RUHR-UNIVERSITÄT BOCHUM

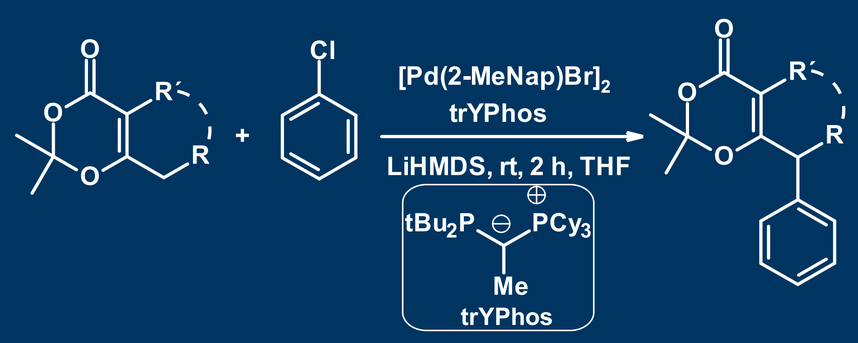
Pd-Catalyzed γ-Arylation of Acylketene Synthons with Aryl Chlorides Enabled by Ylide-Functionalized Phosphines (YPhos)

Sourav Manna[a], Florian Papp[a], Yusei Hisata[b], Julian Löffler[a], Martyna Rybka[a], Viktoria H. Gessner[a,*], Yoichi Hoshimoto[b,*], Lukas J. Gooßen[a,*]

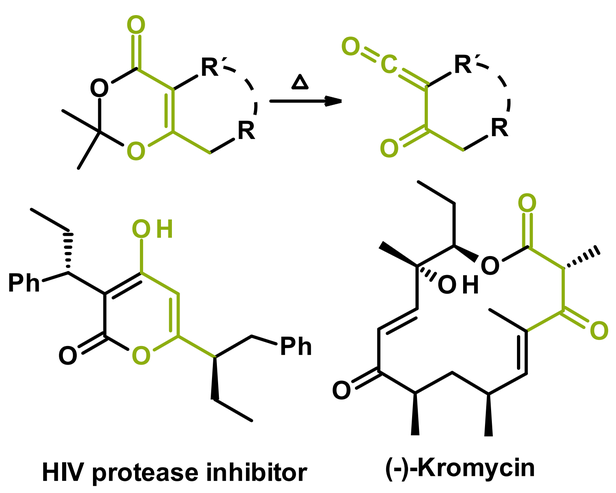
[a]Fakultät Chemie und Biochemie, Ruhr Universität Bochum, [b]Department of Applied Chemistry, Faculty of Engineering, Osaka University

Abstract:

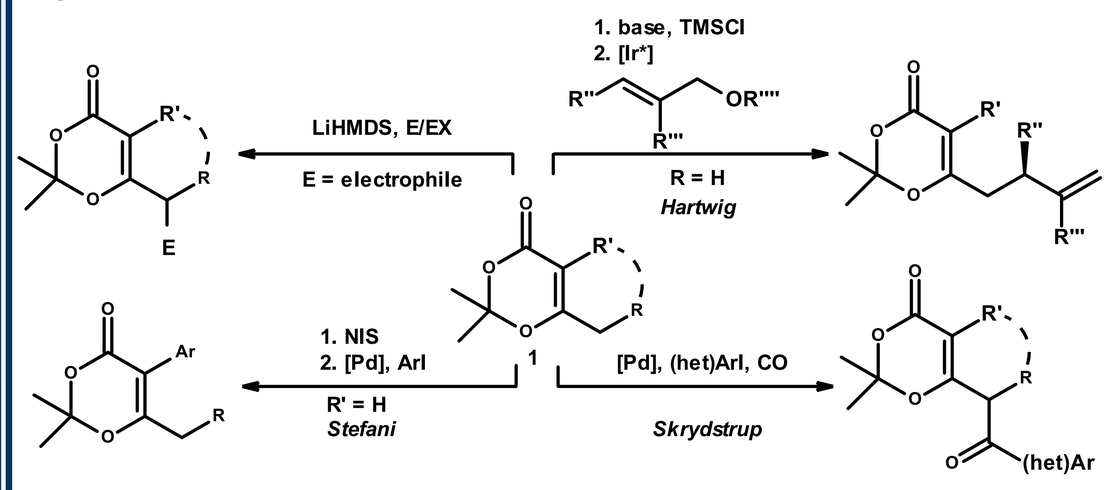
A catalyst system based on palladium 2-methylnaphthyl complexes bearing ylide-functionalized phosphines (YPhos) was found to enable the selective γ-arylation of 1,3-dioxinone derivatives with diversely functionalized aryl, heteroaryl, and vinyl chlorides. The products were further converted into 1,3-diketones and various heterocycles, highlighting their function as synthetic hubs. Experimental and computational studies revealed that bulky, electron-rich YPhos ligands are uniquely effective because they enable the oxidative addition of aryl chlorides at room temperature in the presence of the thermally sensitive enolates while at the same time efficiently promoting the rate-limiting reductive elimination step.



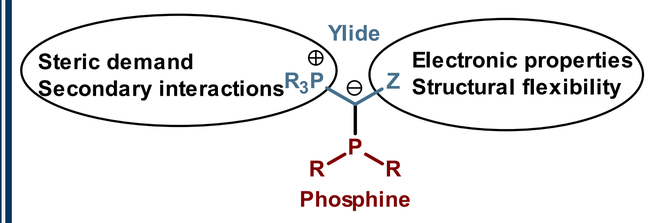
Importance of 1,3-dioxinone



Synthetic modifications of 1,3-dioxinones[1],[2],[3]

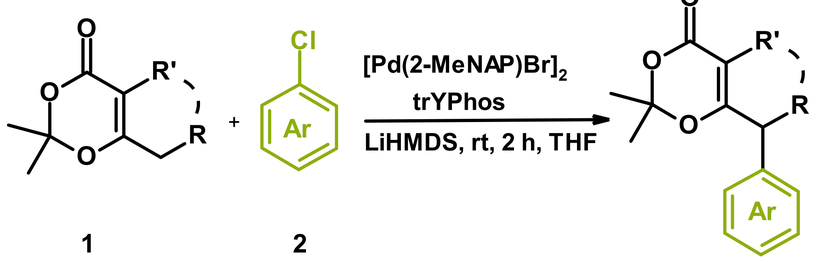


YPhos Ligands[4]

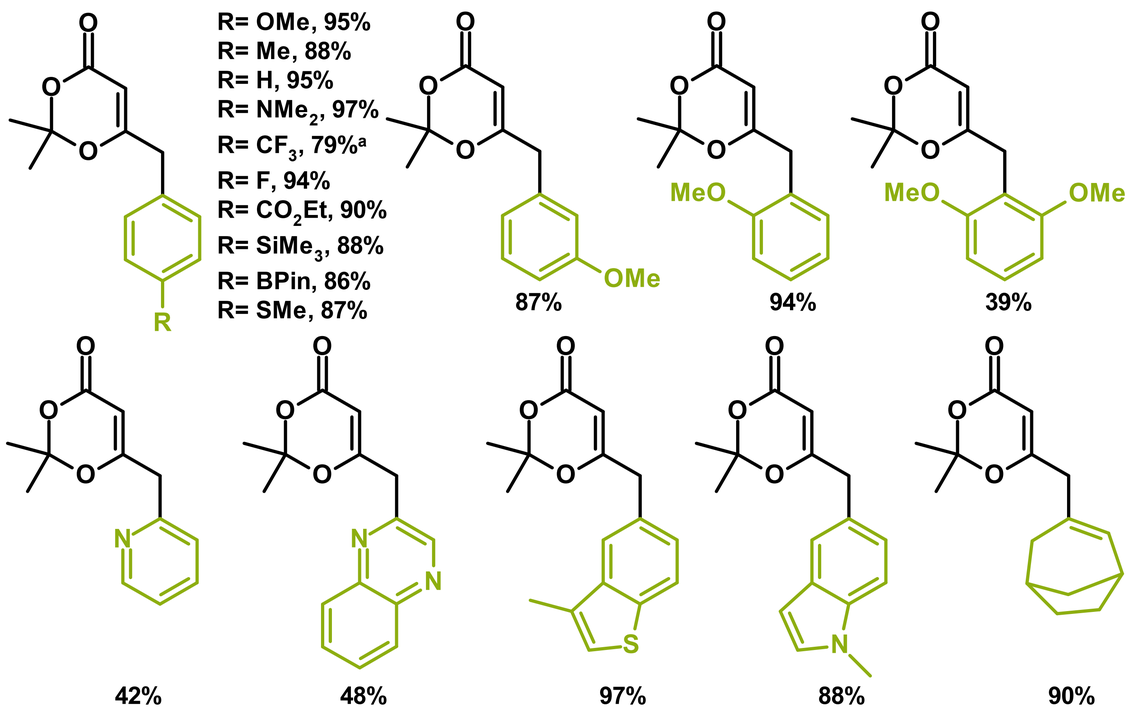


- Oxidative Addition of ArCl at rt.
- Enable Challenging Transmetalation
- Promoting challenging Reductive elimination (This Work).

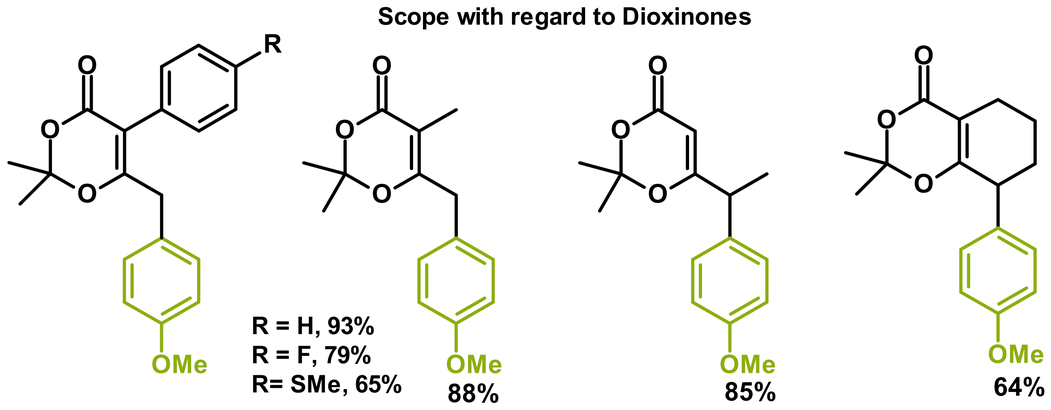
Scope of Aryl Chlorides and Dioxinones



Scope with regard to aryl chlorides

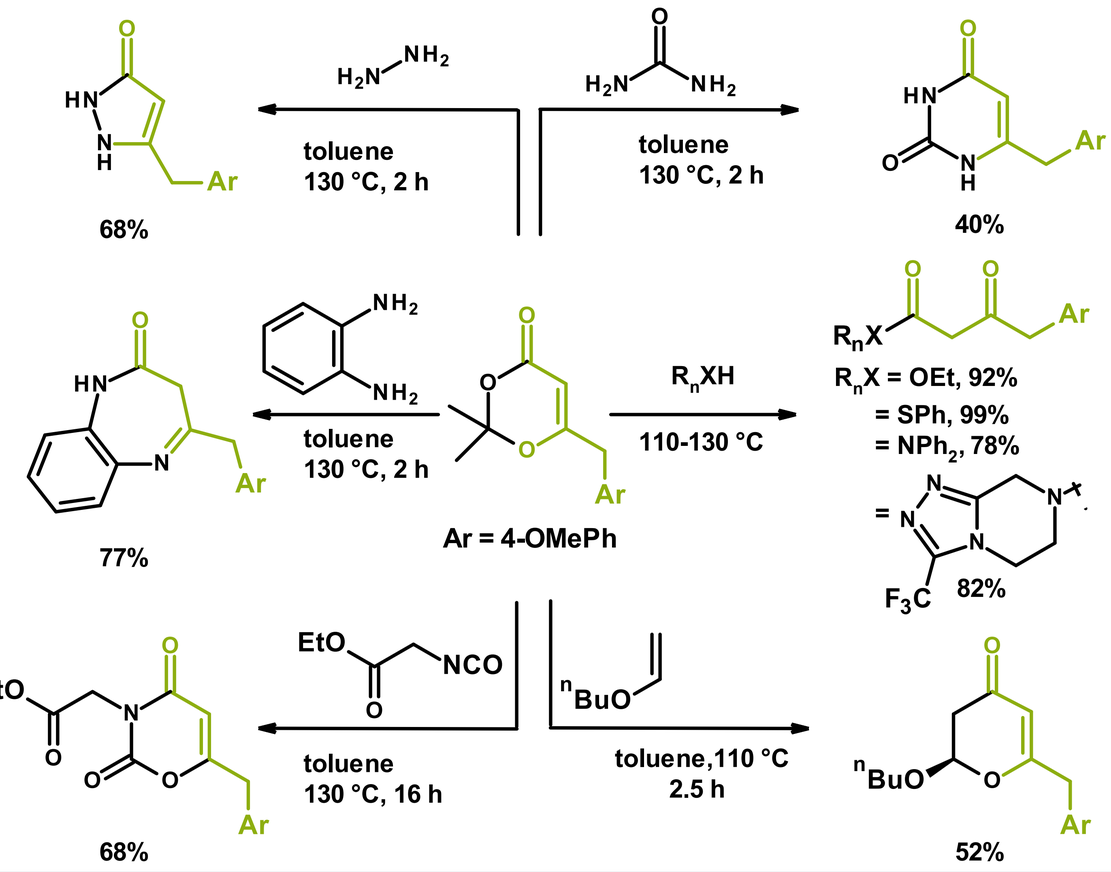


Scope with regard to Dioxinones

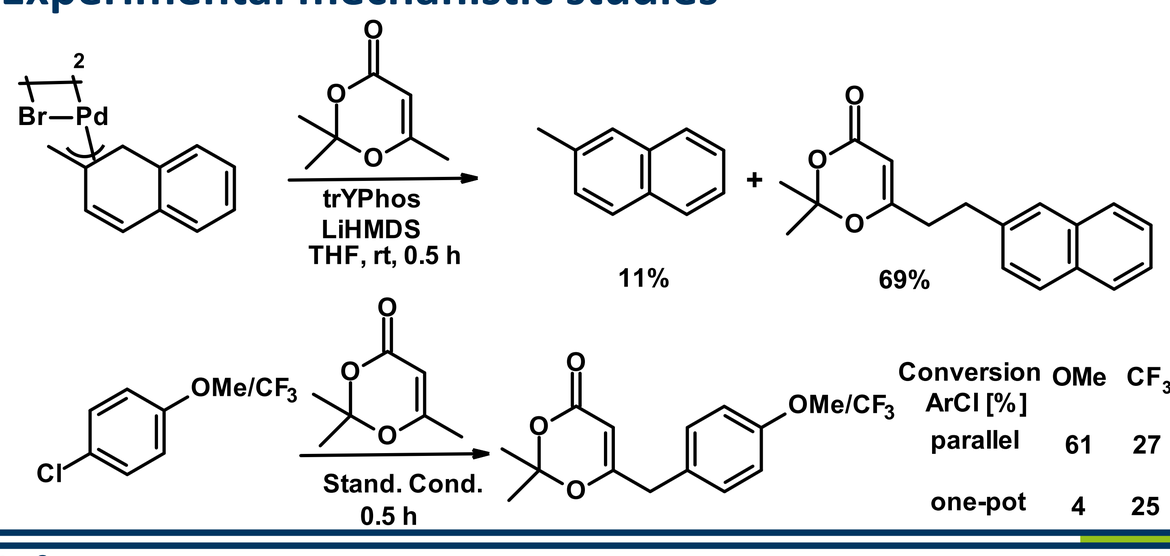


Conditions: 0.50 mmol 2, 1.1 equiv. 1, 2.5 mol% $[Pd(2\text{-MeNAP})Br]_2$, 5.0 mol% trYPhos, 1.5 equiv. LiHMDS, THF, rt, 2 h. Isolated yield.

Follow-up transformations



Experimental mechanistic studies



Conclusion and Outlook

A catalyst generated from a bromo-bridged methylnaphthyl palladium dimer and trYPhos effectively promotes γ-arylations of acylketene synthons with aryl, heteroaryl and vinyl chlorides. This demonstrates that despite their strongly electron-donating character that is vital for the smooth activation of aryl chlorides, YPhos ligands can still be tuned in a way that they enable challenging reductive elimination steps.

References

[1] M. F. Carroll, A. R. Bader, *J. Am. Chem. Soc.* **1952**, *74*, 6305–6305. [2] M. Chen, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2014**, *53*, 12172–12176. [3] I. S. Makarov, T. Kuwahara, X. Jusseau, I. Ryu, A. T. Lindhardt, T. Skrydstrup, *J. Am. Chem. Soc.* **2015**, *137*, 14043–14046.[4] S. Lapointe, A. Sarbajna, V. H. Gessner, *Acc. Chem. Res.*, **2022**, *55*, 770–782 [5] S. Manna, F. papp, Y. Hisata, J. Löffler, M. Rybka, V. H. Gessner, Y. Hoshimoto, L. J. Gooßen, *Adv. Synth. Catal.* **2024**, *366*, 1-7.

We gratefully acknowledge financial support from:

EVONIK KRAFT FÜR NEUES · umicore · RESOLV RUHR EXPLORES SOLVATION CLUSTER OF EXCELLENCE - EXC 2033 · FCI FONDS DER CHEMISCHEN INDUSTRIE