Experimental Procedures

Experiment: 9 **Date: 16/04/2020;**
Lab No: 4 **Time: 9:00a.m. to 1:00p.m.**

Cyclohexene to *cis*-1,2-cyclohexanediol

Osmium tetroxide is a highly toxic reagent. It is volatile and can cause blindness.

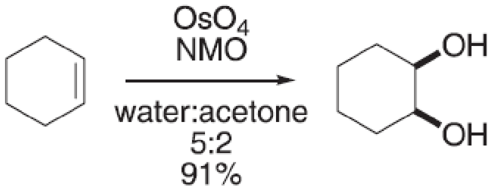

Figure 1 synthesis of *cis*-1,2-cyclohexanediol

Procedure:

To a mixture of *N*-methylmorpholine-*N*-oxide.$2H_2O$ (18.2 g, 155 mmol), water (50 mL), acetone (20 mL), and osmium tetroxide (80 mg) in *t*-butanol (8 mL) was added distilled cyclohexene (10.1 mL, 100 mmol). The reaction was slightly exothermic initially and was maintained at room temperature with a water bath. The reaction was complete after stirring overnight at room temperature under nitrogen. A slurry of 1 g of sodium hydrosulfite, 12 g of magnesium silicate (magnesol), and 80 ml of water was added, and the magnesol was filtered. The filtrate was neutralized to pH 7 with 1 N H_2SO_4, the acetone was evaporated under vacuum, and the pH was further adjusted to pH 2. The solution was saturated with NaCl and extracted with EtOAc. The aqueous phase was concentrated by azeotroping with *n*-butanol and further extracted with ethyl acetate. The combined ethyl acetate layers were dried and evaporated, yielding 11.2 g (96.6%) of crystalline solid. Recrystallization from ether provided 10.6 g (91%) of *cis*-1,2-cyclohexanediol, mp 95–97°C.

Reference: Van Rheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, *17*, 1973−1976.

Yield: 11.2 g, 96.6%

Experiment: 10
Lab No: 5

Date: 20/04/2020;
Time: 9:00a.m. to 1:00p.m.

Indolone to Indole derivatives

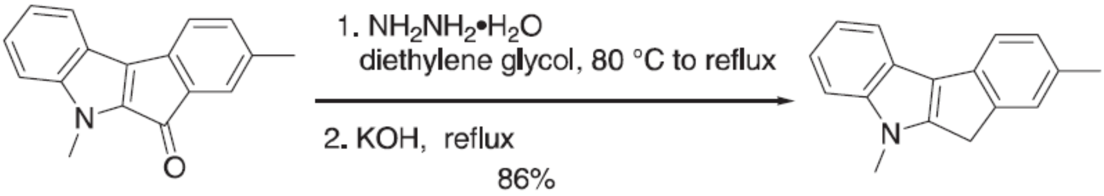

Figure 2 synthesis of indole derivative

Procedure:

A mixture of the indolone (1.04 g, 4.2 mmol) and hydrazine monohydrate (1.12 mL, 22.4 mmol) in diethylene glycol (20 mL) was stirred at 80 °C for 1 h and then refluxed for 2.5 h. The resulting mixture was cooled to room temperature, treated with a solution of KOH (1.2 g, 21.4 mmol) in water (5 mL), and refluxed for 2 h. The resulting mixture was poured into water (100 mL), and the precipitate was filtered off, washed with water (5 × 50 mL), and dried to deliver 0.84 g (86%) of the indole as a greenish solid.

Reference: Kashulin, I. A.; Nifant'ev, I. E. *J. Org. Chem*. **2004**, *69*, 5476–5479.

Yield: 0.84 g, 86%

Experiment: 11 **Date: 23/04/2020;**

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

3´,4´-dihydroxyacetophenone to 3´,4´-dimethoxyacetophenone

The methyl ether is one of the most popular protecting groups for phenols. The resulting phenoxy methyl ether, however, sometimes requires harsh conditions for cleavage.

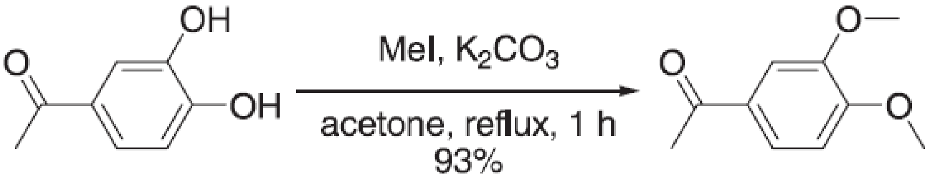

Figure 3 Synthesis of 3´,4´-dimethoxyacetophenone

Procedure:

To a stirred mixture of 3´,4´-dihydroxyacetophenone (100 mg, 0.66 mmol) and anhydrous K_2CO_3 (5 g, 36 mmol) in dry acetone (10 mL) was added MeI (1 mL, 16 mmol). The mixture was heated at reflux for 45 min, cooled to room temperature, filtered, and evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with 2 portions of water, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The product was purified by flash chromatography (silica, hexane/EtOAc 4:1, v/v). Removal of the solvent gave a 93% yield of the product, 3´,4´-dimethoxyacetophenone (110 mg, 0.61 mmol).

Reference: Khatib, S.; Nerya, O.; Musa, R.; Shmuel, M.; Tamir, S.; Vaya, J. *Bioorg. Med. Chem*. **2005**, *13*, 433−441.

Yield: 110 mg, 93%

Experiment: 12
Lab No: 5

Date: 27/04/2020;
Time: 9:00a.m. to 1:00p.m.

2,6-dibromophenol to MOM-protected 2,6-dibromophenol

The methoxymethylene (MOM) ether belongs to a class of substituted ether protecting groups. Unlike methyl ether, however, the MOM ether is actually an acetal, which is cleaved under acidic conditions. The MOM ether is the most robust among all alkoxymethyl ether protecting groups.

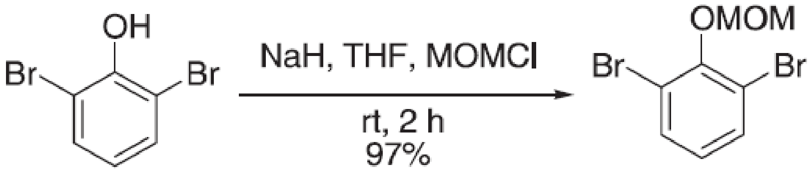

Figure 4 Synthesis of MOM-protected 2,6-dibromophenol

Procedure:

To a solution of 2,6-dibromophenol (5.80 g, 23.02 mmol) in THF (30 mL) at 0 °C was added NaH (1.38 g, 60% dispersion in mineral oil). After 5 min of stirring at 0 °C, MOMCl (2.25 mL, 30 mmol) was added via a syringe. The reaction mixture was then allowed to slowly warm to 25 ˚C, and following 2 h of additional stirring at that temperature the reaction mixture was poured into Et_2O (30 mL) and washed extensively with 3 M NaOH (3 × 7 mL) to remove any residual phenol starting material. The organic layer was then dried (MgSO4) and concentrated to give MOM-protected 2,6-dibromophenol (6.62 g, 97%) as a yellow oil.

Reference: Nicolaou, K. C.; Snyder, S. A.; Huang, X.; Simonsen, K. B.; Koumbis, A. E.; Bigot, A. *J. Am. Chem. Soc.* **2004**, *126*, 10162−10173.

Yield: 6.62g, 97%

Experiment: 13 **Date: 30/04/2020;**
Lab No: 4 **Time: 9:00a.m. to 1:00p.m.**

Protection of amine in 2,5-dimethylpyrrole

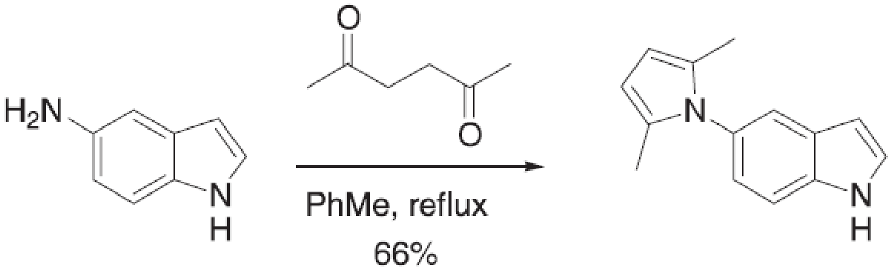

Figure 5 Protection of amine in 2,5-dimethylpyrrole

Procedure:

A mixture of 5-aminoindole (12.0 g, 9.08 mmol), acetonylacetone (20.0 mL, 17.0 mmol), and toluene (40 mL) was heated at reflux under nitrogen using a Dean-Stark trap for 3 h. The reaction was cooled and then poured through a silica gel filter (~ 20 gm) followed first by hexanes (400 mL) and then by 6% ether in hexanes to afford 13.3 g of a pink solid. Recrystallization of this solid in ether/hexanes afforded 12.61gm (66%) of the 2,5-dimethylpyrrole as an off-white solid.

Reference: Macor, J. E.; Chenard, B. L.; Post, R. J. *J. Org. Chem*. **1994**, *59*, 7496−7498.

Yield: 12.6 gm, 66%