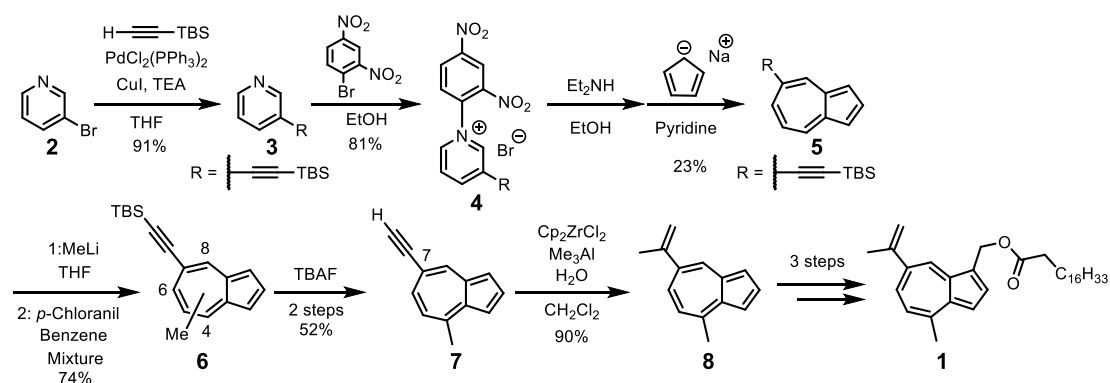
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**Keywords:** Azulene; Blue pigments; Total synthesis; Natural products; Nanoparticles

There has been a worldwide shift in food coloring from synthetic to natural pigments because of the increasing needs of our consumers for food safety. Currently, the major carotenoids used for magenta and yellow are fat-soluble. Fine particulation of carotenoid pigments makes it possible to color them also in aqueous systems.<sup>1</sup> For cyan, however, all natural pigments that are available are water-soluble. Fat-soluble blue pigments are needed to enable coloring of a wide range of foods.<sup>2</sup> To develop a natural blue organic pigment, we focused our attention on fat-soluble pigment **1** containing in the edible mushroom, *Lactarius Indigo*.<sup>3</sup> Here, we presented the total synthesis and basic physical properties of **1**.



Compound **3** with an ethynyl group was obtained by Sonogashira coupling using **2**. To construct the azulene skeleton, the azulene derivative **5** was successfully synthesized by the Hafner method.<sup>4</sup> (**3**→**5**) The regioisomer mixture **6** was obtained via nucleophilic addition reaction with methyl lithium to **5** and re-aromatization with an oxidant. The desilylation of this mixture **6** afforded **7** with C4 methyl group as a single compound by silica gel column chromatographic separation. The conversion of the ethynyl group at C-7 position to an isopropenyl group proceeded by carbometalation reaction (**7**→**8**). The side chain moiety was then constructed, and we achieved the first total synthesis of the desired **1** with a total yield of 3.7%.



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