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Synthesis of legioliulin, a fluorescent isocoumarin compound, isolated from *Legionella dumoffii* using cyclic acylpalladation and Heck reaction

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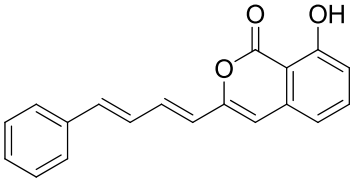
Abstract: Concise synthesis of legioliulin, an isocoumarin compound isolated from *Legionella dumoffii*, was achieved. Isocoumarin ring of legioliulin was constructed using cyclic acylpalladation. Chain elongation was performed using Heck reaction using *t*-butylphosphine as a ligand.

Key words: natural product, polyketides, isocoumarin, acylpalladation, Heck reaction

Legionellae, which are responsible for Legionnaire's disease, are facultative intracellular gram-negative bacteria.[1] 10 species of Legionella exhibit blue-white and dark-red autofluorescence. In 2004, Amemura-Maekawa and co-workers isolated legioliulin (**1**) from *Legionella dumoffii*.[2] Legioliulin (**1**) is a new isocoumarin compound and fluorescent substance. The study on biosynthesis of legioliulin (**1**) was reported by Bode and co-workers in 2013.[3] This compound did not show any cytotoxicity against human monocytic cell line U937, neither exhibit antimicrobial activity against *Staphylococcus aureus* and *E. coli*.[2] The real function and the detailed biological activity of legioliulin (**1**) are still unknown. Thus we began to synthesize legioliulin (**1**) to find out its function and biological properties. Here, we wish to report the consice synthesis of legioliulin (**1**) using cyclic acylpalladation and Heck reaction as the key steps (Figure 1).



legioliulin (**1**)

Figure 1. The structure of legioliulin (**1**).

The synthetic strategy shows in Scheme 1. The side chain would be introduced using Heck reaction. The isocoumarin part of **1** would be constructed using cyclic acyl palladation trapping by *O*-enolate from iodoenone **4**. Iodoenone **4** would be prepared from known aldehyde **5**.[4] Aldehyde **5** would be synthesized from commercially available 3-methoxyphenylacetic acid (Scheme 1).