

Decarbonylative olefination of aldehydes to alkenes

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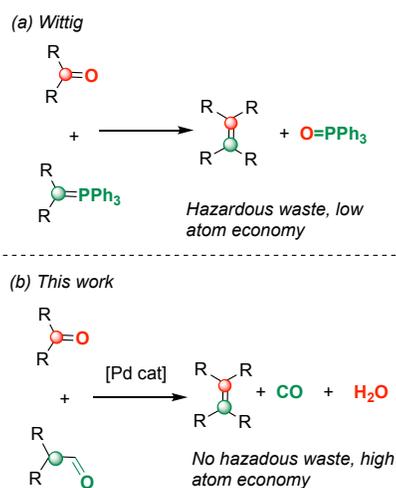
Supporting Information Placeholder

ABSTRACT: New atom-economical alternatives to Wittig chemistry are needed construct olefins from carbonyl complexes, but none have been developed to-date. Here we report an atom-economical olefination of carbonyls via aldol-decarbonylative coupling of aldehydes using robust and recyclable supported Pd catalysts, producing only CO and H₂O as waste. The reaction accommodates homocoupling of aldehydes with an α -methylene groups, as well as heterocoupling. Computations provide insight into the selectivity of the reaction. The tandem aldol-decarbonylation reaction opens the door to exploration of new carbonyl reactivity to construct olefins.

The carbonyl olefination of ketones or aldehydes by phosphorous ylids, discovered by Wittig (Scheme 1a), has been a cornerstone of modern synthesis due to its utility and reliability.¹⁻² However, the utility of the chemistry is hindered by the need to pre-form phosphorous ylids and the production of stoichiometric waste, necessitating the development of more atom-economical alternatives. Recently we reported the high activity of heterogeneous catalysts based on Pd-doped hydrotalcites (Pd-HTs) for selective decarbonylation of aldehydes.⁴ In the course of this study we observed that α,β -unsaturated aldehydes decarbonylate faster than aromatic and saturated aliphatic aldehydes. Given that hydrotalcites, composed of metal hydroxide sheets sandwiched by anions and water, have basic sites, they can promote aldol condensation.⁷⁻⁸ We thus anticipated that aliphatic aldehydes would undergo competing aldol condensation to form forms α,β -unsaturated aldehydes, which can undergo further decarbonylation to form alkenes (Scheme 1a and 2). Thus, we set out to develop a practical catalytic process for decarbonylative coupling of carbonyls to selectively afford alkenes through decarbonylative homo- and hetero-coupling.

Catalysts for tandem aldol condensation-decarbonylation should be bifunctional, consisting of catalytic sites effective for both steps. It would be advantageous to be able to tune the activity of both sites independently in order to optimize selectivity for different carbonyl substrates.

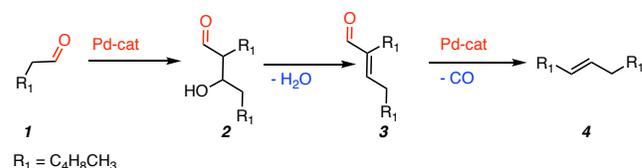
Scheme 1



Given that the aldol condensation is catalyzed by either acid or base sites, we thus considered hydrotalcites, MgO, Al₂O₃ and silica as supports. However, the electronic nature of the support will also affect the activity of the Pd phase, which catalyzes the decarbonylation.⁹⁻¹⁰ In order to explore the potential of optimizing both steps, we synthesized and screened Pd-HT, Pd-Al₂O₃, Pd-SiO₂, and Pd-MgO for the reaction in Scheme 2.

Initial findings showed that Pd-HTs facilitates the conversion of neat aldehydes with α -methylene groups to the α,β -unsaturated carbonyls, which decarbonylate to afford internal alkenes (Scheme 2). The reactions require low Pd loading (0.1 mol% Pd) and proceed at 150 °C or above using microwave and conventional heating. Heptanal thus afforded (E)-tridec-6-ene, an olefin with (2n-1) carbons and some respective aldol intermediates **2** and **3** (Scheme 2).

Scheme 2



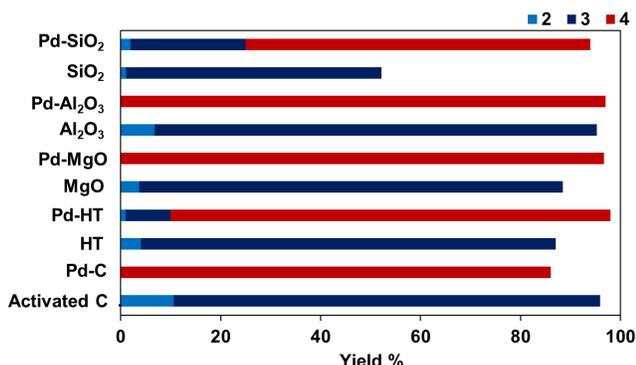


Figure 1. Product distribution of Pd catalysts and supports in decarbonylative olefination of heptanal at 180 °C. (Conditions: 0.1 mol% Pd, 8 hr).

The activity of five supported Pd catalysts were examined with heptanal as model substrate at 150 and 180 °C, (Figure 1 and ESI S1). The activity of the supports was tested as a control in order to distinguish the activity for aldol vs decarbonylation. Consistent with our initial hypothesis, the supports showed good to excellent activity for aldol condensation, but only the Pd catalysts afforded alkene product (**4**, Figure 1).

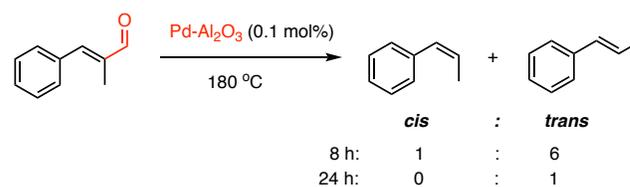
At 150 °C Pd-Al₂O₃ afforded highest yield of **4** (35%), followed by Pd-C with 20% in 8 h (ESI Figure S1). However, the overall conversion of aldehyde with Pd/C was the lowest of all the catalysts tested, suggesting it was a poor catalyst for the aldol condensation. In contrast, Pd-MgO and Pd-HT afforded full conversion of substrate, but only 10-15% yield of the alkene. The trend for activity for aldol condensation was thus established as MgO > HT > Al₂O₃ > activated carbon > SiO₂; and for decarbonylation as: Pd-Al₂O₃ > Pd-C > Pd-HT > Pd-MgO > Pd-SiO₂. At 180 °C quantitative yields of alkene **4** could be obtained with Pd-Al₂O₃, Pd-HT and Pd-MgO in only 8 hours, while Pd-C and Pd-SiO₂ afforded over 70 and 82% respectively (Figure 1).

Reaction time courses of the three most promising catalysts revealed further details about the relative aldol vs decarbonylation activity. At 100 °C, no decarbonylation is observed, and aldol activity follows the trend Pd-HT~Pd-MgO >> Pd-Al₂O₃ (ESI Figure S2). Thus, the strong basic sites on MgO and HT are significantly more effective at facilitating aldol condensation than the Lewis acidic sites of Al₂O₃. At 150 °C decarbonylation yields range from 38 – 78% of **4** in 24 hr, discerning the activity trend for decarbonylation: Pd-Al₂O₃ > Pd-HT > Pd-MgO (ESI Figure S3), while at 180 °C decarbonylation is so rapid that no intermediate **3** is observed at the end of the reaction (ESI Figure S4). Decarbonylation rate is thus rate-determining, and is sensitive to temperature in the range studied. Further reactions were explored using Pd-Al₂O₃ as the most active catalyst.

Curiously, we observation that the configuration of aldol intermediate **3** is *cis* w.r.t. R-groups, while alkene **4** is a *trans* alkene (ESI Figure S5). Based on Zimmerman-

Traxler 6-membered transition state for the alkylation of the enolate, *trans* configuration of **3** suggests it was derived from a *cis* enolate. The latter could be preferred when the acid/base sites are immobilized on a solid support. The *trans* geometry of **4** indicates that the catalyst facilitates both isomerization and decarbonylation of **3**. As further evidence for the latter, we find that α -methylcinnamaldehyde (*cis* w.r.t. the R-groups) affords a 1:6 ratio of *cis*:*trans* propylbenzene in 8 hours of reaction with Pd-Al₂O₃, and complete conversion to the *trans* product in 24 hours (ESI Figure S6). This is consistent with the assertion that the catalyst facilitates both decarbonylation and isomerization to the thermodynamic alkene isomer. No double bond migration was observed.

Scheme 3



We briefly explored the substrate scope of the decarbonylative olefination. Aliphatic aldehydes afford excellent yields (Table 1, entries 1 and 2), while branched aldehydes react more slowly (entries 4 and 5). The latter is due to slower aldol for hindered secondary aldehydes, as evidenced by no unreacted aldol intermediates after 8 hours. In the case of phenylacetaldehyde, the lower yield (40%) is due to the fast decarbonylation of the substrate relative to aldol condensation, affording toluene. The latter emphasizes that obtaining olefin selectively requires balancing rates of three independent reactions: decarbonylation of initial substrate, aldol and decarbonylation of aldol condensation product.

Table 1. Substrate scope for decarboxylative olefination.

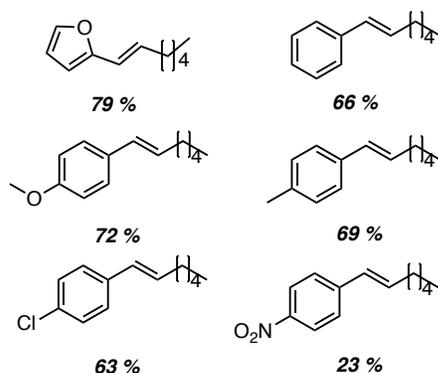
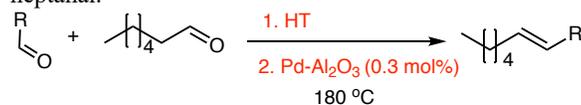
No.	Substrate	Olefin product	% Yield
1			97
2			88
3			82
4			45
5			36
6			

Conditions: 14 mmol substrate, 0.1 mol% Pd-Al₂O₃, 180 °C, 8 h.

We also explored whether this reaction can be optimized in the heterocoupling reactions of two aldehydes. Selectivity for heterocoupling is favored by combining an enolizable aldehyde with a non-enolizable one, such as benzaldehyde. When the reaction was performed using the conditions optimized for homocoupling, selectivity for the desired heterocoupled olefin was low due to rapid decarbonylation of the non-enolizable aldehyde relative to aldol condensation. To increase selectivity for the cross-aldol condensation we introduced a more effective solid aldol catalyst than alumina – hydrotalcite (HT). By using only HT in the first stage of the reaction one can pre-form the hetero-aldol product, which is then decarbonylated by Pd-Al₂O₃. This resulted in high selectivity and yield of the desired olefin (79% yield in 6 hours for furfural and heptanal).

The yields obtained for the heterocoupling of a selection of substrates are summarized in Table 2. All the substrates used afforded full conversion, and good to excellent yields of desired olefin, although competing homocoupling of heptanal decreased selectivity. The selectivity for heterocoupling is limited by the aldol step, which is affected by the relative reactivity of the non-enolizable aldehydes. For example, furfural carbonyl carbon is more electrophilic than that of benzene, and thus more reactive as aldol electrophile (crudely approximated by the Mulliken charges, ESI Table S1??). However, synthetic conditions can be further optimized to improve selectivity for the hetero aldol.

Table 2. Substrate scope for heterocoupling of aldehydes with heptanal.



Conditions: 1. 7 mmol heptanal, 10 mmol aldehyde, 50 mg HT, 180 °C, 2 h; 2. Add 0.3 mol%, Pd-Al₂O₃, 180 °C, 6 h.

Reaction thermodynamics. We briefly explored the relative thermodynamic stability of the intermediates and products in the reaction with heptanal (Scheme 2). All calculations were carried out with the PM7 semiempirical method in gas phase using the Gaussian 16 software.¹

Geometries were fully optimized, and all minima were verified to have to imaginary vibrational frequencies. Free energies were evaluated at 298 K. Computational results indicate that while initial aldol addition is 2.9 kcal/mol uphill, the aldol condensation product is thermodynamically favorable ($\Delta G_{\text{rxn}} = -3.9$ and -4.0 kcal/mol respectively for *trans* and *cis* α,β -unsaturated carbonyl) w.r.t. heptanal (**Figure 1**). The subsequent decarbonylation to the *cis*-olefin is almost thermoneutral (-0.5 kcal/mol), but the isomerization to the *trans*-olefin (**4**) drives ΔG_{rxn} to be slightly more favorable (-1.3 kcal/mol), bringing the overall ΔG_{rxn} of the two-step process to -5.2 kcal/mol (vs. -4.4 kcal/mol for the *cis*-olefin). These calculations are consistent with the experimental observation of the *trans*-olefin product. Furthermore, they suggest that while the reaction is slightly thermodynamically favorable, it is close enough to thermoneutral to potentially allow for reversibility under appropriate conditions.

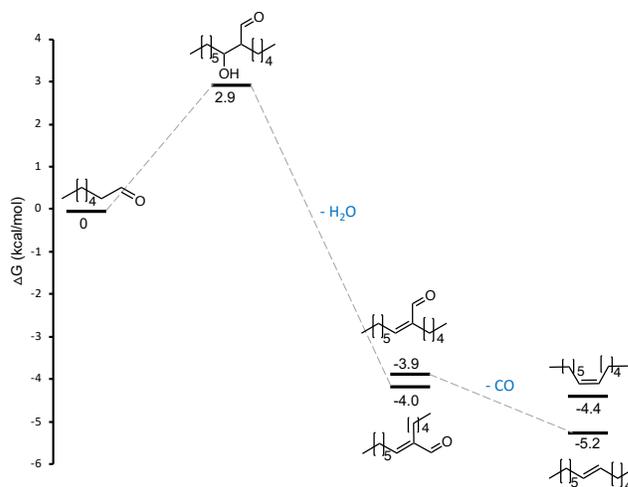


Figure 1. Free energy diagram for decarbonylative olefination of heptanal (Scheme 2).

The recyclability of the Pd-Al₂O₃ was explored for this reaction with heptanal. The catalyst was separated from after reaction centrifugation, washing and drying, and reused. The yields of products obtained over 9 cycles indicate that the catalyst retains activity over 9 cycles (ESI Figure S7), with a small decrease in selectivity remaining 93% - 98% after cycle 4. Elemental analysis of the catalyst after 9 cycles shows negligible loss of Al (within the standard error of the as-prepared catalysts), but a 23 wt% decrease in Pd, suggesting this could be a reason for the small drop in selectivity.

To investigate whether Pd-Al₂O₃ was operationally heterogeneous in this reaction, we applied a combination of hot filtration, selective poisoning, and mercury poisoning tests. Hot filtration was performed by sampling a portion of the reaction mixture after 3 h of reaction and passing the mixture through a hot frit (2 μm). After 5 h further reaction, the concentration of olefin **4** did not change

significantly from the time of filtration (ESI Figure S8a), suggesting that the catalytic species are absent from the filtrate. The catalytic activity was also completely quenched by mercury poisoning, which amalgamates with supported palladium.¹² The reaction produced product **3** as the only product and no product **4** was observed. (ESI Figure S8b). However, catalytic activity was also quenched by Quadrapure-TU,¹³⁻¹⁴ a known scavenger for soluble Pd complexes and nanoparticles.¹⁵ The latter suggests catalytic involvement of both heterogeneous and soluble Pd species in this multi-step process. The presence of complex equilibrium between surface-bound and soluble Pd species is also likely, which is not atypical of heterogeneous catalysis in the condensed phase. The catalyst behavior warrants future operando spectroscopic studies to further interrogate the nature of the catalytic species.

Conclusion

Here we report a new transformation decarboxylative olefination of aldehydes, proceeding via aldol and decarbonylation. The reaction is effectively facilitated by Pd-Al₂O₃ as decarbonylation catalyst, and rehydrated hydrotalcite as the optimized aldol catalyst. The reaction has been optimized for both homocoupling and heterocoupling of aldehydes. The catalyst is recyclable, retained its activity over 9 cycles with minor decrease in selectivity after. Poisoning experiments implicate involvement of surface-bound and soluble Pd species.

obtaining olefin selectively requires balancing rates of three independent reactions: decarbonylation of initial substrate, aldol and decarbonylation of aldol condensation product.

ASSOCIATED CONTENT

Supporting Information is available detailing catalyst synthesis and characterization, additional figures and NMR characterization of products.

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