

Diastereoselective Homologation and Ring Expansion of Alkyl Halides with Diazo Esters Catalyzed by InCl_3

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Homologation via one-carbon-atom insertion into a carbon-carbon single bond (C-C bond) is an efficient methodology in organic synthesis.^[1] However, there is a formidable challenge in adjusting the balance of thermodynamic energy between a cleaved C-C bond and a newly formed C-C bond.^[1a] To overcome this limitation, variety of functional groups were introduced in this system and transition-metal catalysts were used.^[2] Recently, various methods for aldehyde or ketone homologation with diazo compounds have been well established.^[3] In these cases, the formal C-C bond insertion was achieved by the aid of Lewis acid or Brønsted acid catalysts via the rearrangement of alkyl or aryl groups in unstable intermediates. To expand this synthetic approach, the scopes for other functional groups are still significantly.

In this work, our reaction design focused on generation of phenonium ion **5** (Figure 1) derived from alkyl chloride **3** (Figure 1) followed by selective ring opening at C^1 to give homologation alkyl chloride **6** (Figure 1, path A). Furthermore, we also tried to control the diastereoselectivity of the corresponding alkyl chloride products.

When chlorodiphenylmethane **3a** was treated with two equivalents of diazo ester **2** in a catalytic amount of InCl_3 at 0 °C for 6 h, homologated chloride **6a** was obtained in 63% yield with an excellent diastereoselectivity (95:5). In this reaction, the formation of phenonium ion **5** is generated by the denitrogenation in which the phenyl migration on the back side of N_2 occurs. Then, the intermolecular addition of chloride anion to **5** give alkyl chloride **6**. In addition, the same condition was also performed to cyclic substrate **1b**, and ring expansion product **6b** was obtained in 91% yield and with a perfect diastereoselectivity. The products **6** can be served as useful derivatization precursors in organic synthesis.

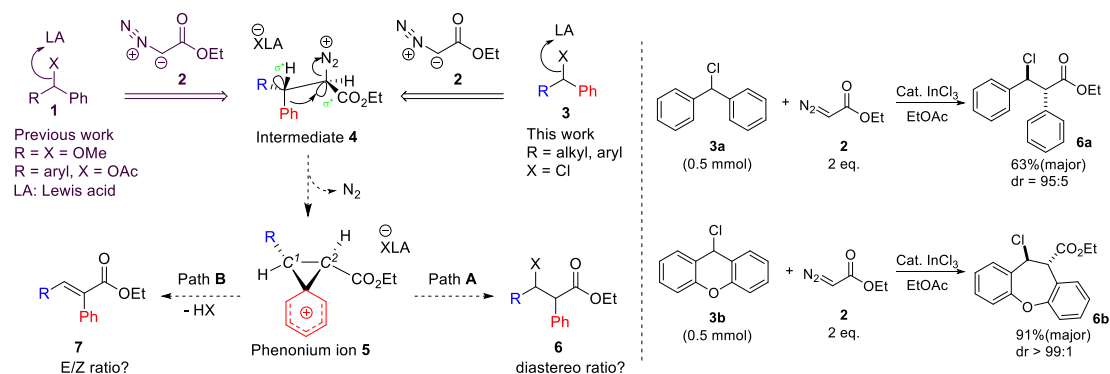


Figure 1. Homologation insertion using alcohol derivatives **1** and alkyl chloride **3** as substrates (left); substrate scopes (right).

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