Organocatalytic Surfactants for Direct Asymmetric Aldol Reactions in Aqueous Media

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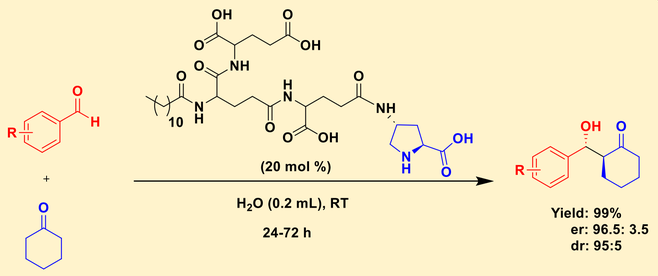
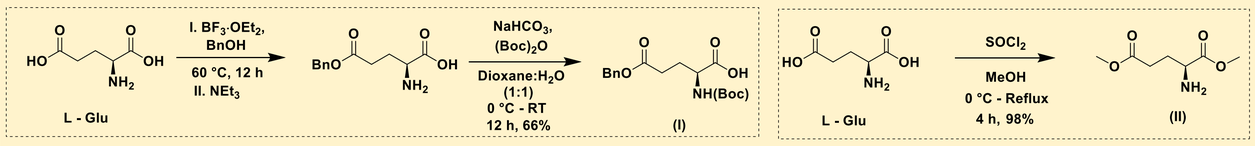
Abstract

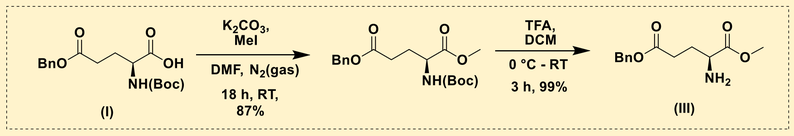
We have developed a peptide surfactant (Pepfactant) based organocatalyst that bears a proline unit as an efficient organocatalyst for the reaction between aromatic aldehydes and cyclohexanone in aqueous media and at room temperature. Using a catalytic loading of 20 mol%, the aldol products were obtained in high yields (99%) and with excellent enantioselectivity (93%) and good diastereoselectivity (95:5). The aqueous solution containing the surfactant could be reused for reactions between four different sets of substrates one after the other without the loss of selectivity. This method provides a greener strategy for carrying out organocatalytic reactions in aqueous media.

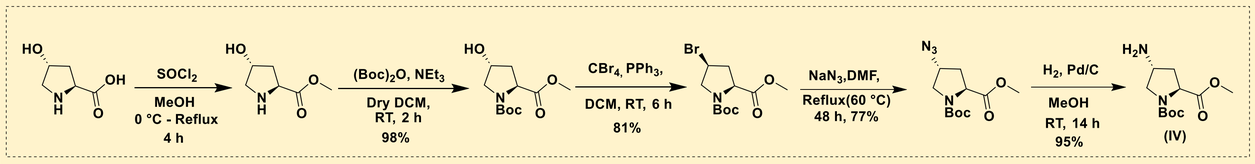


Design and Synthesis

Synthesis of Precursors I - IV

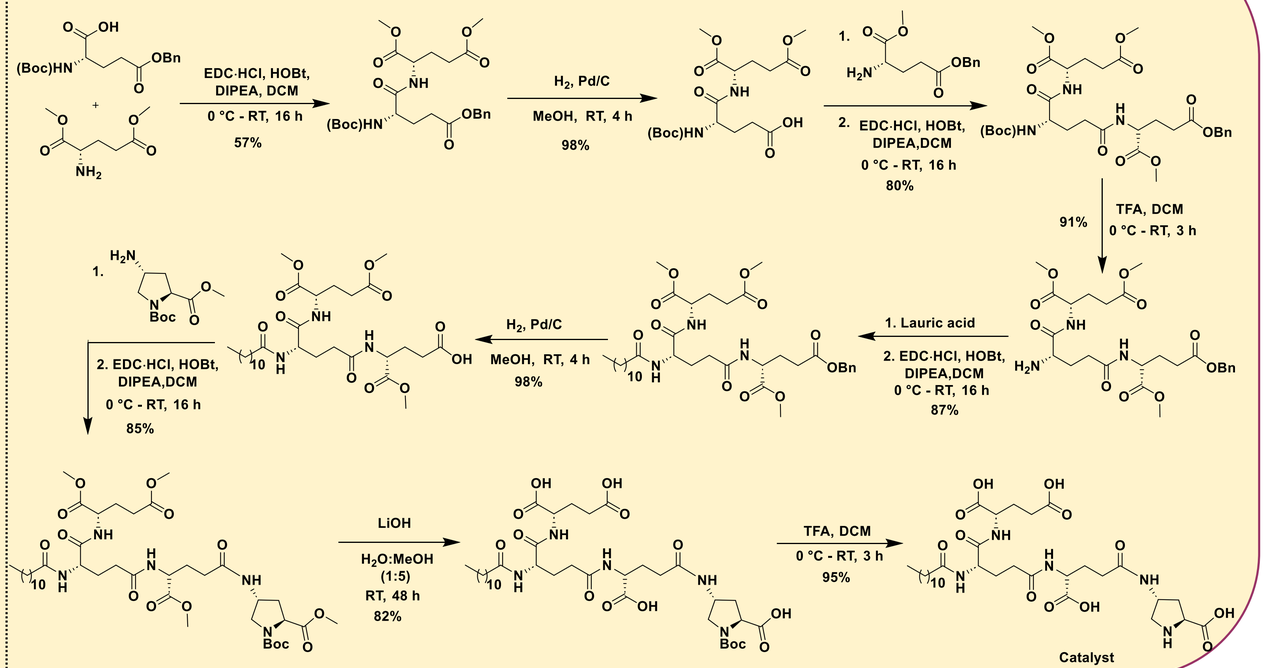




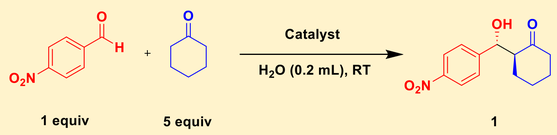


All precursors are synthesized from commercially available L-glutamic acid and *trans*-4-hydroxy-L-proline.

Synthesis of the Catalyst



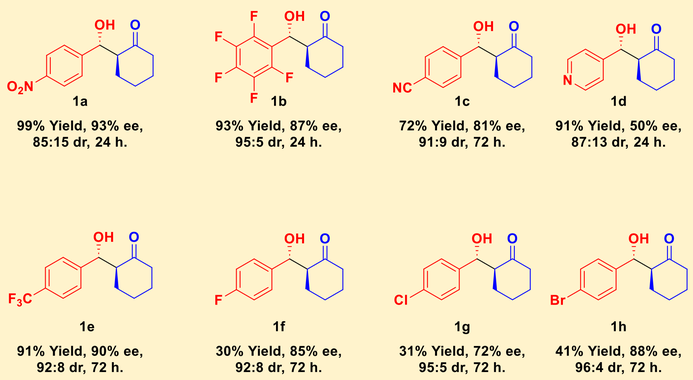
Optimization



S. No.	Catalyst (mol%)	Time (h)	Yield[a] (%)	ee[b] (%)
1	1	58	80	88
2	5	58	99	92
3	10	30	98	91
4	20	24	99	93

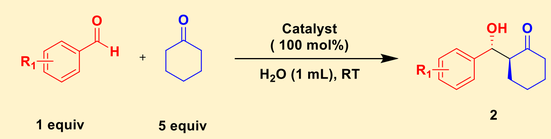
(a) Isolated yield after column chromatography. (b) ee as determined by HPLC analysis using a Chiral AD-H Column.

Substrate Scope



Reactions were performed with catalyst (0.08 mmol), aromatic aldehyde (0.4 mmol) and cyclohexanone (2 mmol) in water (0.2 mL) at room temperature. Isolated yield after column chromatography. Diastereomeric ratio was determined by ^{1}H NMR on a crude sample. ee as determined by HPLC analysis using different Chiral AD-H, OD-H and AS-H Columns.

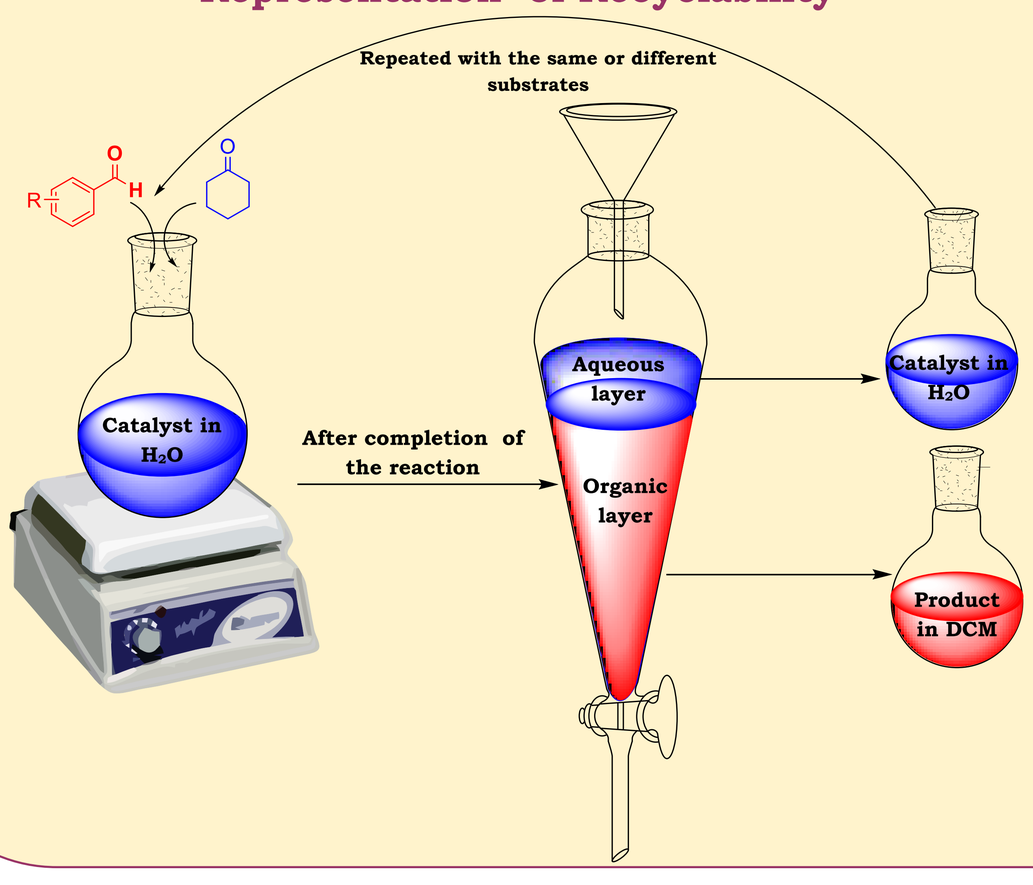
Recyclability Test



S. No.	R_1	Time (h)	Yield[a] (%)	ee[b] (%)
1	NO_2	15	88	90
2	CN	34	89	83
3	C_6F_5	12	91	89
4	CF_3	24	84	91

(a) Isolated yield after column chromatography. (b) ee as determined by HPLC analysis using different Chiral AD-H, OD-H and AS-H Columns.

Representation of Recyclability



Conclusion

- We have designed and synthesized a new water-soluble peptide surfactant (Pepfactant) that contains a proline unit as an organocatalyst.
- These reactions are performed exclusively in water without the use of any additive and at room temperature.

References

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