Studies of a *L*-proline catalyzed Diels-Alder reaction with inverse electron demand by ESI-MS

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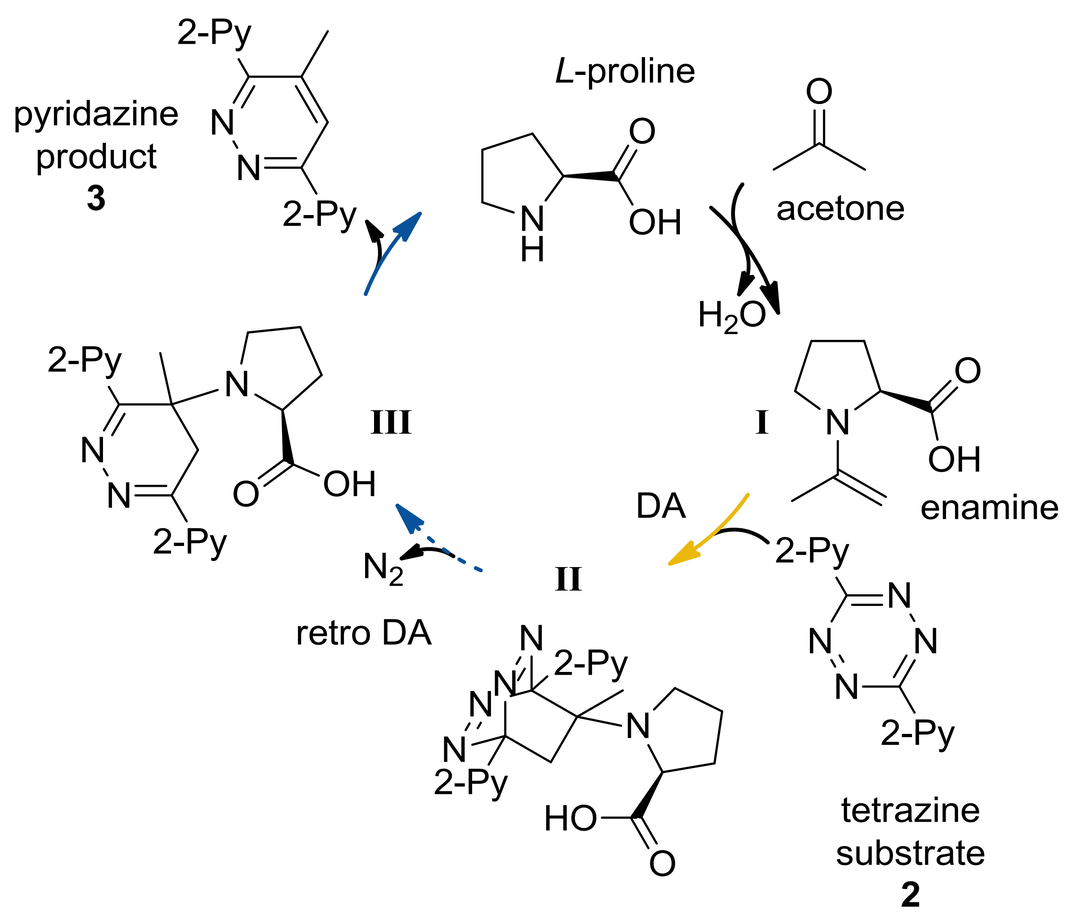
Diels-Alder reaction with inverse electron demand

In 2008, *Xie et al.*[1] published a *L*-proline catalyzed Diels-Alder reaction with inverse electron demand between ketones and aryl-substituted 1,2,4,5-tetrazines which gives easy access to functionalized pyridazines. A mechanism was postulated alongside studies of the scope of the reaction.[1]

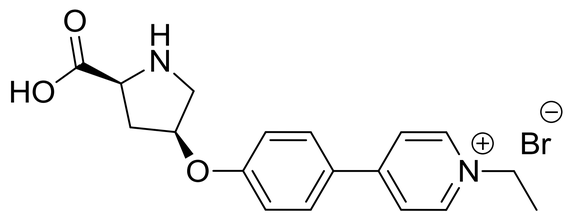


Conclusion

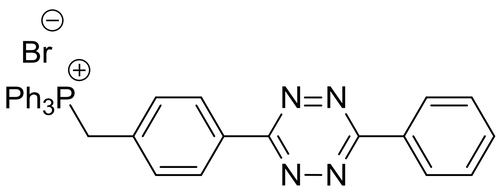
The postulated mechanism of the *L*-proline catalyzed Diels-Alder reaction with inverse electron demand was thoroughly verified. All three intermediates were detected and characterized. [6]

Charge-tagging

Covalently linked charge-tags can be attached to the participating molecules usually in the form of alkylated amines or phosphanes.[2,3] As a result, all species containing the charge-tag should have similarly high ESI response factors[2,4]. For this study the charge-tagged tetrazine **4·Br** was synthesized. The charge-tagged *L*-proline derivative **1·Br**[5] was used as well.

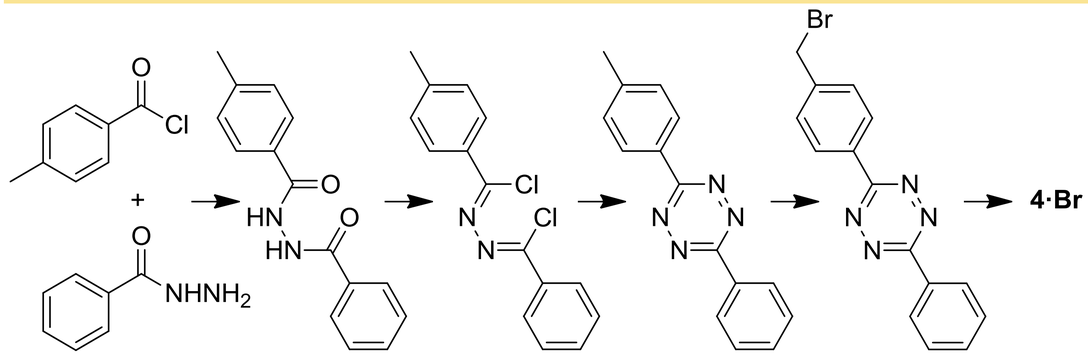


1·Br



4·Br

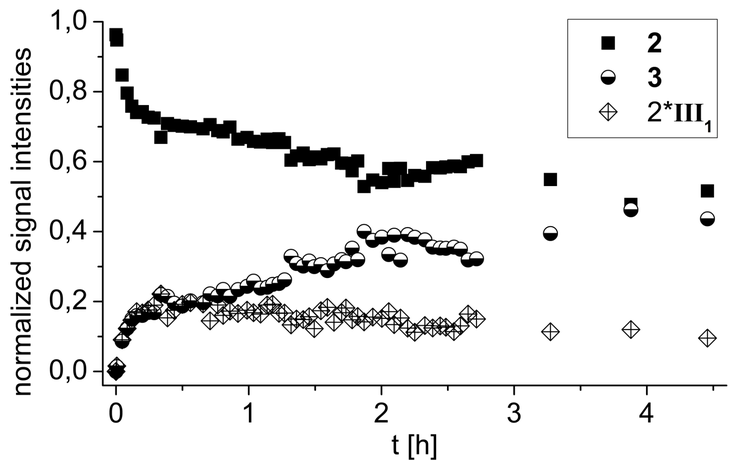
Synthesis of charge-tagged tetrazine 4·Br



ESI-MS studies of reacting solutions

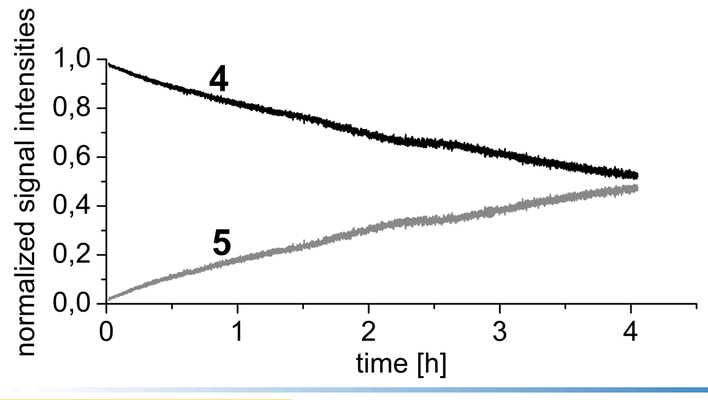
R1: *L*-proline & untagged substrate

The substrate **2,** product **3,** and the third intermediate $\mathbf{III}_1$ were detected during a kinetic study. $\mathbf{I}_1$ could be detected in a reaction with 0.05 eq. **2**.



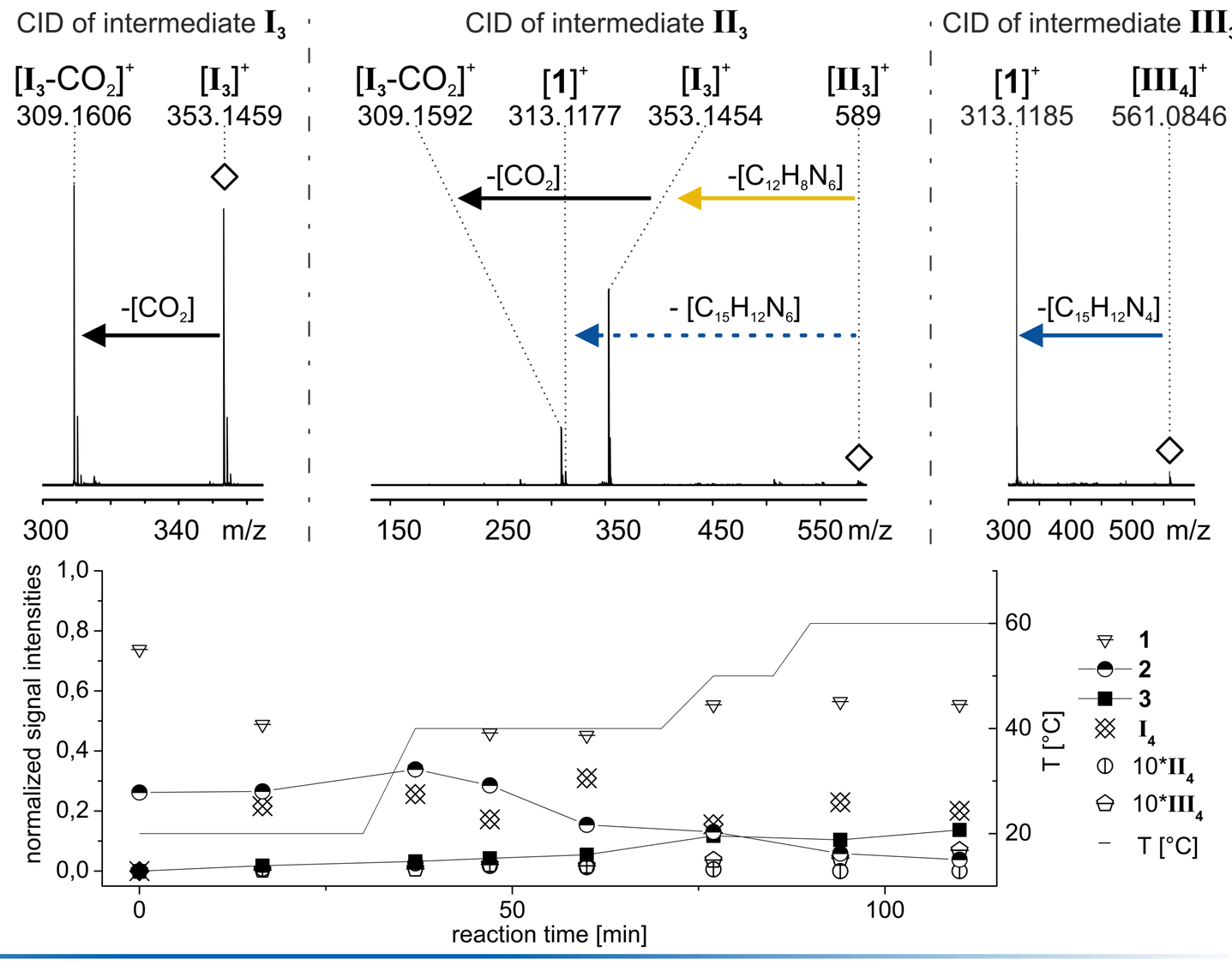
R2: *L*-proline & charge-tagged substrate

Substrate **4** and product **5** were monitored. $\mathbf{III}_2$ can only be detected in traces.



R3: charge-tagged proline 1·Br & untagged substrate

Substrate **2**, product **3**, catalyst **1·Br,** and all three intermediates were detected. CID experiments for all intermediates were conducted. Thus, single steps of the catalytic cycle could be mimicked in the gas phase.



References

[1] H. Xie, L. Zu, H. R. Oueis, H. Li, J. Wang, W. Wang, *Org. Lett.* **2008**, *10*, 1923–1926.
[2] L. P. E. Yunker, R. L. Stoddard, J. S. McIndoe, *J. Mass Spectrom.* **2014**, *49*, 1–8.
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[5] J. A. Willms, R. Beel, M. L. Schmidt, C. Mundt, M. Engeser, *Beilstein J. Org. Chem.* **2014**, *10*, 2027–2037.
[6] A. Schnell, J. A. Willms, M. Engeser, *Beilstein J. Org. Chem.* **2018**, submitted.