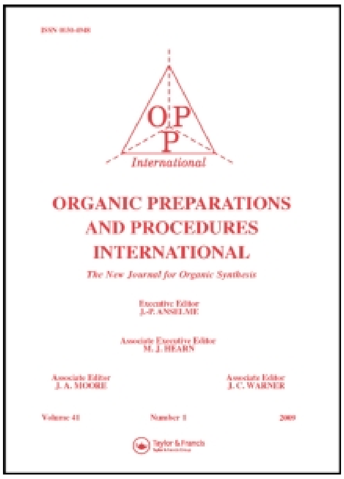

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2-METHYL-3-PHENYLPROPANAL. AN EXAMPLE OF A THREE CARBON CHAIN EXTENSION VIA THE OXAZINE-ALDEHYDE SYNTHESIS

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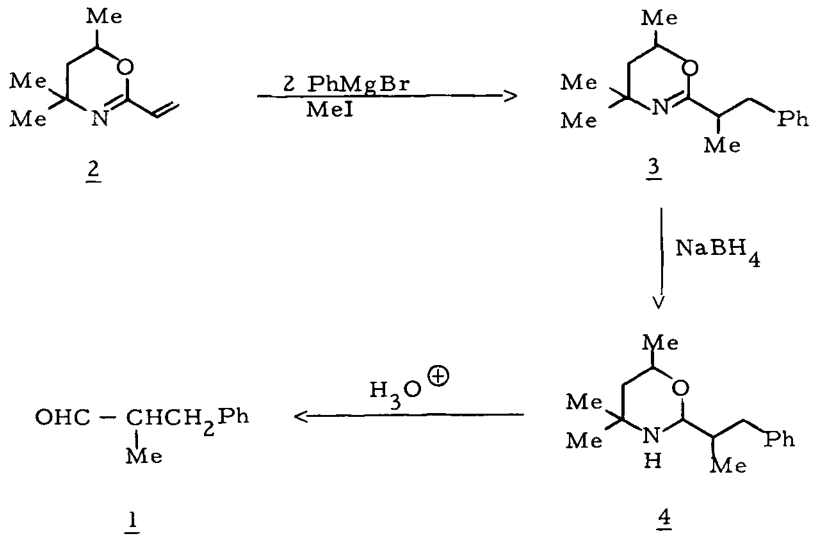
The utility of dihydro-1,3-oxazines as precursors to a variety of substituted acetaldehydes has recently been reported[1] and experimental details have been described.[2] We wish to now describe experimental details for preparing propionaldehyde derivatives (1) utilizing the readily available 2-vinyl oxazine derivative, 2. This procedure extends the scope of the oxazine-aldehyde synthesis by allowing a useful three carbon chain extension.[3]



PROCEDURE[4]

a) 2-(1-Phenyl-2-propyl)-4,4,6-trimethyl-5,6-dihydro-1,3-4H-oxazine (3). - A solution containing 10.0 g (0.06 mole) of 2, 6.1 ml (0.09 mole) methyl iodide,[5] and 100 ml tetrahydrofuran is cooled to -60° (Dry Ice-acetone) under nitrogen. To the stirred solution, 51 ml (0.16 mole, 3.0 M) of ethereal phenylmagnesium bromide is added dropwise over a period of 30 minutes. The reaction mixture is stirred after complete addition for 1 hour at -60 to -65° and then slowly allowed to warm to room temperature. The excess Grignard reagent is decomposed by the careful addition of 10 ml water and the contents of the flask are poured into 200 ml of an ice-water mixture. The solution is acidified with dilute hydrochloric acid (pH 2-3) and then extracted with three 75 ml portions of petroleum ether. The latter extracts are discarded and the aqueous solution is rendered alkaline by the addition of 40% sodium hydroxide solution. The oil that appears is removed by extraction with three 100 ml portions of ether and the extracts dried over potassium carbonate. Concentration of the ethereal extracts provides 14.8 g (93%)[6] of the crude product, 3, which is sufficiently pure to proceed to the next step. The dialkylated oxazine shows strong absorption at 1665 cm^{-1} (C=N).

b) Borohydride Reduction to 4. - The details for reducing the C=N link in 3 to the tetrahydro-1,3-oxazine, 4, is identical to that already described.[2] The reduction is performed using 2.5 g (0.06 mole) sodium borohydride and 13.7 g (93%) of crude 4 is obtained. The tetrahydro-1,3-oxazine exhibited no absorption in the 1665 cm^{-1} region and showed the NH band at 3270 cm^{-1}.

c) Oxalic Acid Cleavage to 1. - The crude tetrahydro-1,3-oxazine (13.1 g) is added dropwise to a boiling oxalic acid solution (33.4 g per 150 ml water) and the aldehyde collected in the steam distillate.[2] Ethereal extraction (three 50 ml portions) of the distillate is followed by drying over sodium sulfate. Removal of the solvent yields 6.0 g (77%) of 2-methyl-3-phenylpropanal in overall yield of 66% based upon 2. Ir (neat) 1725 cm^{-1}; nmr ($CDCl_3$) δ 10.7 (d, 1H, CHO). The semicarbazone melted at 122-123° (lit.[7] 123-124°).

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4. The 2-vinyl-4,4,6-trimethyl-5,6-dihydro-1,3-oxazine [J.J. Ritter and E.J. Tillmans, J. Org. Chem., 22, 839 (1957)] may be obtained from Columbia Organic Chemicals, 912 Drake Street, Columbia, South Carolina.

5. Ethyl magnesium bromide and allyl magnesium bromide were also employed at the temperatures designated. When ethyl iodide was employed, 3.0 equivalents were required for best results. Methylmagnesium bromide gave poor results in this reaction.

6. The yield of crude product includes 10-30% polymer derived from 2 which did not interfere with the subsequent steps or the isolation of the pure aldehyde.

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