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Optimization of Microwave-Enhanced Williamson Ether Synthesis of 1-ethoxydodecane

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ABSTRACT

1-ethoxydodecane is an asymmetrical ether used in production of sunscreen and moisturizing due to its nonpolar properties. One of the standard protocols for synthesizing both asymmetrical and symmetrical ethers is via the Williamson Ether Synthesis. The standard synthesis requires a 60-70 minute reflux time frame to allow for this reaction to run until completion; however, the ability to reduce this reaction time via microwave radiation has become increasingly prominent in organic synthesis. The conventional means of Williamson Ether Synthesis is also not ideal for optimal purity or speed, thus microwave synthesis of this compound was investigated. In order to obtain the greatest yield in the shortest amount of time, multiple reactions were run in order to optimize time, temperature, and wattage parameters. The optimal time parameter determined that allows for greatest yield and purity of product was 3 minutes, temperature was optimized to be 123°C, and wattage was optimized to be 1000W. Purity and proper formation of 1-ethoxydodecane was determined via ^{1}H NMR, ^{13}C NMR, and IR (as a basic assessment of functional group transformation from alcohol to ether).

BACKGROUND

INDUSTRIAL MICROWAVES AS A TOOL FOR ORGANIC SYNTHESIS

- Microwaves are a prominent tool in organic synthesis.
- Microwaves reduce reaction time by directly transferring heat to the interior of the microwave vessel while providing control over reaction conditions[4,5].
- Industrial microwaves can also reach higher temperatures at faster rates[2,4].

EFFICIENCY ENHANCMENT OF ORGANIC SYNTHESIS IN INDUSTRIAL MICROWAVES IS STILL BEING INVESTIGATED

- The investigation of optimizing microwave conditions for different varieties of organic synthesis reactions still currently being investigated[1,6]:
  - Diels-Alder Reaction
  - Esterifications
  - Oxidation
  - Williamson Ether Synthesis

THE MICROWAVE-ENHANCED WILLIAMSON ETHER SYNTHESIS

- Ethers are a commonly synthesized class of organic compounds used as liquid engine starters, manufacture of explosives, extraction of oils, and production of moisturizer & sunscreen[1,6].
- Conventional means of ether synthesis are time-consuming and inefficient[1,6].

RESEARCH GOALS

- Effectiveness of microwave technology was demonstrated through synthesis of 1-ethoxydodecane.
  - 1- ethoxydodecane is an aliphatic ether synthesized from 1-dodecanol 1-bromoethane; has yet to have been optimized via microwave organic synthesis.
  - 1-ethoxydodecane is used in moisturizers and sunscreen[3].
  - **Optimizing reaction conditions and microwave parameters for the microwave synthesis of 1-ethoxydodecane demonstrated improved reaction time and greater yield over conventional synthesis.**

Figure 1. Physical appearance of 1-ethoxydodecane

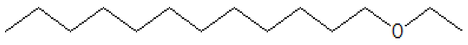
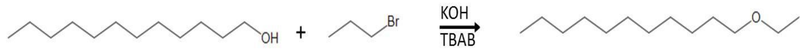


Figure 2. Line-angle structure of 1-ethoxydodecane.

RESULTS

Scheme 1. Williamson Ether Synthesis of 1-ethoxydodecane.



Experiment	Reaction Time (minutes)	Temperature (°C)	Wattage (W)	Yield	Purity
1	0.5	140	1200	N/A	N
2	4.0	140	1200	57%	N
3	5.0	140	1200	82%	N
4	10.0	140	1200	115%*	N
5	3.0	140	1200	77%	Y**
6	2.5	140	1200	87%	N
7	3.5	140	1200	62%	N

Table 1. Reactions performed to optimize reaction time. * denotes impossible yield due to remaining starting material. ** indicates greatest purity. Rows colored green indicate crude yields. Row highlighted yellow indicates optimal time.

Experiment	Reaction Time (minutes)	Temperature (°C)	Wattage (W)	Yield	Purity
8	3.0	130	1200	78%	N
9	3.0	120	1200	83%	N
10	3.0	125	1200	74%	N
11	3.0	124	1200	73%	Y
12	3.0	123	1200	67%	Y
13	3.0	122	1200	82%	N

Table 2. Reactions performed to optimize reaction temperature. Rows colored green indicated crude yields. Rows highlighted yellow indicates optimal temperature.

Experiment	Reaction Time (minutes)	Temperature (°C)	Wattage (W)	Yield	Purity
14	3.0	123	900	70%	N
15	3.0	123	1000	72%	Y

Table 3. Reactions performed to optimize wattage. Row highlighted yellow indicates optimal wattage.

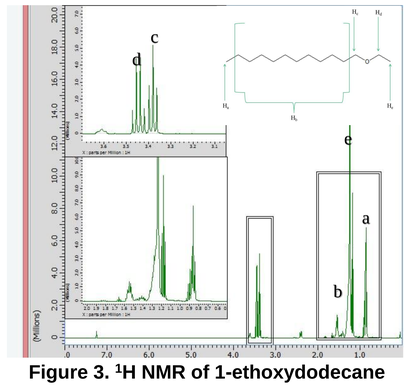


Figure 3. ^{1}H NMR of 1-ethoxydodecane

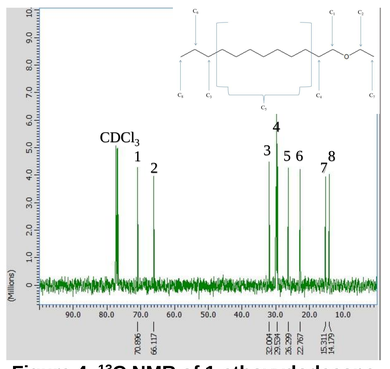


Figure 4. ^{13}C NMR of 1-ethoxydodecane

Shift (ppm)	# of hydrogens	Multiplicity	Assignment
0.86	3	t	H_a
1.54	20	m	H_b
3.38	2	t	H_c
3.44	2	q	H_d
1.20	3	q	H_e

Table 4. ^{1}H NMR assignments of 1-ethoxydodecane

Shift (ppm)	Assignment
70.896	C_1
66.117	C_2
32.004	C_3
29.534	C_4
26.299	C_5
22.767	C_6
15.311	C_7
14.179	C_8

Table 5. ^{13}C NMR assignments of 1-ethoxydodecane

DISCUSSION

- Synthesis:
  - 1-ethoxydodecane was synthesized from dodecanol and ethyl bromide by microwave irradiation. The reaction ran most efficiently without the presence of a solvent and in ~150% excess alkyl halide (Scheme I). The structure was confirmed by ^{1}H and ^{13}C NMR.(Figures 3 & 4).
  - TBAB (tetrabutylammonium bromide) was used as a catalyst.
- Optimization of reaction conditions:
  - Time:
    - The optimal time at 140°C was three minutes. Longer or less than three minutes produced an impure product (Table 1).
  - Temperature:
    - The minimum temperature for the reaction to run to completion was 123°C. This was determined by progressively lowering the reaction temperature from 140°C to an optimal 123°C (Table 2).
  - Wattage:
    - After optimizing both time and temperature, wattage was optimized. The optimal wattage was 1000W (Table 3).

CONCLUSION

- Utilizing a microwave for the enhancement of the synthesis of 1-ethoxydodecane was able to successfully reduce the reaction time (65 minute reflux, Table 1) to 3 minutes while also improving yield over conventional means of synthesis (~70% vs. 38%).

EXPERIMETNAL SECTION

- Added ~1.5g KOH (0.0267 mol), 0.35g TBAB (0.0011 mol), ~2.0g 1-dodecanol (0.0108 mol), and ~2.95g of ethyl bromide (0.0271 mol) to a microwave reaction vessel.
- Microwaved reaction vessel in a Start SYNTH Microwave from Milestone Microwave Laboratory Systems at varying conditions; final conditions were T1 = 123°C, T2 = 70°C, Ramp time = 1 minute, Reaction time = 3minutes, Wattage = 1000W.
- Simply distilled microwaved product to remove excess ethyl bromide for ~30 minutes.
- Purified with $CaCl_2$ to remove excess 1-dodecanol for ~10 minutes.
- Ran IR, ^{1}H, and ^{13}C NMR to examine purity and proper synthesis. Used a JEOL ECS 400 NMR Spectrometer for NMR analysis.

FUTURE WORK

- Utilizing the same starting alcohol, the next goal will be to ultimately continue the microwave-enhanced Williamson Ether Synthesis using 1-dodecanol and different alkyl halides.
- Optimizing reaction conditions to run multiple reactions at once will also be key in improving efficiency of the Williamson Ether Synthesis of 1-ethoxydodecane as well.

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