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Communication

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Decarbonylative olefination of aldehydes to alkenes

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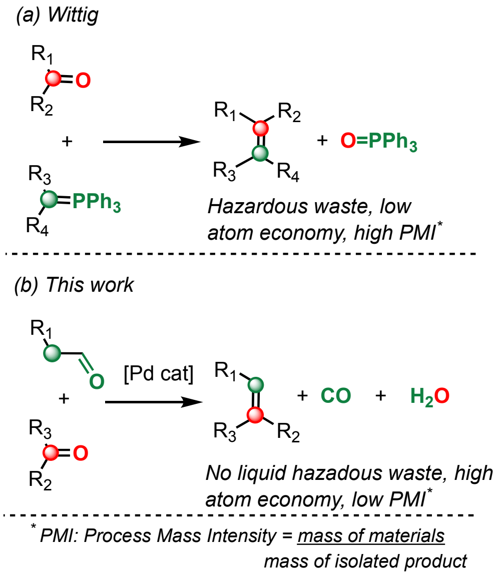
Supporting Information Available

ABSTRACT: New atom-economical alternatives to Wittig chemistry are needed to construct olefins from carbonyl compounds, 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 H_2O as waste. The reaction affords homocoupling of aliphatic aldehydes, as well as heterocoupling of aliphatic and aromatic ones. Computations provide insight into the selectivity and thermodynamics of the reaction. The tandem aldol-decarbonylation reaction opens the door to exploration of new carbonyl reactivity to construct olefins.

The Wittig carbonyl olefination of ketones or aldehydes by phosphorous ylids (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 by the production of stoichiometric waste, necessitating the development of more atom-economical alternatives. Recently, we reported the activity of heterogeneous catalysts based on Pd-doped hydrotalcites (Pd-HTs) for selective decarbonylation of aldehydes.[3] In the course of this study we observed that α,β-unsaturated aldehydes decarbonylate faster than aromatic and saturated aliphatic aldehydes. Furthermore, we noted that the basic sites of Pd-HTs facilitate aldol condensation of enolizable aldehydes to form α,β-unsaturated aldehydes, which undergo further decarbonylation to form alkenes (Schemes 1b and 2). Thus, herein 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 ideally be possible to tune the activity of both sites independently in order to optimize selectivity for different carbonyl substrates.

Scheme 1.

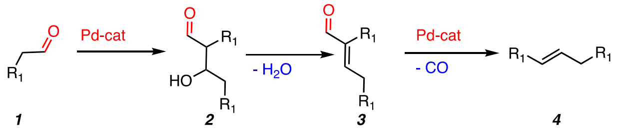


Given that the aldol condensation can be catalyzed by acidic or basic sites, we considered hydrotalcites, MgO, Al_2O_3, carbon and silica as potential non-innocent supports that could facilitate this step. However, the electronic nature of the support also affects the activity of the Pd phase, which catalyzes the decarbonylation.[4-5] In order to explore the potential of optimizing both steps, we synthesized and screened Pd-HT, Pd-Al_2O_3, Pd-SiO_2, Pd-C and Pd-MgO for the reaction in Scheme 2. The catalysts were fully characterized by ICP-OES, TEM, XPS, surface analysis and PXRD (ESI section Catalyst Characterization). XPS showed notable electronic differences in speciation and binding energies of the immobilized Pd species (ESI Table S3 and Figure S7).

Initial findings showed that Pd-HTs facilitate the conversion of enolizable aldehydes under neat conditions 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 or conventional heating. Heptanal thus afforded (E)-tridec-6-ene, an olefin with

(2n-1) carbons, and small amounts of the intermediate ***3*** (Scheme 2).

Scheme 2



$R_1 = C_4H_8CH_3$

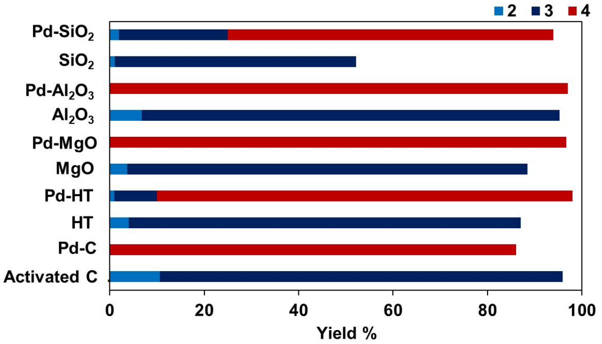


Figure 1. Product distribution of supported Pd catalysts and supports in decarbonylative olefination of heptanal. (Conditions: 0.1 mol% Pd, at 180 °C, 8 hr). See ESI Fig. S8 for profiles at 150 °C.

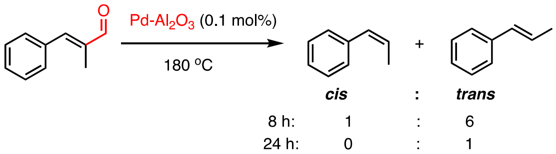
The activity of five supported Pd catalysts were examined with heptanal as model substrate at 150 and 180 °C, (Figures 1 and S8). The activities of the supports were compared to distinguish the activity for aldol vs decarbonylation. Consistent with our initial hypothesis, all of the supports showed some activity for aldol condensation, but only the Pd catalysts afforded decarbonylation products (Figure 1). Use of $Pd(OAc)_2$ alone afforded only minimal yield of aldol intermediate ***3*** (10%) with no olefin ***4***.

At 180 °C quantitative yields of alkene ***4*** could be obtained with $Pd\text{-}Al_2O_3$, Pd-HT and Pd-MgO in only 8 hours, while Pd-C and $Pd\text{-}SiO_2$ afforded 70 and 82% respectively (Figure 1). No decarbonylation was observed with homogeneous $Pd(OAc)_2$ precursor. Catalyst screening at 150 °C (ESI Figure S8) allowed us to establish activity trends at lower conversions. $Pd\text{-}Al_2O_3$ still afforded highest yield of olefin ***4*** (35% in 8 hours and 98% in 24 hours), followed by Pd-C (20% in 8 hours). However, Pd-C showed lowest overall conversion, suggesting it is a poor catalyst for aldol condensation. In contrast, Pd-MgO and Pd-HT afforded full conversion in 8 hours, but only 10-15% yield of the alkene. These results establish the following trend for activity for aldol condensation: **MgO > HT > Al_2O_3 > activated carbon > SiO_2**; and for decarbonylation: **$Pd\text{-}Al_2O_3$ > Pd-C > Pd-HT > Pd-MgO > $Pd\text{-}SiO_2$**.

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-MgO~ Pd-HT >> $Pd\text{-}Al_2O_3$ (ESI Figure S9). Thus, the strong basic sites on MgO and HT are more effective for aldol condensation than the Lewis acidic sites of Al_2O_3. At 150 °C decarbonylation yields 38 – 78% of ***4*** in 24 hr, discerning the activity trend for decarbonylation: $Pd\text{-}Al_2O_3$ > Pd-HT > Pd-MgO (ESI Figure S10), while at 180 °C decarbonylation is rapid, so intermediate ***3*** is quickly consumed (ESI Figure S11). As a control, we compared the reaction with $Pd\text{-}Al_2O_3$ to one with $Pd(OAc)_2$ and Al_2O_3. The reaction yields ***4*** but decarbonylation is significantly slower, resulting in build-up of ***3*** (ESI Figure 12). Decarbonylation rate is thus the rate-determining process, and is sensitive to support and reaction temperature in the range studied. Further reactions were explored using $Pd\text{-}Al_2O_3$ as the most active catalyst.

Curiously, we observed that the configuration of aldol intermediate ***3*** is *cis* w.r.t. R-groups, while alkene ***4*** is a *trans* alkene (Scheme 2 and ESI Fig. S13). 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 with $Pd\text{-}Al_2O_3$, and complete conversion to the *trans* product in 24 hours (Scheme 3 and ESI Figure S14). This is consistent with the assertion that the catalyst facilitates both decarbonylation and isomerization to the thermodynamic alkene isomer. No alkene migration was observed in the substrates.

Scheme 3



We briefly explored the relative thermodynamics of the intermediates and products in the reaction with heptanal (Scheme 2 and Figure 2). Calculations were carried out with the PM7 semiempirical method in gas phase using the Gaussian 16 software.[6] Geometries were fully optimized, and all minima were verified to have to imaginary vibrational frequencies. Free energies, evaluated at 298 K, show that while initial aldol addition is 2.9 kcal/mol uphill, the aldol condensation is thermodynamically favorable (ΔG_{rxn} = -3.9 and -4.0 kcal/mol respectively for *trans* and *cis* α,β-unsaturated carbonyls) w.r.t. heptanal. The subsequent decarbonylation to the *cis*-olefin is near thermoneutral, 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, Figure 1). These calculations are consistent with the experimental observation of the *trans*-olefin product. Furthermore, the thermodynamics suggest that decarbonylation is close enough to thermoneutral to potentially allow for reversibility under appropriate conditions.

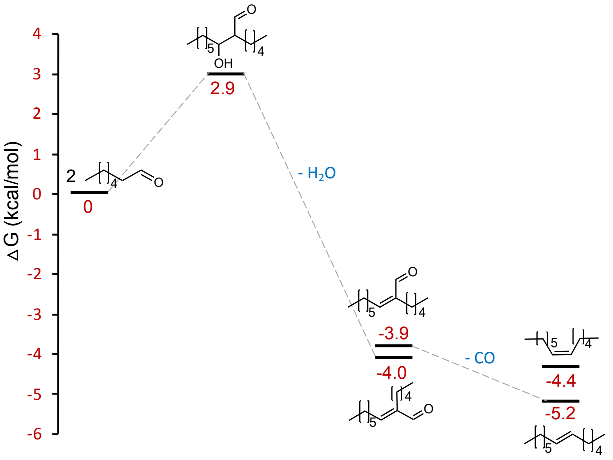
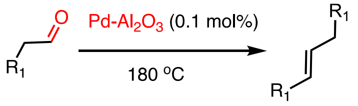
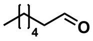
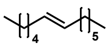
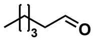
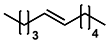
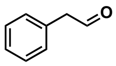
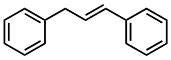
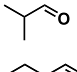
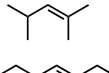
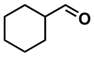
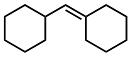


Figure 2. Free energy diagram for decarbonylative olefination of heptanal (see reaction in Scheme 2).

We briefly explored the substrate scope of the decarbonylative olefination. Enolizable aldehydes with no α-branching afford excellent yields (Table 1, entries 1-3), while those with α-branching react more slowly (entries 4 and 5) due to slower aldol condensation. The latter is evidenced by the low conversion in the latter cases. Thus, optimization of olefin selectively requires balancing rates of three independent reactions: aldol condensation, decarbonylation of aldol product and undesired decarbonylation of initial substrate.

Table 1. Substrate scope for decarboxylative olefination of aliphatic aldehydes.



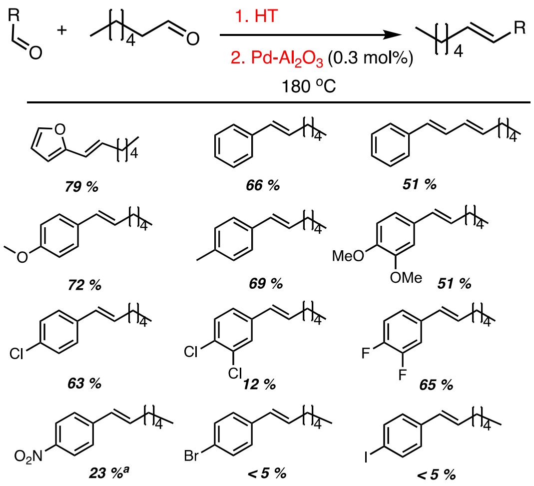
No.	Substrate	Olefin product	% Yield
1			97
2			88
3			82
4			45
5			36

Conditions: 14 mmol substrate (neat), 0.1 mol% Pd-Al_2O_3, 180 °C, 8 h, under air.

We also explored whether this reaction can be optimized in the heterocoupling reactions of two aldehydes. Selectivity for heterocoupling was favored by coupling enolizable with non-enolizable aldehydes. 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 (aromatic) aldehyde relative to aldol condensation. To increase selectivity for the cross-aldol condensation we introduced hydrotalcite (HT) as a more effective aldol catalyst than alumina. Initial reaction with only HT pre-forms the hetero-aldol product, and subsequent addition of Pd-Al_2O_3 affords decarbonylation. This protocol significantly improved the selectivity and yield of the desired olefin (79% yield in 8 hours for furfural and heptanal).

Further exploration of heterocoupling for a selection of substrates is summarized in Table 2. Similar to the Wittig reaction, the aldol condensation does not tolerate electrophilic and nucleophilic groups (e.g. unprotected amines, alcohols, alkyl halides), and thus these were excluded. Substrates shown in Table 2 afforded full conversion, and good to excellent yields of desired olefin, but some competing homocoupling of heptanal was still observed in select cases. Since selectivity for heterocoupling is affected by the aldol step, it can be related to the reactivity of the non-enolizable aldehydes: e.g. furfural carbonyl carbon is more electrophilic than that of benzaldehyde, and thus more reactive. Computationally, the latter can be approximated by the Mulliken charges, which reflect the same trend (ESI Table S4). Since selectivity issues are primarily related to the aldol step, synthetic conditions can be further modified to optimize selectivity and yields for the desired intermediate. The second limitation on substrate scope is functionality that is susceptible to Pd-catalyzed processes: e.g., aryl halides susceptible to C-X oxidative addition. The latter is responsible for the low yields of *3,4*-dichlorobenzaldehyde (12%) as well as iodo and bromobenzaldehyde (< 5%) due to aryl-aryl by-products. As expected, this is not an issue for C-F bonds, and *3,4*-difluorobenzaldehyde affords good yields and selectivity.

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-Al_2O_3, 180 °C, 6 h. [a]Reaction polymerized 2 hours after adding Pd-Al_2O_3.

The recyclability of the Pd-Al_2O_3 was explored with heptanal as substrate. The catalyst was reused after separation from reaction by centrifugation, washing and drying. The yields of products obtained over 9 cycles, all of which below full conversion, indicate that the catalyst retaines activity (Figure 3), with a small decrease in selectivity 93% - 98% after cycle 4. Elemental analysis of the spent catalyst shows negligible loss of Al amd Pd (within the standard error of the as-prepared catalysts), suggesting the small drop in selectivity is likely attributed to factors other than leaching. TEM images of the used catalyst do not indicate notable morphological changes or agglomeration of Pd nanoparticles (ESI Figure S15).

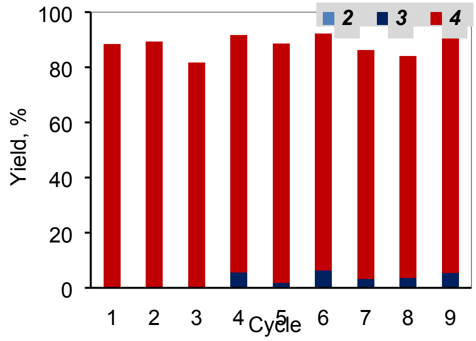


Figure 3. Recyclability of Pd-Al_2O_3 in the decarbonylative olefination of heptanal.

To investigate whether Pd-Al_2O_3 was operationally heterogeneous in this reaction, we performed 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 S16a), suggesting that the catalytic species are absent from the filtrate. This result was consistent with the fact that decarbonylation activity was completely quenched by mercury poisoning, which amalgamates with supported palladium.[7] (ESI Figure S16b). However, catalytic activity was also quenched by Quadrapure-TU,[8-9] a known scavenger for soluble Pd complexes and nanoparticles.[7] The latter could suggest involvement of both heterogeneous and soluble Pd species in this multi-step process. We note that the use of an entirely soluble source of Pd was earlier found ineffective, but this does not exclude potential complex equilibrium between surface-bound and soluble Pd species - not atypical of heterogeneous catalysis in the condensed phase. The catalyst behavior will be subject to future operando spectroscopic studies to interrogate the nature of the catalytic species.

In sum, this preliminary report documents a new, atom-economical olefination of carbonyls via aldol-decarbonylative coupling of aldehydes using robust and recyclable supported Pd catalysts, producing only CO and H_2O as waste. Computations suggest the reaction is thermodynamically favorable, with the decarbonylation step near thermo-neutral. Decarbonylation is rate-determining, and is sensitive to temperature in the range 100 – 180 °C. The tandem reaction is most effectively facilitated by multifunctional Pd catalysts, such as Pd-Al_2O_3, Pd-HT and Pd-MgO, where the relative rates of the two steps is dependent on catalytic support. The process can be used to obtain olefins from both homocoupling and heterocoupling of aldehydes. The most effective catalyst, Pd-Al_2O_3, retains activity for at least 9 cycles with minor decrease in selectivity. Poisoning experiments implicate involvement of surface-bound and soluble Pd species.

ASSOCIATED CONTENT

Supporting Information is available detailing catalyst synthesis, characterization, additional figures and tables related to reaction and NMR characterization of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

1. Hoffmann, R. W., Wittig and His Accomplishments: Still Relevant Beyond His 100th Birthday. *Ang. Chem. Int. Ed.* **2001,** *40* (8), 1411-1416.
2. Sha, Q.; Wei, Y., Copper(I)-Catalyzed Wittig Olefination Reactions ofN-Tosylhydrazones with Trifluoromethylketones. *ChemCatChem* **2014,** *6* (1), 131-134.
3. An, N.; Ainembabazi, D.; Reid, C.; Samudrala, K.; Wilson, K.; Lee, A. F.; Voutchkova-Kostal, A., Microwave-Assisted Decarbonylation of Biomass-Derived Aldehydes using Pd-Doped Hydrotalcites. *ChemSusChem* **2019**, DOI: 10.1002/cssc.201901934.
4. Lejemble, P.; Gaset, A.; Kalck, P., From Biomass to Furan through Decarbonylation of Furfural under Mild Conditions. *Biomass* **1984**, *4* (4), 263-274.
5. Meng, Q. W.; Qiu, C. W.; Ding, G. Q.; Cui, J. L.; Zhu, Y. L.; Li, Y. W., Role of alkali earth metals over Pd/Al2O3 for decarbonylation of 5-hydroxymethylfurfural. *Catal. Sci. Technol.* **2016,** *6* (12), 4377-4388.
6. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; J. A. Montgomery, J.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma,

K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 16, Revision B.01*, Gaussian, Inc., Wallingford CT: 2016.

7. Lee, A. F.; Ellis, P. J.; Fairlamb, I. J. S.; Wilson, K., Surface catalysed Suzuki-Miyaura cross-coupling by Pd nanoparticles: an operando XAS study. *Dalton Trsans.* **2010,** *39* (43), 10473-10482.

8. Richardson, J. M.; Jones, C. W., Poly(4-vinylpyridine) and Quadrapure TU as selective poisons for soluble catalytic species in palladium-catalyzed coupling reactions - Application to leaching from polymer-entrapped palladium. *Adv. Synth. Catal.* **2006,** *348* (10-11), 1207-1216.

9. Richardson, J. M.; Jones, C. W., Strong evidence of solution-phase catalysis associated with palladium leaching from immobilized thiols during Heck and Suzuki coupling of aryl iodides, bromides, and chlorides. *J. Catal.* **2007,** *251* (1), 80-93.

SYNOPSIS TOC (Word Style "SN_Synopsis_TOC").