Optimization of photoflow thiol-ene click reaction

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light-up

Introduction

The Light-Up project aims to optimize photochemical reactions using light as a sustainable energy source. Flow reactors, which enhance light energy absorption, are commonly employed in photochemical reactions to contribute to the transition toward a climate-neutral society (fig. 1).

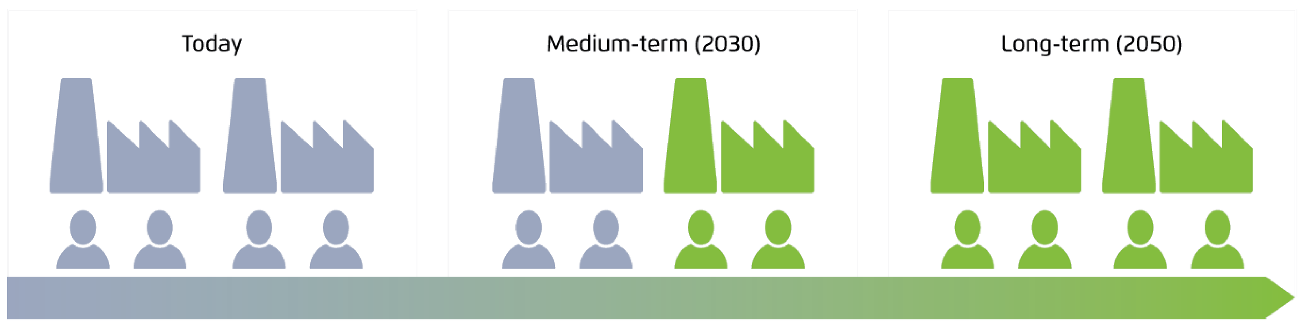

Fig. 1: The transformation of a basic industrial company on the road to climate-neutral production. [1]

One method for forming carbon–sulfur bonds is through the thiol-ene click reaction. Therefore, it allows access to fine chemicals, such as sulfur-containing drug molecules and specialized polymers. This research aims to translate the thiol-ene click reaction reported by Fadeyi[2] to a multiphasic solid/liquid reaction in flow and improve conversion, yield, and sustainability. Bismuth(III) oxide – a mild, inexpensive and non-toxic photocatalyst – was employed.

Materials & Method

The thiol-ene click reaction (fig. 2) was performed in the HANU™ [3] flow reactor under UV-light (fig. 3).

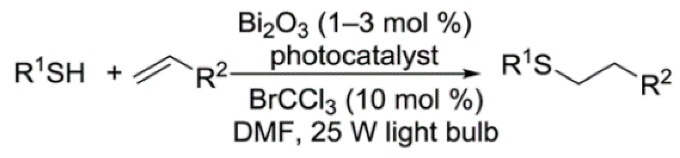

Fig. 2: The selected literature reaction for thiol-ene click reaction. [2]

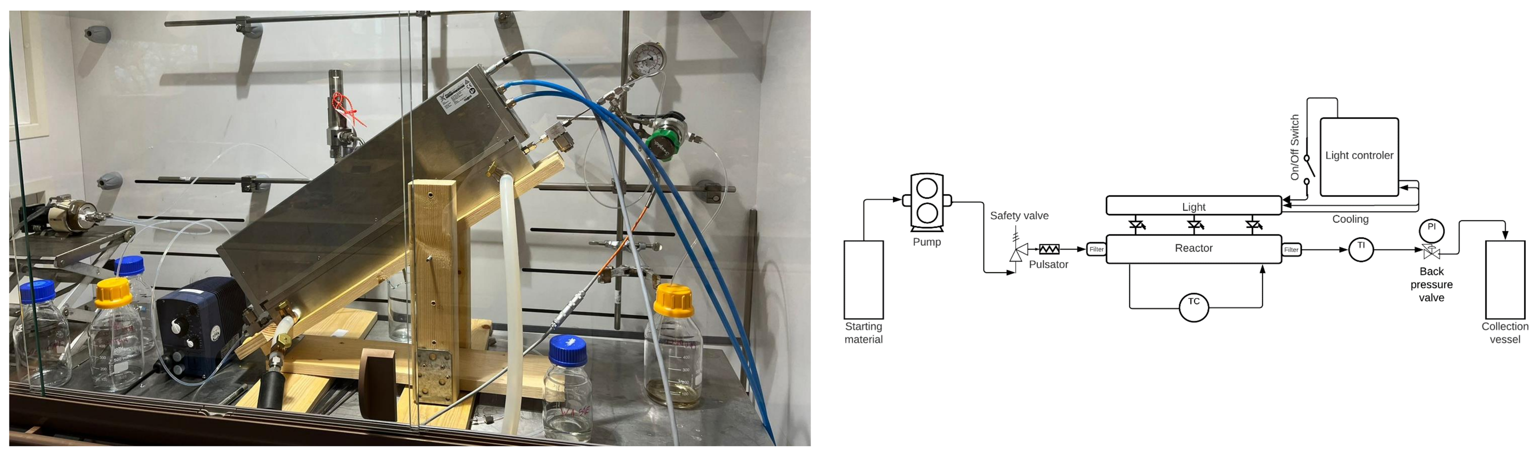

Fig. 3: HANU™ reactor set-up and P&ID.

The reaction mixtures were analyzed with GC-MS to determine the purity, yield and conversion. The parameters evaluated in the optimization were:

Light source and intensity	Reagent concentration	Temperature
Residence time	Catalyst loading	Green solvents

Results & Discussion

The reaction was firstly performed with an alternative catalyst (Benzil), before being tested with Bi_2O_3 catalyst in a multiphasic solid/liquid set-up. Almost full conversion and yield was achieved (>97%).

The multiphasic reaction (fig. 4) was performed different solvents, mTHF and acetone were suitable green solvents for the reaction (table 2). Under UV-light, the reaction had significant yield/conversion without catalyst.

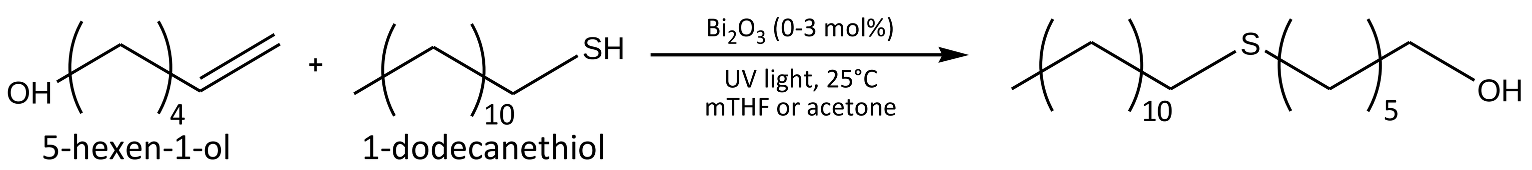

Fig. 4: Reaction performed in this work.

Table 2. Reactions conditions and results of the solvent testing.

Thiol source	Catalyst	Catalyst loading (%)	Solvent	Yield (%)	Conversion (%)
1-dodecanethiol	bismuth(III) oxide	3	mTHF	54	~54
			propylene carbonate	0	0
	none	0	mTHF	52	~52
			acetone:PEG400	65	~65
			acetone	88	~88

The reaction sustainability was improved with the replacement of DMF and by not using the chain transfer agent $BrCCl_3$. No side products were noted, thus the reaction has a high selectivity. The calculation based on GC-MS spectras (fig.5) showed that conversion was similar to yield.

The optimal reagent concentration is 4 equiv. of thiol (less waste of alkene). Residence times below 1 minute can be investigated in the future. The temperature range did not influence the reaction. The optimal light intensity is between 60 to 90% of it (fig. 6).

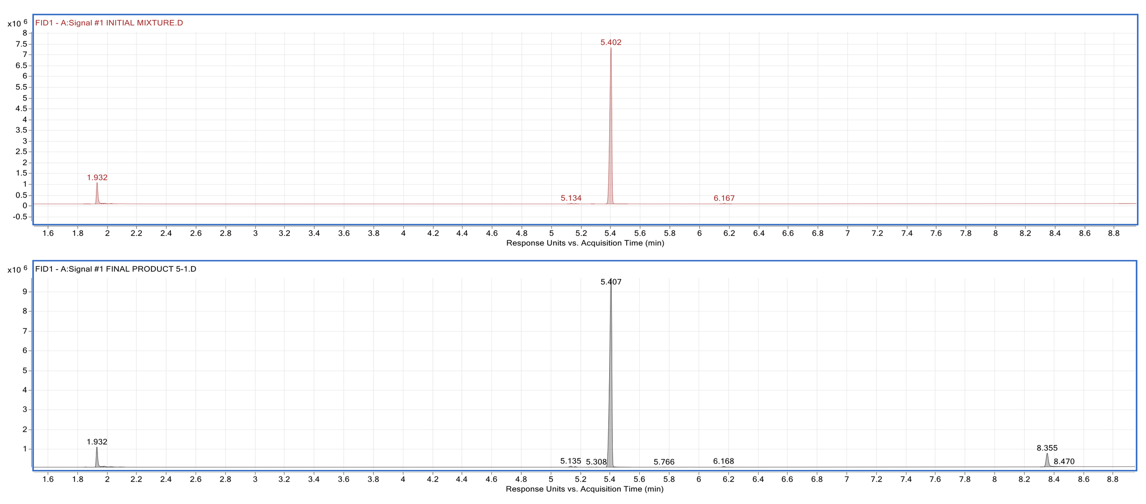

Fig. 5: GC chromatogram of initial and final mixtures. Legend: alkene (1.9 min), thiol (5.4 min) and product (8.3 min).

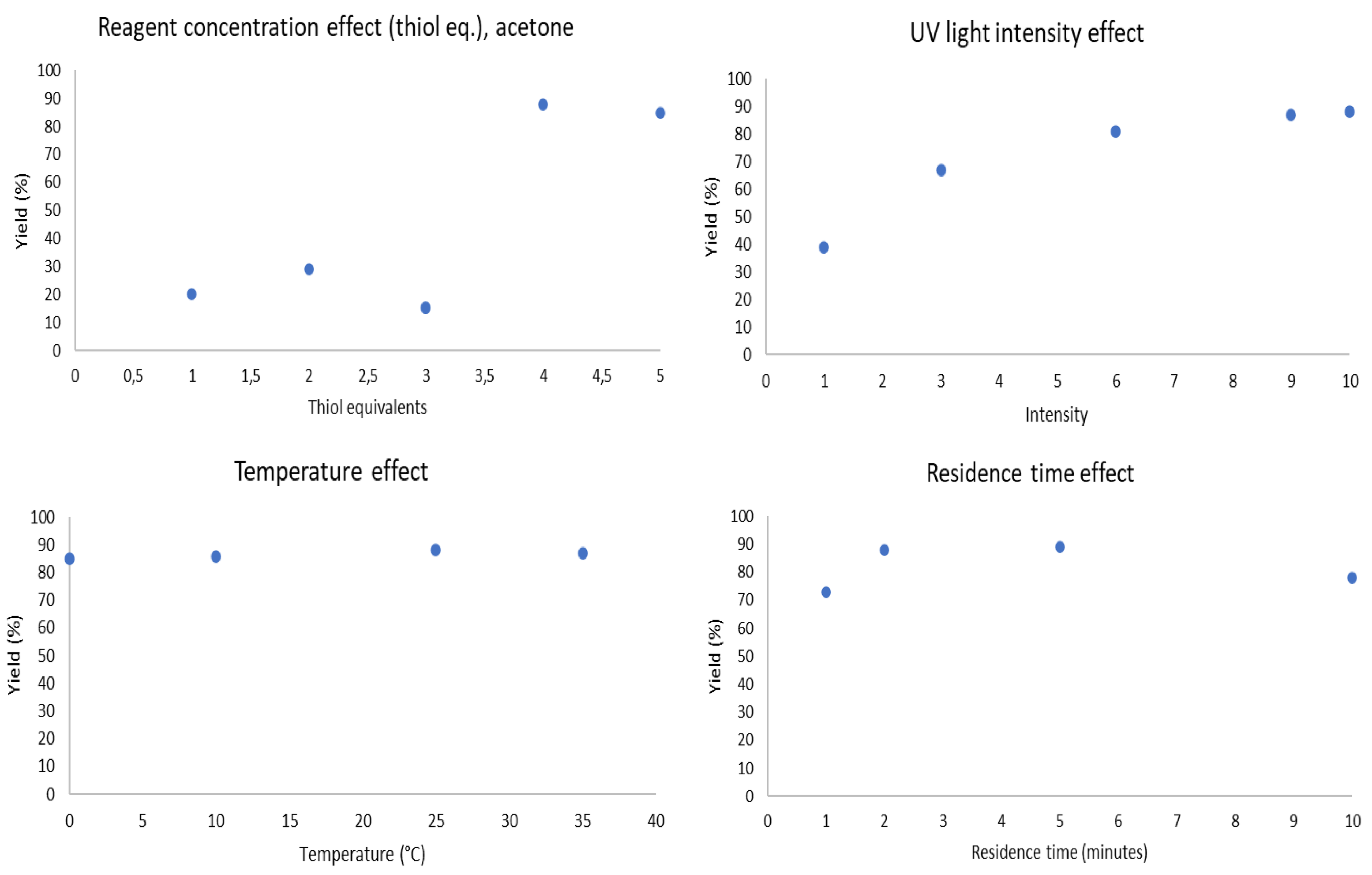

Fig. 6: Graphs of parameters effect on the reaction yield.

Conclusion & Recommendation

- The use of UV light overcame the effect of the catalyst and none was needed to achieve significant yield and conversion.
- The flow reaction was optimized in sustainability and outcome.
- To continue the optimization process, the RoboChem software based on Bayesian optimization can be used and more factors can be explored (e.g. alkene concentration and reactor set-up parameters).

Acknowledgment

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[1] Agora Energiewende. (2018). Climate-neutral industry: Strategies for a net-zero emissions future. Agora Energiewende: Retrieved from https://www.agora-energiewende.de/en/publications/climate-neutral-industry-executive-summary/
[2] Visible-Light-Driven Photocatalytic Initiation of Radical Thiol–Ene Reactions Using Bismuth Oxide, O. O. Fadeyi,* J. J. Mousseau, Y. Feng, C. Allais, P. Nuhant, M. Z. Chen, B. Pierce, R. Robinson, Org Lett, vol. 17, no. 23, pp. 5756–5759, Jan. 2015
[3] Creaflow, "HANU™ Flow Reactors," https://www.creaflow.be/hanutm-flow-reactors.

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