In search of the optimal synthesis of rubrocurcumin derivatives

A study into rubrocurcumin derived colourants

JJC Matera, JP de Rooij, CA Kruithof
Project/Research Group: Ecopro-BBBP
Contact information: jjc.matera@student.avans.nl
Date: June 12th

MNEXT MATERIALS & ENERGY X TRANSITION

introduction

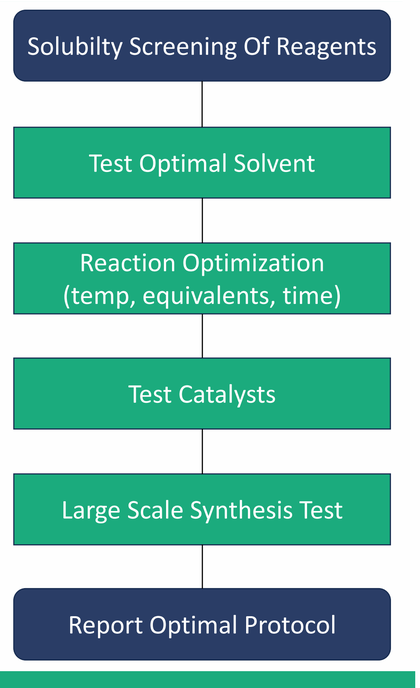
In search of biobased colourants, curcumin has presented itself as a viable yellow colourant. Its derivatives, a borate complex with an alphahydroxy ligand, turn a deep, vibrant red colour [1]. Although its photostability is strongly dependent on the chosen ligand [2], many derivatives have been made. Yet, an optimal synthesis was still needed to achieve large scale production.
This project aims to explore the many different methods used for these synthesis to optimize all parameters into a single synthesis route that is viable for larger scale production of the desired colourants.

Figure 1: from curcumin (right) to rubrocurcumin (left)

Experimental Outlook

When designing an optimal synthesis, multiple factors must be considered, as illustrated in the scheme presented left. The optimal synthesis and purification method will be defined by the product being >99% pure, with a >90% yield and ideally a 100% conversion from curcumin to rubrocurcumin derivative. Our first goal is obtaining the product in high purity.

Confirmation of these parameters will be done with the following methods; Thin Layer Chromatography, HPLC and H-NMR. When the desired >99% Purity is reached, the molecule can be identified using ^{1}H-NMR.



Results

The solubility of curcumin, ligand and boric acid has been tested at room temperature and 50°C. The same goes for the reactivity of curcumin with the previously mentioned reactants in different solvents at room temperature.

Table 1: solubility of different reactants.

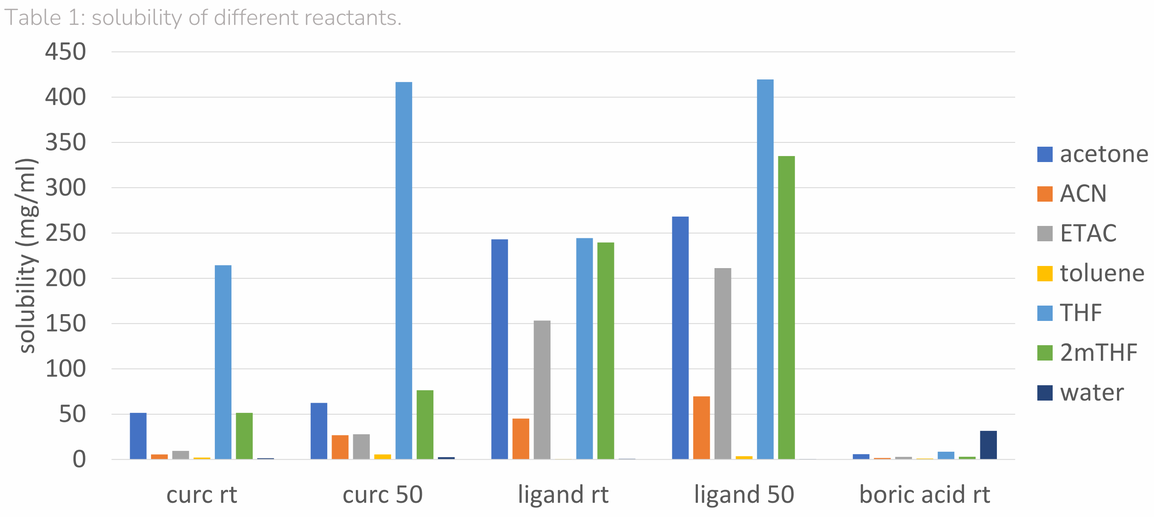
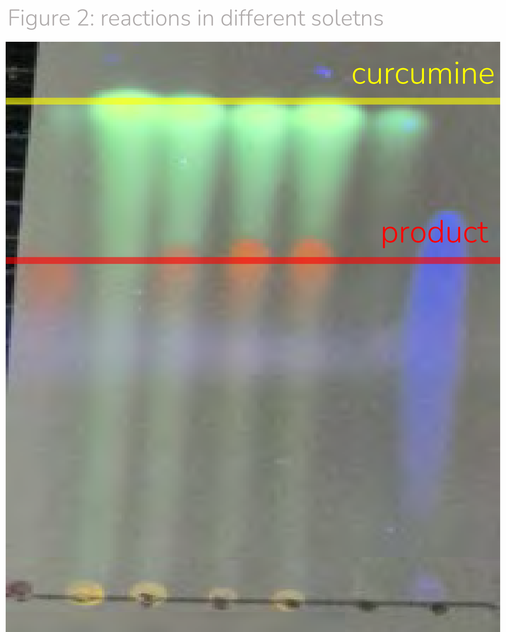


Figure 2: reactions in different soletns



Shown above in figure 2 and left in figure 3, the reaction with different solvents has different effects on the conversion after 24 hours. The solids from the suspension were measured for free curcumin. Curcumin and the ligand (3m) are also shown. Solvents 1 and 2 stand out. Solvent 1 shows the smallest curcumin spot after just 24 hours, while solvent 2 shows no conversion to the desired rubrocurcumin whatsoever.

Figure 3: TLC of reactionproducts of different solvents

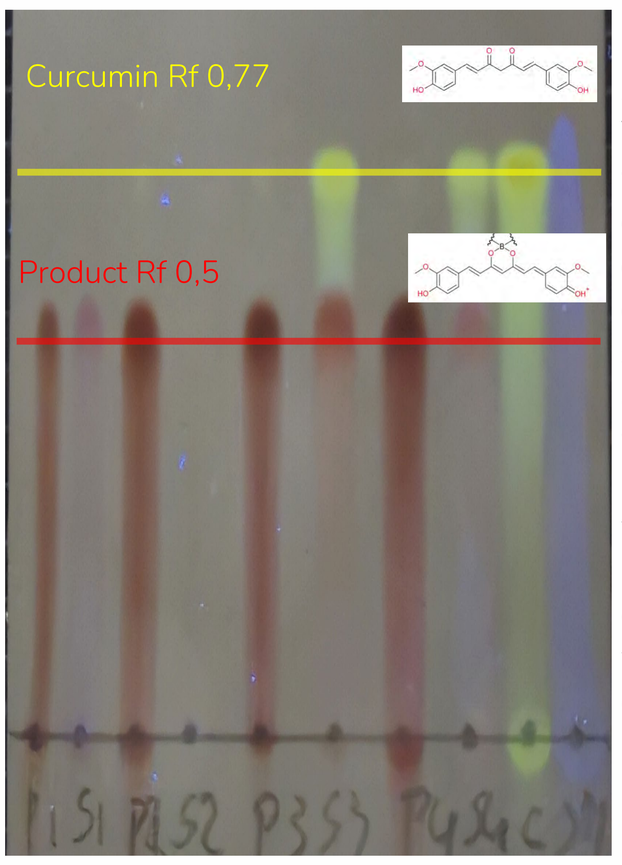


Figure 4: TLC of optimal ratios of reactants.

Shown on the left in Figure 4 The solids and liquid of the reaction were analysed on TLC. The reactions carried out and compared were with different equivalents of reactants to determine the optimal ratios. 1 and 2 seemed the most promising. Almost all curcumin seemed to have reacted with little to no side-product and barely any reactant left or product in the solvent.
In Figure 5, shown below, the HPLC chromatogram is shown. 425nm is the optimal wavelength to measure curcumin content (8min), and 512nm is the optimal wavelength for rubrocurcumin (13min). No measurable or quantifiable impurities or starting materials were found.

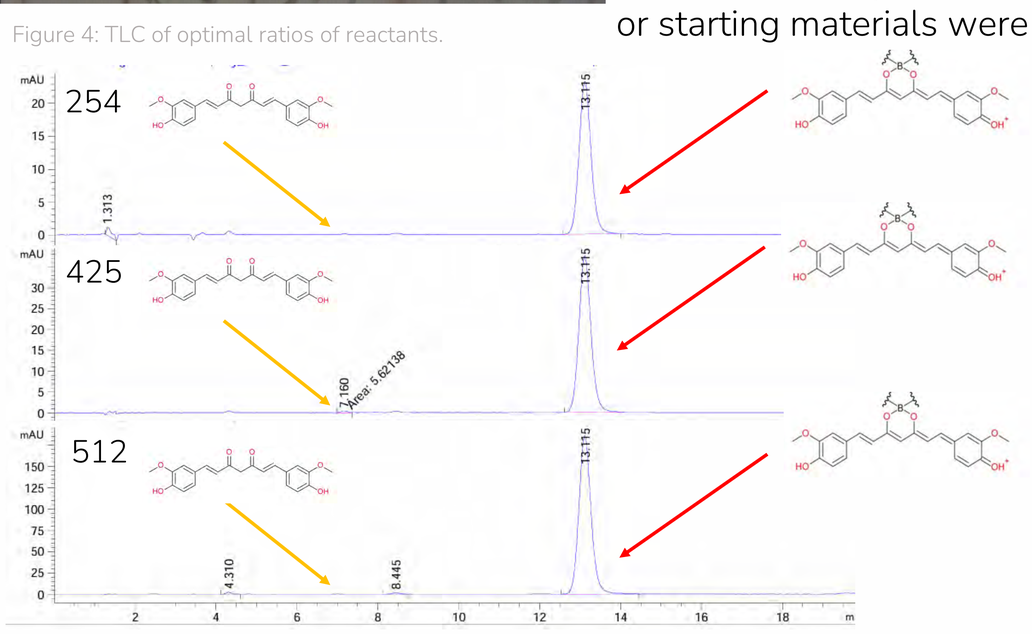


Figure 5: HPLC spectrum of a pure rubrocurcumin derivative.

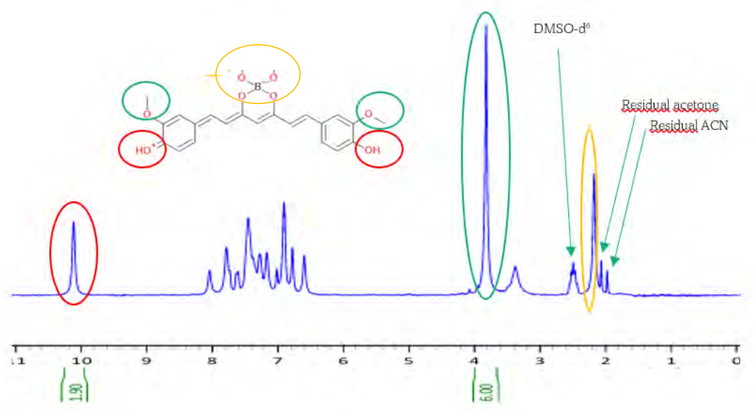
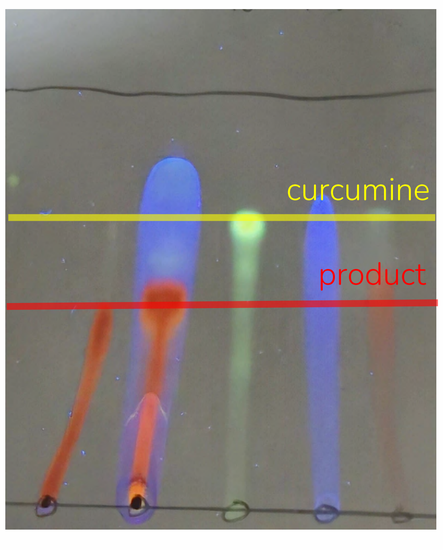


Figure 6: H-NMR spectrum of pure Rubrocurcumin derivative

Shown on the left in Figure 6, the ^{1}H-NMR spectrum of the target molecule is presented. In the spectrum, no solvents were visible. This indicates that the product is solvent-free.



In Figure 7 to the left, the TLC is taken 10 minutes after the reaction with a catalyst has started. Compared to the uncatalyzed reaction, this has improved the reaction time from 24 hours to 10 minutes. Also, two catalysts were tested. One is a conventional one, the other a greener alternative. Both performed the same after 10 minutes and 24 hours.

Figure 7; TLC after 10 minutes of the green catalyzed rubrocurcumin synthesis

Conclusion

A promising solvent has been found for the synthesis of rubrocurcumin derivatives at room temperature. This solvent also proved to be a good solvent for the introduction of a catalyst. Which can reduce reaction times drastically. Due to the implementation of a lower excess of reactants, waste of chemicals can be prevented.

The addition of the catalyst has proven to be of great value. This catalyst reduces reaction time, without producing more side products or changing even more conditions. Initial tests show that on a 1-gram scale, this reaction can be done within 10 minutes, whereafter it can be washed and dried to gain a fairly pure product, only containing some leftover solvent. A great starting point for an optimal synthesis has been laid down with a yield of 85% and HPLC purities of >99%.

References

1.G. Spicer and J. Strickland, 1952, compounds of curcumin and boric acid.
2.C.F. Chignell et. All. 1991, spectral and photochemical properties of curcumin.

Interreg North-West Europe
EUROPEAN UNION