Experimental Procedures

Experiment: 9 **Date: 17/04/2020;**
Lab No: 4 **Time: 9:00a.m. to 1:00p.m.**

Oxidation of Olefin with *meta*-Chloroperbenzoic Acid

meta-Chloroperbenzoic acid (*m*-CPBA) is known to decompose at elevated temperatures (starting at approximately 97 °C) and therefore reactions with *m*-CPBA should be run below 50 °C (see Kubota, A; Takeuchi, H. *Org. Proc. Res. Dev*. **2004**, *8*, 1076−1078).

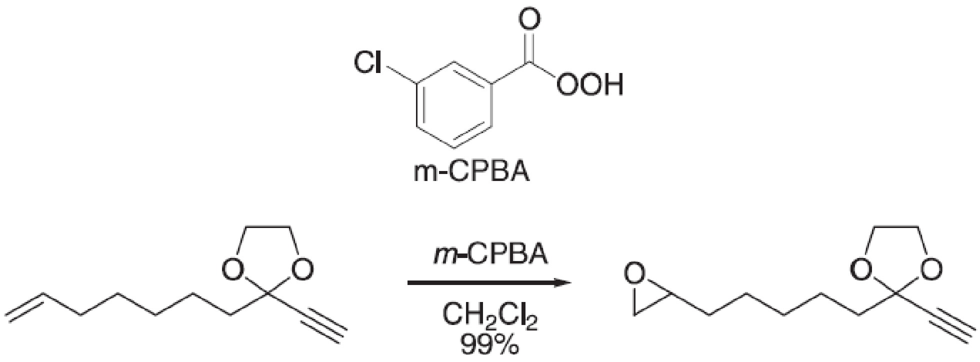

Figure 1 synthesis of epoxide

Procedure:

A solution of *m*-CPBA (10.4 g, 70%, 42.3 mmol) in CH_2Cl_2 (80 mL) was added to a solution of the olefin (3.73 g, 19.2 mmol) in CH_2Cl_2 (40 mL). The reaction was stirred for 12 h and cooled to 0 °C. 2-Methyl-2-butene (8.1 mL, 76.9 mmol) was added (to quench the reaction) and the resulting mixture was slowly warmed to 25 °C and stirred for 4 h to consume excess *m*-CPBA. The mixture was diluted with saturated $NaHCO_3$ and extracted by CH_2Cl_2. The combined CH2Cl2 extracts were washed with saturated Na_2SO_3 (30 mL), 5% NaOH (2 × 30 mL), and water (2 × 30 mL), dried ($MgSO_4$), and concentrated to afford the crude epoxide. Flash chromatography on silica gel (10:1 hexanes/EtOAc) yielded 4.03 g (99%) of pure epoxide as a colorless oil.

Reference: Snider, B. B.; Zhou, J. *Org. Lett*. **2006**, *8*, 1283−1286.

Yield: 4.03 g, 99%

Experiment: 10 **Date: 21/04/2020;**
Lab No: 5 **Time: 9:00a.m. to 1:00p.m.**

Condensation of acetoacetic esters with aldehydes or ketones

The Knoevenagel reaction is the condensation of malonic esters or acetoacetic esters (an active methylene) with aldehydes or ketones. The catalysts are mostly organoamines. Review: Tietze, L. F.; Beifuss, U. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon Press: Oxford, U. K., 1991; Vol. 2, Chapter 1.11: The Knoevenagel Reaction, pp. 341−394.

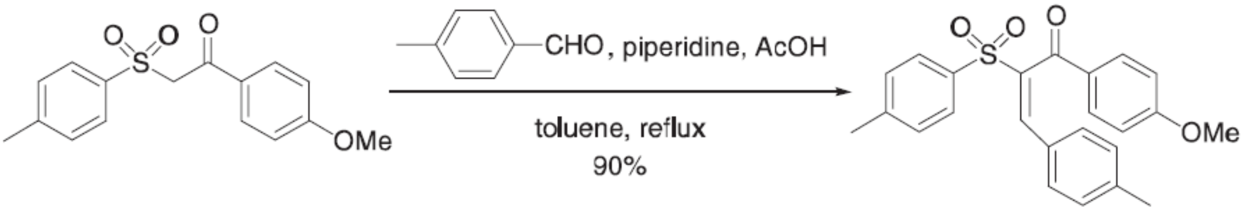

Figure 2 Condensation of acetoacetic esters with aldehydes or ketones

Procedure:

A mixture of the keto-sulfoxide (4.6 g, 15 mmol), *p*-tolualdehyde (2.0 g, 16.5 mmol), piperidine (0.18 g, 2 mmol), and acetic acid in toluene (40 mL) was heated at reflux for 2 h with azeotropic removal of water using a Dean–Stark trap. The mixture was cooled to room temperature and concentrated in vacuo. The residue was purified by flash chromatography eluting with a hexane:EtOAc:toluene (3:1:1) mixture to give 5.5 g (90%) of the olefin as a solid.

Reference: Swenson, R. E.; Sowin, T. J.; Zhang, H. Q. *J. Org. Chem*. **2002,** *67*, 9182−9185.

Yield: 5.5 g, 90%

Experiment: 11 **Date: 24/04/2020;**

Lab No: 4 **Time: 9:00a.m. to 1:00p.m.**

2-Chloro-5-bromonitro-benzene to Ester

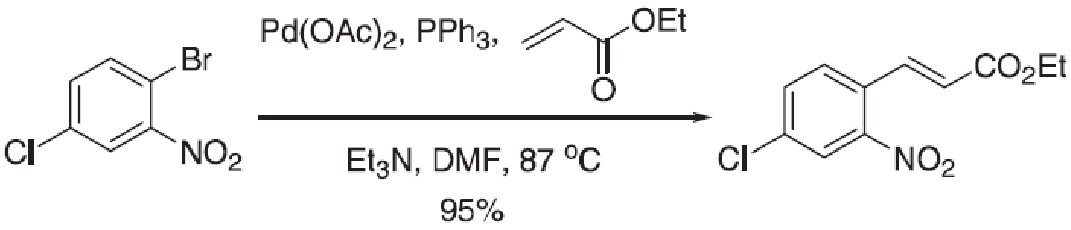

Figure 3 synthesis of ester

Procedure:

2-Chloro-5-bromonitro-benzene (3.0 g, 12.7 mmol), $Pd(OAc)_2$ (28.5 mg, 0.127 mmol), and triphenylphosphine (66.6 mg, 0.254 mmol) in dimethylformamide (360 mL) were added to triethylamine (2.47 mL, 17.8 mmol) and ethyl acrylate (13.8 mL, 0.127 mol). The reaction was stirred at 87 °C for 10 h, cooled to room temperature, and poured into a separatory funnel containing toluene (30 mL). The mixture was washed with 1 N HCl (30 mL) and water (2 × 20 mL). The organic extracts were concentrated to an oil that was crystallized in hexanes (60 mL). The solid was filtered to afford 3.08 g (95%) of the ester.

Reference: Caron, S.; Vazquez, E; Stevens, R. W.; Nakao, K.; Koike, H.; Murata, Y. *J. Org. Chem*. **2003,** *68*, 4104−4107.

Yield: 3.08 g, 95%

Experiment: 12
Lab No: 5

Date: 28/04/2020;
Time: 9:00a.m. to 1:00p.m.

Anisole derivative to Ketone derivatives

The Friedel–Crafts reaction includes both alkylation and acylation although here only acylation is exemplified. For the Friedel–Crafts acylation, the electrophile could be either an acid chloride or an anhydride. The catalyst could be either a Lewis or protic acid.

Review: Bandini, M.; Melloni, A.; Ronchi-Umami, A. *Angew. Chem. Int. Ed.* **2004,** *43*, 550−556.

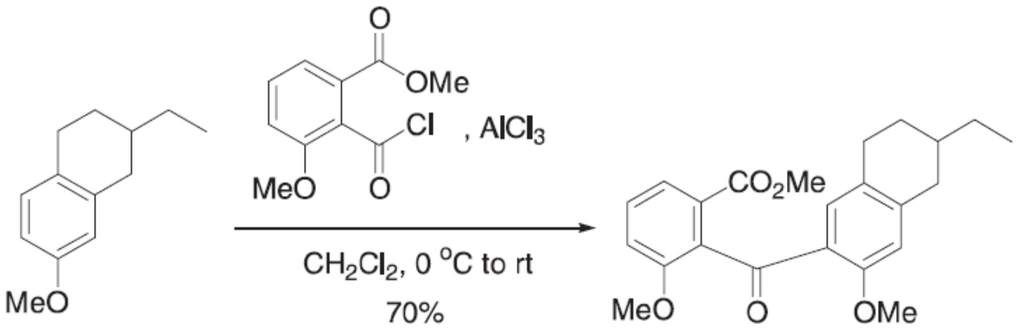

Figure 4 synthesis of ketone derivatives

Procedure:

The anisole derivative (380 mg, 2 mmol) in dry CH_2Cl_2 (5 mL) under a nitrogen atmosphere was cooled to 0 °C. Anhydrous aluminum chloride (400 mg, 3 mmol) was added slowly and the mixture was stirred for 15 min. The acid chloride (456 mg, 2 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and at room temperature overnight. After the reaction was deemed complete by TLC, the reaction mixture was poured on a mixture of crushed ice (5 g) and concentrated HCl (2 mL). The quenched reaction was stirred for 10 min and then extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with water (20 mL), brine (20 mL), and dried over sodium sulfate. The filtrate was then evaporated. The crude product was purified by column chromatography eluting with 20% EtOAc/petroleum ether to afford 535 mg (70%) of the ketone as a semi-solid.

Reference: Patil, M. L.; Borate, H. B.; Ponde, D. E.; Deshpande, V. H. *Tetrahedron* **2002,** *58*, 6615−6620.

Yield: 535 mg, 70%