

國科會計畫

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重點一子題 4：金屬促進水相加成反應：發展與應用(I)
Metal-Mediated Addition Reactions in Aqueous Media: Development and Application (I)

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中文摘要

帶有手性中心的丁烯醇(2)是有機合成上重要的合成單體，其傳統合成方法是由帶有手性中心的 3-羥基 2-甲基丙酸甲酯經多步驟合成而來(式 2, 3)。目前我們使用市售甲醛水溶液為反應試劑，與溴化物(1)和銻金屬進行烯丙基化反應，成功得到丁烯醇(2) (式 1)。本研究計畫提出新合成策略，發展不對稱水相羥甲基化反應，而反應產物丁烯醇(2)產生新的手性中心，是取決於烯丙基的反應位向，此為新穎不對稱合成技術。以此不對稱合成技術能精簡合成步驟，更能有效合成帶有手性中心的丁烯醇。除了進行烯丙基化反應，我們也企圖發展苯甲基化反應(benzylation)，可應用在合成帶有手性中心的苯丙酸。帶有手性中心的苯丙酸像 Naproxen, Ibuprofen 為非類固醇性抗炎藥，用於治骨關節炎和類風濕性關節炎。我們也成功發展以純水為溶劑，利用金屬錫與二氫呋喃(3a)、二氫吡喃(3b)進行烯丙基化反應(式 4)。此反應不止僅限於二氫呋喃和二氫吡喃，見式 5。本研究計畫將探討利用金屬錫進行水相加成反應，可望應用到含氮醣(azasugar)的合成。

關鍵字：水相羥甲基化反應； 市售甲醛水溶液； 烯丙基化反應

Abstract

Chiral functionalized homoallylic alcohol **2** is a useful building block in organic synthesis. Isoprene is a C₅ unit found in many natural products, and the synthetic application of homoallylic alcohol **2** is reported in the synthesis of terpenoid hydrocarbons, macrolides and polyether antibiotics. The general synthetic route to access homoallylic alcohol **2** is from methyl 3-hydroxy-2-methylpropionate (eq 2, 3). The metal-mediated Barbier-type allylation of formaldehyde would provide a facile route to the homoallylic alcohol **2**. As the source of formaldehyde, the use of a commercial formaldehyde aqueous solution is the most convenient. Herein, an aqueous hydroxymethylation of γ -substituted allyl halides **1** was developed in our group (eq 1). The formaldehyde addition reaction in an asymmetric version was proposed. The benzylation of formaldehyde remains a synthetic insolubility so far. Our attempts in this arena were also described in the proposal. In addition, a new tin-mediated allylation of dihydrofuran (**3a**) and dihydropyran (**3b**) to the corresponding 1,4- or 1,5-diols was developed in our group (eq 4). This method was not only applicable on dihydropyrans and dihydrofurans but also methyl 3-methoxyacrylate (eq 5). The scope of tin-mediated allylation would be studied.