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Sodium Tetraalkoxyborates: Intermediates for the Quantitative Reduction of Aldehydes and Ketones to Alcohols through Ball Milling with $NaBH_4$

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Stoichiometric molecular solid-state vibrational ball milling, solvent-free kneading ball milling, and mechanochemical ball milling of varied aldehydes and ketones with unmodified sodium borohydride under temperature control uses all hydrogen atoms of the reducing agent in fast reactions. It provides quantitative yields of thermally stable sodium tetraalkoxyborates. The easily isolated solids are extremely sensitive towards hydrolysis, leading to quantitative yields of the corresponding alcohols. The rapid syntheses are regiospecific and stereoselective. Varied substituents are not attacked, including the bromine of α-bromo ketones. Conjugated aldehydes and ketones provide quantitative yields of the allylic alcohols free of contamination by saturated alcohols that would occur by reaction in solution. Depending on the stoichiometric ratio, benzil is quantitatively reduced to benzoin (4:1 ratio) or dihydrobenzoin (2:1 ratio).

Introduction

Reduction of aldehydes and ketones (**1**) with $NaBH_4$ (**2**) to give the alcohols is a widely used technique.[1] It is mostly performed in protic solution, but the reactions are relatively slow and often proceed with low regioselectivity.[2] Only reductions with $NaBH_4$ in aprotic solvents allowed very tedious and unpractical isolation of a few tetraalkoxyborates.[3,4] There are also reports for the reduction of aldehydes and ketones with $NaBH_4$ under solvent-free conditions.[5] However, most of them have disadvantages for practical utility including excessive amounts of reducing agent, addition of catalysts, long reaction times, and the necessity of chromatographic workup. For example, benzophenone and a 10-fold molar amount of sodium borohydride were kept in a dry box at room temperature with occasional co-grinding of the reactants in an agate mortar with pestle for 5 d.[5a] More recently, solvent-free reductions of carbonyl compounds by sodium borohydride with added solid acids such as boric acid, benzoic acid, and 4-toluenesulfonic acid monohydrate[6] or wet silica have been reported.[7] All of these techniques, however, were not waste free, and the yields were less than quantitative. Highly versatile and varied stoichiometric ball milling at controlled temperature and moderate milling impact[8,9] has not yet been used to improve the situation. Furthermore, other recent reviews (covering different reaction types, but homogeneous liquids should not be milled)[10] did not particularly stress these technical points, which increase yields and decrease milling times.[8,9] We report herein the sustainable, rapid, and quantitative stoichiometric ball milling of 32 aldehydes and ketones with complete use of all four hydrogen atoms of the reducing agent for obtaining the alcohols. This method has the additional benefit of possessing the easiest thinkable synthesis of the versatile solid intermediate sodium tetraalkoxyborates that escape detection and isolation in the presence of water or moisture or excessive amounts of $NaBH_4$.

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Results and Discussion

A repetition of early grinding techniques with a fourfold excess amount of $NaBH_4$ (**2**)[5a] (1:1 mixture in the case of **1a**) gave only 36% yield of alcohol **4a**, whereas 10 min milling of such a mixture gave 100% yield after hydrolysis and workup. This appeared promising for the improvement of the reaction, as moisture- and solvent-free conditions would allow all four hydrogen atoms of **2** to be used, resulting in the isolation of tetraalkoxyborates **3**, and the use of excess amounts of **2** and inorganic waste would be avoided. The aldehydes used in Table 1 were either liquid (14 entries), solid (17 entries, m.p. 40–111 °C), or polymer (1 entry), but $NaBH_4$ (**2**) did not readily dissolve in them. Therefore, three types of milling procedures with substrates in a 4:1 ratio were used (Scheme 1, Table 1): (1) proper solvent-free kneading ball milling,[9] (2) proper solid-state molecular

