Light Up - Ways to achieve a greener usage of energy in the chemistry industry:

Optimization of thiol-ene click reaction in flow with an advanced reaction set-up and techno-economic analysis

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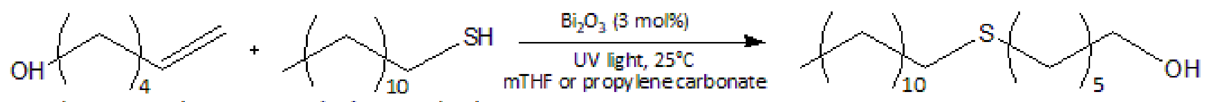
Introduction

Click chemistry [1] is very interesting to be studied because of:

- Simple reaction;
- Thermodynamically favorable;
- High yield;
- Good speed;
- Production of harmless products.

Also photoinitiated reactions have advantages of using light as an energy source considering a **sustainable, controllable, and efficient** method for chemical synthesis.



5-hexen-1-ol   1-dodecanethiol

Figure 1. Selected thiol-ene click reaction

Materials & Methods

The HANU Reactor is the main equipment, but the system has also the presence of pump, safety pressure valve, pulsator, filter, back pressure regulator, UV light and heating bath.

Figure 2. Set up used to perform the reaction

The three focus of the project are:

- Determine which parameters are important for the results of the reaction;
- Usage the optimization program Robochem to find the best operational conditions;
- Analyze the techno economics factor of this process and its scale up.

Results & Discussion

Pressure Experiment

Pressure Experiment Results					
Sample	Conversion Test 1	Conversion Test 2	Conversion Test 3	Conversion Test 4	Conversion Test 5
0 bar	42%	90%	93%	84%	82%
2 bar	51%	93%	95%	87%	86%
4 bar	50%	94%	88%	88%	82%
6 bar	65%	94%	95%	92%	83%

Figure 3. Impact of the pressure in the reaction

Wavelength Experiment

Sample	Conversion	Final Alkene [] mol/L
365nm	68%	0,025197166
405nm	23%	0,061153392
460nm	-20%	0,096270933
Initial Alkene []	0,080001299	mol/L

Figure 4. Impact of the wavelength in the reaction

Optimization Program

Index	Alkene (mMol)	Thiol Equivalents	Temperature (°C)	Flow (mL/min)	Wavelength (nm)	Light Intensity (w/m²)	Conversion (%)	Throughput (g/min)
1	835	4,2	39	5,3	405	2	23	20,49
2	910	1,8	19	5	365	9	31	28,40
3	227	2,8	23	3,6	365	9	14	2,30
4	685	3,2	33	6,2	460	3	11	9,41
5	835	1,2	30	4,8	460	9	19	15,33
6	530	3,8	24	4	405	8	63	26,89
7	530	4,7	25	6,7	365	7	25	17,87
8	455	1,8	22	4,5	460	3	12	4,95
9	610	3,4	18	4	365	10	24	11,79
10	610	2,2	17	4	365	10	42	20,63
11	605	1,5	18	2,8	365	2	14	4,77
13	605	1,3	24	1	365	10	55	6,70
14	530	4,2	37	2,4	365	6	85	21,77
15	305	1,2	15	1,2	460	9	9	0,66

Figure 6. Optimization experiments and results

Catalyst Experiment

Bismuth III Oxide Test			Zinc Oxide Test		
Estimated Initial Alkene []	0,412	mol/L	Estimated Initial Alkene []	0,412	mol/L
Calculated Initial Alkene [] 1	0,141957126	mol/L	Calculated Initial Alkene [] 1	0,157966645	mol/L
Calculated Initial Alkene [] 2	0,121839974	mol/L	Calculated Initial Alkene [] 2	0,153928226	mol/L
Experiment	Conversion		Experiment	Conversion	
0g	27%		0g	35%	
0,6g	-15%		0,6g	9%	
1,2g	5%		1,2g	18%	

Figure 5. Different catalyst and amounts

Reliability of the Experiment

	I A	I B	Diference %	II A	II B	Diference %	III A	III B	Diference %	Product A	Product B	Diference %
Exp 1	0,53	0,57	-8,12	0,53	-	-	0,58	0,59	-1,43	0,45	0,44	3,89
Exp 2	0,69	0,65	6,46	0,75	0,84	-12,70	0,70	0,66	6,11	0,57	0,58	-1,32
Exp 3	0,21	0,17	19,78	0,18	0,20	-10,03	0,21	0,22	-2,01	0,18	0,19	-6,75
Exp 4	0,51	0,44	12,54	0,45	0,48	-6,96	0,52	0,41	20,82	0,44	0,45	-3,03
Exp 5	0,74	0,64	13,14	0,68	0,88	-28,82	0,69	0,76	-9,34	0,73	0,59	18,70
Exp 6	0,46	9,89	-2043,76	8,37	2,05	75,56	25,40	17,65	30,52	0,17	0,20	-16,89
Exp 7	0,39	0,40	-2,30	0,40	0,38	3,66	0,41	0,40	1,71	0,28	0,30	-7,68
Exp 8	0,41	0,37	10,97	0,40	0,52	-29,88	-	0,20	-	0,36	0,36	-1,62
Exp 9	0,45	0,44	2,95	0,45	0,47	-4,38	0,46	0,45	2,63	0,35	0,34	2,48
Exp 10	0,48	0,50	-3,15	0,47	0,51	-7,69	0,47	0,45	5,56	0,28	0,27	2,96
Exp 11	0,42	0,46	-11,47	0,44	0,49	-11,07	0,46	0,48	-3,84	0,40	0,38	4,72
Exp 13	0,51	0,55	-6,44	0,50	0,47	5,60	0,48	0,46	4,21	0,03	0,23	-579,10
Exp 14	0,36	0,43	-19,52	0,42	0,46	-7,38	0,36	0,45	-24,34	0,05	0,06	-6,86
Exp 15	0,28	0,29	-2,06	0,26	0,26	-0,97	0,25	0,26	-3,70	0,26	0,27	-3,30

Figure 7. Different concentration comparing duplicates

Techno Economics Study

Total Reactant Costs (€/h)	Total Catalysts Costs (€/h)	Total Energy Costs (€/h)	Total Labor Costs (€/h)	Total Equipment Costs (€/h)	Total Land Costs (€/h)	Total Costs (€/h)
3,46	0,00	0,46	10,40	0,64	0,01	14,97

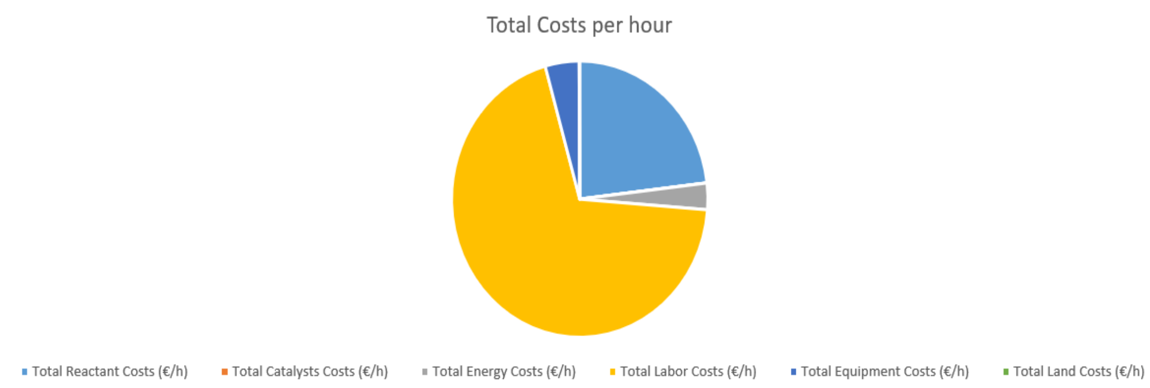


Figure 8. Total costs per hour

Conclusions and Suggestions

- The parameter of **pressure is not very relevant for the reaction**, and it is very difficult to operate under higher pressure in terms of pressure stability, leakages and the impossibility of using it combined with the pulsator;
- The parameter **wavelength is very important for the reaction** considering the blank reaction, but it can be even more impactful when combined with different catalysts;
- The usage of solid catalyst is very complicated in terms of **clogging, cleaning, spreadbility in the reactor and containing the catalyst inside it**, so a method need to be developed for the test of the catalyst;
- The reliability analysis show that the percentual difference of alkene concentration of the duplicates is very high, so there is a **problem in the method** in terms of **replication of the decane as internal standard**;
- The techno economic study show that the **highest production cost is labor**, what reinforce the importance of the **automatization of this process.**

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Reference:

[1] Kolb, H. C., Finn, M. G., & Sharpless, K. B. (2001). Click Chemistry: Diverse Chemical Function from a Few Good Reactions. Angewandte Chemie International Edition, 40, 2004-2021.

[2] O. O. Fadeyi et al., "Visible-Light-Driven Photocatalytic Initiation of Radical Thiol–Ene Reactions Using Bismuth Oxide," Org Lett, vol. 17, no. 23, pp. 5756–5759, Dec. 2015, doi: 10.1021/acs.orglett.5b03184.

[3] P. Bianchi, J. D. Williams, and C. O. Kappe, "Continuous flow processing of bismuth-photocatalyzed atom transfer radical addition reactions using an oscillatory flow reactor," Green Chemistry, vol. 23, no. 7, pp. 2685–2693, 2021, doi: 10.1039/D0GC03070H.

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