

# Solvent-free Dieckmann condensation reactions of diethyl adipate and pimelate

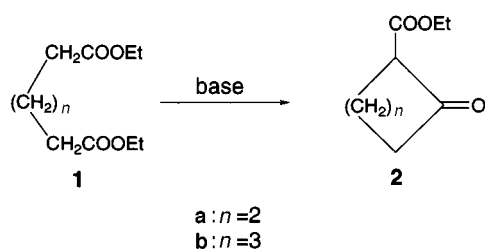
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Dieckmann condensation reactions of diethyl adipate and pimelate proceeded efficiently in the absence of solvent, and the reaction products were collected by a direct distillation from the solvent-free reaction mixture.

Dieckmann condensation reactions of diesters should be carried out in dried solvent under reflux in an inert atmosphere.<sup>1,2</sup> Furthermore, Dieckmann reactions are often carried out under high dilution conditions in order to avoid intramolecular reaction.<sup>1,2</sup> We found, however, that the reaction of diethyl adipate **1a** and pimelate **1b** (diethyl hexanedioate and heptanedioate,



Scheme 1

respectively) proceeds efficiently in the absence of solvent under air. We also succeeded in isolating the reaction products from the reaction mixture directly by distillation. These results establish a completely solvent-free procedure throughout the reaction and work-up of the reaction mixture. This is a very clean, green, simple and economical procedure.

After mixing **1a** and powdered Bu'OK for 10 min at room temperature using a mortar and pestle, the solidified reaction mixture was kept in a desiccator for 60 min in order to complete the reaction and evaporate the Bu'OH formed. The dried reaction mixture was neutralized by addition of *p*-TsOH·H<sub>2</sub>O and distilled under reduced pressure to give **2a** in 82% yield. The details of the procedure are given in the Experimental section. In contrast to the simple solvent-free procedure, the normal reaction of **1a** is carried out in dried toluene under reflux using Na metal under an N<sub>2</sub> atmosphere and the reaction product **2a** is isolated in 74–81% yield by the following successive work-up: neutralization with AcOH, evaporation of toluene and distillation.<sup>2</sup> The residue left after the distillation contains some recovered ester. When the solvent-free reaction mixture of **1a** and Bu'OK is distilled after neutralization with *p*-TsOH·H<sub>2</sub>O, **2a** was obtained in 82% yield by the solvent-free procedure and isolation of the product has many advantages. The same treatment of **1b** with Bu'OK in the absence of solvent followed by distillation gave **2b** in 69% yield.

Solvent-free and solid–solid organic reactions have been well established.<sup>3</sup> However, the reaction products are isolated from the reaction mixture by extraction with solvent in most cases, although the reaction product can be separated by filtration in some special cases, such as those where the reaction can be carried out in a water suspension.<sup>4</sup> In contrast to these solid state reactions, the solvent-free Dieckmann condensation needs no liquid throughout the entire process.

Table 1 Yields of solvent-free Dieckmann condensation reaction products **2a** and **2b**<sup>a</sup>

Base	Yield of <b>2a</b> (%)	Yield of <b>2b</b> (%)
Bu'OK	82	69
Bu'ONa	74	68
EtOK	63	56
EtONa	61	60

<sup>a</sup> All reactions were carried out at room temperature for 10 min and the reaction mixture was kept in a desiccator for 60 min.

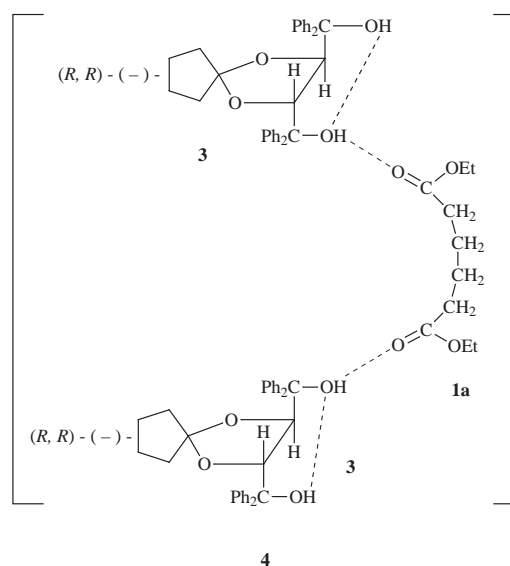
Table 2 Yields of **2a** and **2b** obtained by Dieckmann condensation reaction in toluene<sup>a</sup>

Base	Yield of <b>2a</b> (%)	Yield of <b>2b</b> (%)
Bu'OK	98	63
Bu'ONa	69	56
EtOK	41	60
EtONa	58	60

<sup>a</sup> All reactions were carried out in toluene under reflux for 3 h.

The solvent-free Dieckmann condensation of **1a** and **1b** also proceeds efficiently in the presence of powdered Bu'ONa, EtOK and EtONa as summarized in Table 1. For comparison with the solvent-free reaction, the Dieckmann condensation of **1a** and **1b** with the same base in toluene under reflux was studied. As shown in Table 2, there is no marked difference between the yields of solvent-free and solvent reactions. This clearly shows that the solvent-free reaction is much better than the other in terms of simplicity, cleanliness and economy.

In order to accomplish an enantioselective solvent-free Dieckmann reaction, the condensation was carried out in an



inclusion complex crystal with an optically active host compound, because some enantioselective solid state reactions have been achieved by this method.<sup>3</sup> Host–guest inclusion complexation of (*R,R*)-(-)-*trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[4.4]nonane **3**<sup>5,6</sup> with **1a** gave a 2:1 complex **4** of **3** and **1a** as colourless needles (mp 159–161 °C). However, treatment of **4** with Bu<sup>t</sup>OK in the solid state did not give **2a** and **1a** was recovered unchanged. The 2:1 molar ratio of **3** and **1a** in **4** suggests that two host molecules are binding to each one ester moiety of **1a** and preventing the intramolecular reaction of the ester groups.

## Experimental

### Solvent-free Dieckmann condensation reaction of **1a**

When **1a** (10.2 g, 50.4 mmol) and Bu<sup>t</sup>OK powder (8.44 g, 75.2 mmol) were mixed using a mortar and pestle for 10 min,

the reaction mixture solidified. The solidified mixture was kept in a desiccator for 60 min. The reaction mixture was neutralized by addition of *p*-TsOH·H<sub>2</sub>O and was distilled under 20 mmHg to give **2a** (5.8 g, 82% yield).

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