4 Carbonyl additions and organometallic chemistry in water

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4.1 Introduction

This chapter is devoted to aqueous carbonyl additions, with the focus on organometallic additions. Thus Barbier-type reactions in water, the success of which is increasing, are described at length in section 4.2. The subsequent section deals with conjugate additions, and section 4.4 deals with cross-aldol reactions, with special attention being paid to organometallic additions. Section 4.5 is devoted to organometallic pinacol couplings in water. Some miscellaneous reactions in which the carbonyl group is the reactive site are reviewed briefly at the end of the chapter.

4.2 Barbier-type alkylation reactions

The Barbier reaction is that between an alkyl halide and a carbonyl compound in the presence of magnesium (Barbier, 1898). In Barbier-type reactions, an organometallic intermediate species is supposed to be produced in the presence of the substrate. As this organometallic intermediate is usually highly reactive with water, Barbier-type reactions were previously conducted after careful exclusion of water.

As long ago as 1977, a Barbier allylation mediated by zinc was accomplished in refluxing ethanol containing 5% of water, unfortunately giving poor yields (Killinger et al., 1977). Luche and Damiano (1980) observed that ultrasonic waves were able to promote the formation of lithium or magnesium organometallic reagents even in the presence of aqueous solvents. These salient features have paved the way to a new field of investigation, which turned out to be extremely fruitful in the case of the allylation of carbonyl compounds mediated by tin, zinc and indium in aqueous media, as outlined in a recent review (Li, 1996).

4.2.1 Allylation of carbonyl compounds mediated by tin

The aqueous allylation reaction mediated by tin was inspired by the observation that allylation of benzaldehyde with diallyltin dibromide seemed to be accelerated by the addition of water (Nokami et al., 1983). Acidic conditions (HBr, AcOH) were needed to perform the heterogeneous reaction using
metallic tin, allylic bromides and carbonyl compounds in a mixture of ether and water. Metallic aluminum as an additive was recommended for the allylation of ketones and the less reactive aldehydes (Nokami et al., 1983). The procedure was then applied to intramolecular reactions to synthesize five- or six-membered rings (Nokami et al., 1984):

With functionalized allylic bromides, the same procedure allowed preparation of bromo-homoallylic alcohols and 1,3-ketoacetates (Mandai et al., 1984) or α-methylene-γ-butyrolactones (Nokami et al., 1986).

An improvement of the allylation reaction was achieved with the use of ultrasonic waves in a water–tetrahydrofuran (5/1) mixture without the help of acidic co-reagents (Pétrier et al., 1985). Noteworthy are the sonicated reactions involving commercially available aqueous solutions of aldehydes, such as formaldehyde, and those involving aldehydes containing free hydroxyl groups (Einhorn and Luche, 1987):

When applied to carbohydrates, the sono-allylation proceeded with useful diastereoselectivity (threo-selectivity) and allowed preparation of higher-carbon sugars from water-soluble substrates directly in aqueous ethanol without protection (Schmid and Whitesides, 1991). Later, the authors showed that the allylation of aldoses could be advantageously carried out by heating the reaction mixture; for example, the allylation of D-arabinose required 16–20 h under sonication, but only 2 h under reflux (Kim et al., 1993):

Of interest was the use of a suspension of tin powder in a saturated aqueous NH₄Cl/THF solution at 60°C (Zhou et al., 1992).