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A Solvent-Free Baeyer–Villiger Lactonization for the Undergraduate Organic Laboratory: Synthesis of γ -*t*-Butyl- ϵ -caprolactone

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Since it was first reported in 1899 (1), the Baeyer–Villiger rearrangement has long been a staple of an organic chemist's reaction repertoire (2). First-year organic students learn this reaction as an efficient method to transform ketones to esters and lactones. Unfortunately, owing to a lack of suitable experiments, students are seldom able to explore this reaction in the undergraduate teaching laboratory.

Solvent-free or solid-state reaction systems have become popular in the synthetic organic community (3). They have also become a viable option for the undergraduate laboratory series (4) to reduce waste and cost, simplify reaction processes, and to provide students with an introduction to green chemistry. Recently, several solvent-free examples of the Baeyer–Villiger rearrangement have been reported in the literature utilizing different processes: the first utilized a triphase titanium silicate (TS-1)/H₂O₂ system (5); the second promoted the oxidation via chemoenzymatic means (6); and lastly, a solid-state reaction was performed with *m*-chloroperoxybenzoic acid (*m*-CPBA) (7).

The ease and straightforwardness of the *m*-CPBA process led us to investigate the possibility of converting the existing procedure into a form applicable to the teaching laboratory. Previous articles have appeared in this *Journal* utilizing Baeyer–Villiger oxidations as teaching tools for the advanced student (8), but none were specifically geared toward the second-year student and none under solvent-free conditions. The simplicity, ease, availability, and relative nontoxicity of our process make it an ideal candidate for the undergraduate laboratory.

In this experiment, *m*-chloroperoxybenzoic acid (*m*-CPBA) and 4-*tert*-butylcyclohexanone are mixed together for 30 minutes under solvent-free conditions to produce γ -*t*-butyl- ϵ -caprolactone in 95% yield (Scheme I). 4-*tert*-Butylcyclohexanone was selected as a suitable reagent owing to its low cost, low toxicity, and for the fact that the reaction may be stopped after only 0.5 hours with excellent conversion. Furthermore, the product is a solid, which can be easily isolated

from the reaction and purified by the students through recrystallization. Lastly, since the reaction yields are very good, the students obtain enough material to characterize their product by NMR, GC–MS, and IR if desired.

Typical Experimental Procedure

To a flask was added 0.50 g (3.2 mmol) of 4-*tert*-butylcyclohexanone and 1.12 g (6.49 mmol) of *m*-chloroperoxybenzoic acid. A reflux condenser was immediately attached to the flask.¹ After about 2 min, the reaction began to become warm and bubble,² and the mixture was stirred with a spatula³ once every 5 min for 30 min. Upon completion, the reaction mixture was treated with 20% aqueous sodium bisulfite solution to decompose the excess peroxyacid. The mixture was transferred to a separatory funnel, shaken, and the ether layer isolated. The ether layer was washed thoroughly⁴ with aqueous sodium bicarbonate solution. The organic fraction was collected, dried with MgSO₄, filtered into a round-bottomed flask, and the solvent removed by rotary evaporation. The off-white residue was washed with a small quantity of cold pentane and collected by suction filtration. The γ -*t*-butyl- ϵ -caprolactone may be recrystallized from a minimal quantity of hot hexane. Purity of the product was assessed through melting point determinations (mp 57.5–58.5 °C). Typical student yields are in the 50–80% range.

Hazards

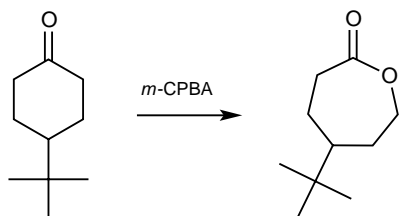
m-CPBA should not be heated since an explosion may occur. *m*-CPBA is also a potent oxidizer; keep away from combustible material. Ether, pentane, and hexanes are flammable liquids; there are to be no open flames in the laboratory. Magnesium sulfate is hygroscopic. The reaction may become violent if performed on a scale different from what is detailed in this article; scaleup is not recommended. Further health and safety notes may be found in the Supplemental Material.^W

Acknowledgment

The authors would like to thank Butler University's 2003 summer organic chemistry classes for helping assist with the preparation and testing of this lab.

^WSupplemental Material

Instructions for the students and notes for the instructor are available in this issue of *JCE Online*.



Scheme I. Reaction of 4-*tert*-butylcyclohexanone with *m*-CPBA under solvent-free conditions to produce γ -*t*-butyl- ϵ -caprolactone.

Notes

1. A reflux condenser is not necessary; however, it is recommended to encourage good safety procedures.

2. Scaleup of the reaction conditions is not recommended as the reaction may become violent if a large quantity of reagent is used.

3. The reflux condenser is removed, the students briefly stir the mixture, and the condenser is reattached.

4. If the extraction procedure is not done properly, the students will isolate *m*-chlorobenzoic acid in addition to their desired lactone.

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