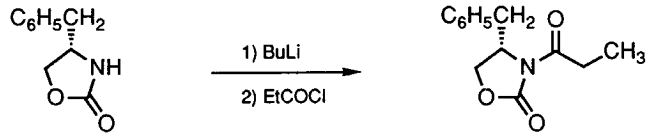
K 157 A

(S)-3-(1-Oxopropyl)-4-(phenylmethyl)-2-oxazolidinone



A dry, 500-mL flask equipped with a magnetic stirring bar is charged with 17.7 g (0.100 mol) of (S)-4(phenylmcthyl)-2-oxazolidinone[1] capped with a rubber septum, and flushed with nitrogen. Anhydrous tetrahydrofuran, 300 mL (Note 1), is then added to the flask via cannula, and the resulting solution is cooled to –78 °C in an acetone-dry ice bath. A solution of 68.3 mL (0.100 mol) of 1.47 M butyllithium in hexane (Note 2) is transferred via cannula first to a dry, septum-stoppered, 100-mL graduated cylinder with a groundglass joint, and then to the reaction flask over a 10-min period. The solution may turn yellow and slightly cloudy. Freshly distilled propionyl chloride (9.6 mL, 0. 11 mol, Note 3) is added in one portion by syringe after completion of the addition of butyllithium. The resulting clear, nearly colorless solution is stirred for 30 min at –78 °C, then allowed to warm to ambient temperature over a 30-min period. Excess propionyl chloride is quenched by the addition of 60 mL of saturated aqueous ammonium chloride. The bulk øf the tetrahydrofuran and hexane is removed on a rotary evaporator (bath temp. ca. 25-30 °C), and the resulting slurry is extracted with two 80-mL portions of dichloromethane. The combined organic extracts are washed with 75 mL of an aqueous 1 M sodium hydroxide solution and 75 mL of brine, dried over anhydrous sodium sulfate, and tiltered. The solvent is removed by rotary evaporation, and the residue, a lightyellow oil, is placed in a refrigerator overnight to crystallize. The resulting crystalline solid is pulverized and triturated with a minimum quantity of cold hexane. After filtration and drying 21.2-22.3 g (91-96%) of the desired product is obtained as a colorless crystalline solid, mp 44-46 °C (Notes 4 and 5).

1. Reagent-grade tetrahydrofuran was purchased from Fisher Scientific Company and cither freshly distilled from sodium metal and benzophenone or dried at least 3 days over activated Linde 4A molecular sieves before use in Reaction A. It was used as reccived for reaction C.

2. Butyllithium in hexane was purchased from Aldrich Chemical Company, Inc. and titrated prior to use.

3. Propionyl chloride (d, 1.065) was obtained from Aldrich Chemical Company, Inc., and distilled prior to use.

4. Trituration by the checkers gave 21.2-22.3 g (91-96 %) of acylated product of somewhat higher purity: mp 45-46 °C; [a]D +99.5 ° (ethanol, c 1.01). Alternatively, the acylated oxazolidinone can be isolated by distillation (Kugelrohr, 125 °C, 12 mm). Isolated yields were 97-99 %.

5. The product has the following spectroscopic properties: IR (solution in dichloromethane) em-': 3030, 2980, 1780, 1705, 1455, 1385, 1245, 1210, 1080; 'H NMR (CDCl3) 8: 1.2 (t, 3 H, J = 7.2, CH3), 2.8 (dd, 1 H, J = 13.3, 9.6, CH2C6H5), 2.9 (m, 2 H, CH2CH3), 3.3 (dd, 1 H, J = 13.4, 3.3, CH2C6H5), 4.1 (m, 2 H, CHCH20), 4.7 (m, 1 H, NCH), 7.1-7.5 (m, 5 H, ArH); [a]D +92.9 ° (ethanol, c 1.01).

[1] 2. Gage, J. R.-, Evans, D. A. Org. Synth., Coll. Vol. VIII 1993, 528.