UCLA Chemistry 144 Organic Synthesis

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Experiment 3: Synthesis of 5,6-dicarboxymethyl-8-phenylchroman via a Facile Diels-Alder Reaction

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Abstract

The synthesis of chroman compounds can be achieved through diels alder reaction with furan derivatives and their subsequent reduction. Experiment progressed in attempt to produce furan derivative (3). With repeated attempts, was unsuccessful to produce the alkene furan deravitive (3).

Introduction

The experiment's original aim was to synthesize 5,6-dicarboxymethyl-i-phenylchroman, though difficulties in obtaining the alkene (3) thwarted progress to that point. The experiment uses an organolitium reagent with DHP to start a scaffold toward the chroman synthesis. The resulting alcohol (2) was attempted to be dehydrated to alkene (3). Had time and results permitted, an alkyne would be reacted with (3) in a diels alder reaction and subsequently reduced to a chroman compound.

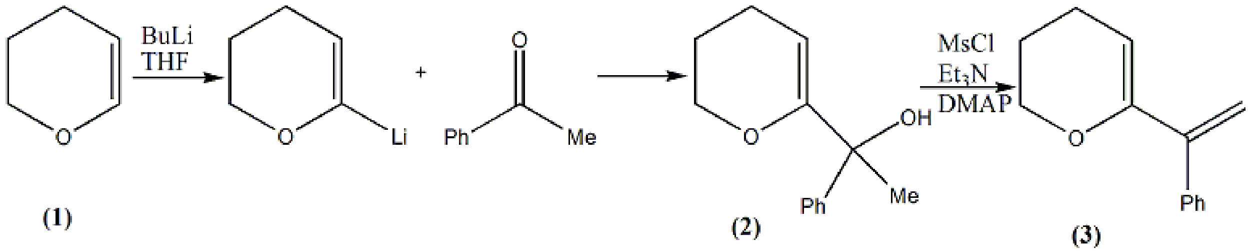

Figure 1: Reaction Scheme

Discussion

The synthesis of alcohol (2) uses BuLi to deprotinate and lithiate DHP (1). The electropositive nature of lithium puts most of the charge density of the bond on the carbon atom. The lithium ion of BuLi complexes to THF to further polarize the Li-C bond. This carbanion attacks the carbonyl of acetophenone to produce alcohol (2). The reaction likely proceeded to yield (2), though it is not pure. FTIR -OH peak at 3538 cm^{-1} and CH at 1686 cm^{-1} is comparable to reference values[1]. The ^{1}H and ^{13}C NMR peaks are well accounted for, though additional peaks are present such as a carbonyl carbon in the ^{13}C NMR from acetophenone. Rercystallization or another purification technique would be done if repeated, though recrystallization from ethanol as the procedure[1] was not successful as the compounds are not identical. Identity of alcohol (2) is further suggested by successful TBS protection of (2) as evidenced by TLC shift in polarity.

The following step is a dehydration of the alcohol to alkene (3) using catalytic DMAP, triethylamine, and MsCl. This procedure is used because it produces an alkene from tertiary alcohols and does not react with acid sensitive groups such as DHP[2]. This step was repeated twice without success in obtaining the alkene (3). The NMR was compared to shifts typical of styrene, and there was no typical ^{1}H shift around 5.09 ppm. Additionally IR showed a broad peak at 3407 cm^{-1} which could be due to (2). It is believed that the either the MsCl reagent was not good, an impurity from the previous reaction caused unexpected results, or (2) was never successfully synthesized. The NMR and IR of alcohol (2) as well as the TBS protection do suggest that the alcohol (2) was successfully synthesized though. The alcohol could have been dehydrated using DMSO instead or a wittig reaction of 2-acyl-5,6-dihydro-2h-acyl-5,6-dihydro-2h-pyran[3].

Conclusions

Although the result of this experiment did not progress to synthesis of a chroman compound, it is believed the alcohol (2) was successfully produced. The alkene (3) was not successfully synthesized after repeat attempts and an alternate synthetic route or different reagents are considered if experiment was repeated.

Experimental

1-(5,6-dihydro-4H-pyran-2-yl)-1-phenylethanol (2) A solution of 3,4-dihydro2Hpyran ((1); 5mL, 55mmol) and 20mL of THF were stirred at 0°C under N_2 gas. A 1.6 molar solution of BuLi in hexane (32mL) was added dropwise and stirred for two hours at 50-65°C. Acetophenone (45mmol) in 10mL THF was added dropwise and stirred for two days at room temperature. Added 100mL dH_2O and stirred for five minutes. Extracted twice with 50mL diethyl ether, dried with Mg_2SO_4 and evaporated solvent to 10.7042g (52mmol) of a brown liquid **(2)** at 94.5% yield. FT-IR v(cm^{-1}) 1224 (w), 1241 (m), 1265 (s), 1360 (m), 1448 (m), 1599 (m), 1649 (m), 1686 (s), 2871 (m), 2930 (m), 2957 (m), 3060 (w), 3438 (b); ^{1}H NMR (400 mHz, $CDCl_3$) δ (ppm) 0.86 (m), 1.32 (s), 1.43 (m), 1.78 (m), 1.80 (d), 1.93 (s), 3.67 (m), 3.91 (m), 4.92 (s), 6.30 (m), 7.38 (m), 7.42(m), 7.48 (m), 7.90 (m), 7.92 (m); ^{13}C NMR (100 mHz, $CDCl_3$) δ (ppm) 13.8, 18.9, 19.5, 20.0, 22.1, 22.7, 25.3, 25.5, 25.5, 26.5, 27.8, 34.8, 62.4, 65.7, 66.4, 67.9, 75.2, 96.3, 100.7, 125.2, 125.4, 126.8, 127.2, 127.9, 128.1, 128.2, 128.3, 128.3, 128.4, 128.5, 133.1, 137.1, 144.0, 198.1.

6-(prop-1-en-2-yl)-3,4-dihydro-2H-pyran (3) A solution of 1.0152g (5.0mmol) of alcohol (2), 10.97mmol pyridine (1.53mL), 26.8mg DMAP, and 10mL CH_2Cl_2 was stirred at 0°C under N_2 gas and 0.57mL MsCl was added dropwise. Stirred at room temperature for 90 minutes and crushed ice was added. Extracted CH_2Cl_2 (3x15mL), washed combined organic layers with dH_2O (3x15mL), and dried Mg_2SO_4. Flash chromatography with 4:1 hexane EtOAc eluent. Fractions 13-15 combined for 80.4mg orange oil. FT-IR v(cm^{-1}) 1174 (s), 1260 (w), 1353 (m), 1441 (m), 1711 (m), 2873 (s), 2951 (m), 3047 (b).

References

1. LeBouc, A.; DeLaunay, J.; Riobe, O. *Synthesis* **1979**, 610
2. Yadav, J.S., Mysoekar, S.V. *Syn. Commun.* **1989**, 19, 1057-1060

3. Chemistry 144 Organic Synthesis Laboratory Experiments Profesor Michael e. Jung Fall 2008 UCLA Department of Chemistry and Biochemistry

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