

HIGHLIGHT

Transition-Metal-Catalyzed Decarbonylation of Carboxylic Acids to Olefins: Exploiting Acyl C–O Activation for the Production of High Value Products

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Transition-metal-catalyzed decarbonylation reactions of aliphatic carboxylic acids produce olefins via one carbon degradation. Recently, tremendous progress has been made in the development of new protocols for the synthesis of linear olefins by the formal acyl C–O activation mechanism of ubiquitous carboxylic acids. Various transition metals including nickel, palladium, iridium and iron have been shown to catalyze the reaction and achieve excellent yields and selectivity. The use of new ligand systems has resulted in unprecedented control of selectivity of elementary steps in the catalytic cycle. The development of new acyl precursors expands the access to α -olefins and offers promising perspectives for applications in preparative organic synthesis. In this article, we highlight the recent noteworthy developments in the transition-metal-catalyzed decarbonylation of carboxylic acids and discuss future challenges in this field.

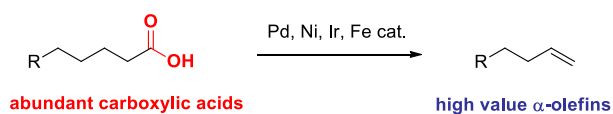
Linear olefins are extremely important commodity chemicals that have found numerous applications in industrial and consumer products, including surfactants, lubricants and polymers.^{1,2} The most common industrial technology for the production of high value linear α -olefins relies on polymerization of ethylene.³ The diminishing resources of oil supply have fuelled the recent surge of interest in the conversion of biomass into chemicals that are currently produced by the petrochemical industry, including ethylene, and by extension linear olefins.⁴ Thus, developing new chemical strategies for the production of high quality linear olefins from biomass has been a crucial issue in current chemistry research.⁵

Recently, tremendous progress has been made in the generation of linear olefins from carboxylic acids and esters. Since carboxylic acids can be derived from abundant natural product feedstocks, such as vegetable oils and animal fats, the direct conversion of carboxylic acids represents an attractive strategy to produce linear olefins from biomass resources.^{2–5} Moreover, the availability of fatty acids with an even number of carbon atoms provides an inexpensive route to linear olefins containing an odd number of carbons, which are inaccessible by the current ethylene polymerization technologies.^{1–3}

A plethora of attractive strategies for the catalytic decarbonylation of carboxylic acids to generate alkenes have been developed. The search for new metals, improved catalytic systems and new acyl precursors have facilitated the

synthesis of high value commodity olefins from biomass resources, and resulted in a direct production of densely-functionalized fine chemicals that open new vistas for the increased application in organic synthesis. In this article, we will highlight the recent developments in the transition-metal-catalyzed dehydrative deoxygenation of carboxylic acids to alkenes by the formal acyl C–O activation mechanism^{6,7} of ubiquitous carboxylic acids (Figure 1).

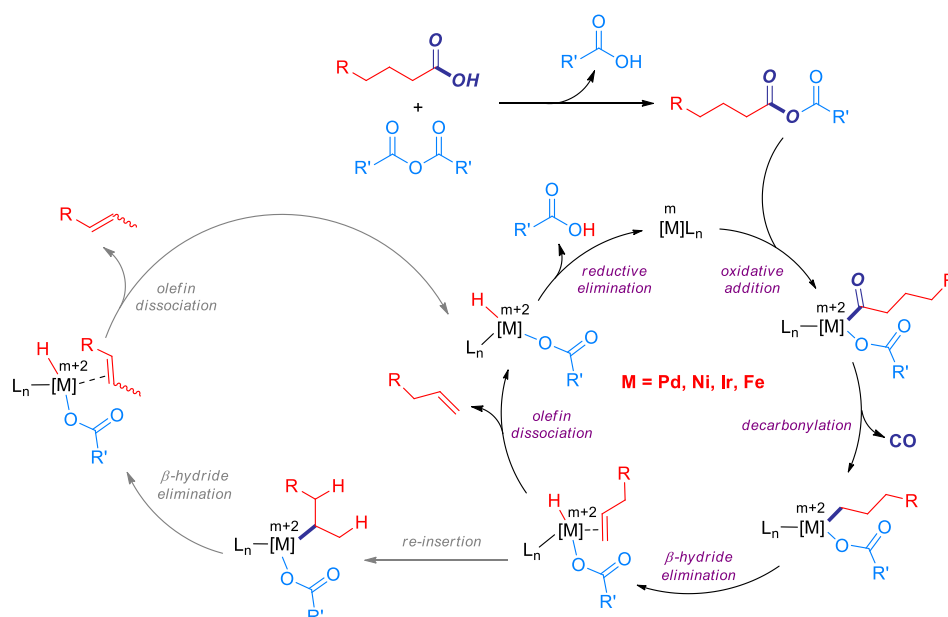
The most frequently used approach focuses on the direct decarbonylation of carboxylic acids, and usually requires stoichiometric quantities of a sacrificial anhydride to activate the carboxylic acid substrate (Scheme 1). After the carboxylic acid substrate is transformed into a mixed anhydride, the catalytic cycle involves the following steps: (i) oxidative addition, (ii) decarbonylation, (iii) β -hydride elimination, and (iv) reductive elimination to regenerate the catalyst. Simultaneously, isomerization to form internal alkenes occurs through re-insertion and β -hydride elimination. Thus, in order to obtain high quality olefins, the prime challenge is to control the selectivity of the olefin isomerization by a catalyst system.^{2,4} Moreover, while distilling the α -olefin product from the reaction mixture at high temperatures is often used to minimize isomerization, this process is less ideal because only volatile olefins can be obtained by this method.



■ biomass-derived carboxylic acids ■ commodity chemicals ■ fine chemicals
■ mild conditions ■ new catalysts & precursors ■ no isomerization

Figure 1 General decarbonylation of carboxylic acids to olefins.

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Scheme 1 General mechanism for transition-metal-catalyzed decarbonylation of carboxylic acids.

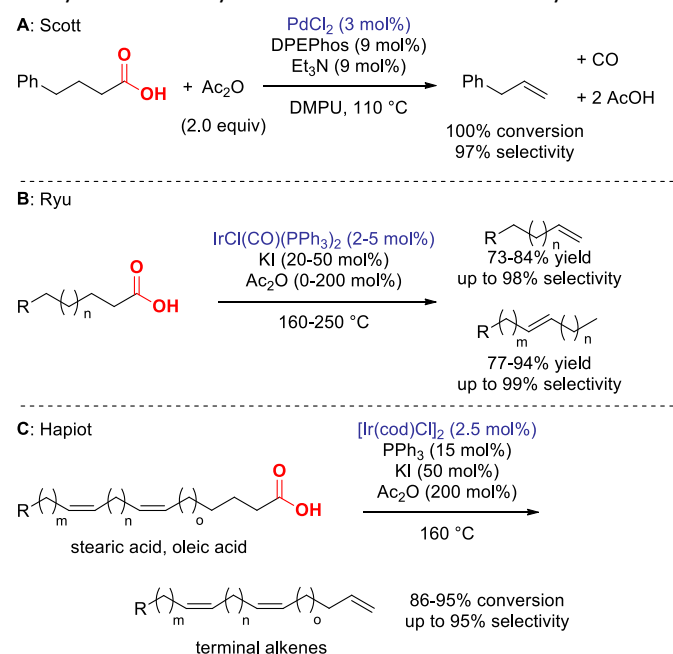
An important mechanistic point involves the origin of selectivity in the oxidative addition step of the mixed anhydride to a palladium catalyst. Mechanistic studies suggest reversibility of the oxidative addition with deprotonation of alkyl-palladium as the rate-determining step.^{2,6–8}

Palladium is the most commonly used transition metal in deoxygenation of carboxylic acids.^{8,9} In 2010, a palladium-DPEPhos-catalyzed decarbonylation was reported by Scott and co-workers (Scheme 2A).¹⁰ The method allows for the conversion of aliphatic carboxylic acids to terminal alkenes in high yields and with high α -selectivity at temperatures as low as 110 °C. The addition of triethylamine as additive was critical to stabilize the catalytic species and effectively prevent isomerization of the terminal double bond.¹¹ The method represented a significant improvement over previous methods that require very forcing conditions (250 °C) or stopping the process at lower conversions to avoid olefin isomerization.⁸

In the same year, the Ryu group developed an efficient iridium-catalyzed decarbonylation reaction of aliphatic carboxylic acids (Scheme 2B).¹² By using Vaska's complex, $\text{IrCl}(\text{CO})(\text{PPh}_3)_2$, as catalyst, KI and Ac_2O as additives, long-chain aliphatic carboxylic acids can be converted to internal or terminal alkenes with high selectivity at controlled temperature. At 250 °C, the addition of KI alone (20 mol%) greatly improves the yield of internal alkenes, while maintaining perfect selectivity (>99%, with respect to the olefin regioisomer). At 160 °C and using both KI (50 mol%) and Ac_2O (200 mol%), terminal alkenes are obtained with high selectivity (up to 98%). The authors suggested that the addition of KI results in ligand exchange from Cl to I in Vaska's complex to give a more active catalyst. Interestingly, the reaction showed good functional group compatibility in that ester groups can also be tolerated during the reaction. More recently, the Hapiot group reported elegant Ir-catalyzed decarbonylation of biomass-derived fatty acids to obtain long

linear olefins in good yields and with high selectivity (Scheme 2C).¹³ These reactions were best accomplished in the presence of $\text{Ir}(\text{cod})\text{Cl}_2$ (2.5 mol%) and PPh_3 (15 mol%) with KI (50 mol%) and Ac_2O (200 %) as additives. Importantly, the Ir catalyst could be recovered by simple distillation of the reaction mixture and recycled, albeit with lower conversions.

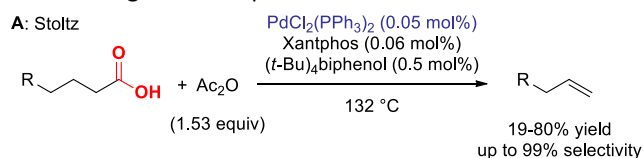
In 2014, Stoltz and co-workers achieved a palladium-catalyzed decarbonylation reaction of linear carboxylic acids at



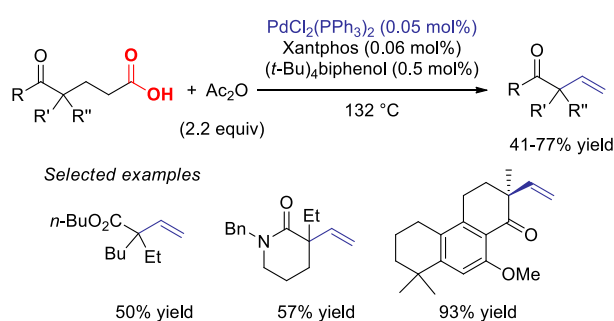
Scheme 2 Pd- and Ir-catalyzed decarbonylation of carboxylic acids: A) Scott; B) Ryu; C) Hapiot. Scheme 2B: selectivity with respect to the indicated olefin regioisomer is shown.

very low catalyst loadings using $\text{PdCl}_2(\text{PPh}_3)_2$ (0.05 mol%) and Xantphos (0.06 mol%) under solvent-free conditions (Scheme 3A).¹⁴ During screening of the reaction conditions, two findings

were crucial: (i) a protic additive, (*t*-Bu)₄biphenol (0.5 mol%), promoted reactivity; (ii) the frequency of adding acetic anhydride had a major impact on α -selectivity; by portion-wise addition of acetic anhydride, the reaction could give α -olefins with exquisite selectivity (up to 99%) even without in situ distillation. The authors proposed that acidic additives, such as (*t*-Bu)₄biphenol, result in higher reactivity of a catalyst system. Since the reaction can be performed under neat conditions, it can be easily scaled up without compromising α -selectivity. The method represents an important addition to the toolbox of technologies for the production of linear α -



B: Synthesis of α -vinyl carbonyls



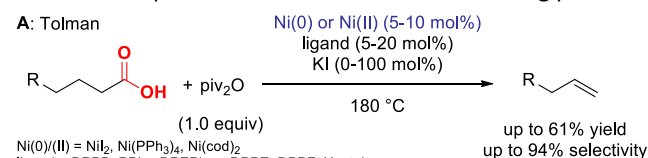
Scheme 3 Pd-catalyzed decarbonylation of carboxylic acids by Stoltz: A) α -linear olefins; B) α -vinyl carbonyl compounds.

olefins from biomass resources. Later, the same group reported another important advance in the area by developing Pd-catalyzed decarbonylative dehydration to furnish α -vinyl carbonyl compounds (Scheme 3B).¹⁵ This method was elegantly showcased in the total synthesis of Aspewentins A, B, C, norditerpene natural products. The study by Stoltz and co-workers convincingly demonstrated that the concept of decarbonylative olefin synthesis from readily available carboxylic acids provides a novel platform for the production of densely-functionalized molecules that would be challenging to prepare by alternative methods.

Tolman, Hillmyer and co-workers have been extensively studying new protocols for deoxygenation of carboxylic acids. In 2012, they developed a Pd-catalyzed decarbonylation of biomass-derived carboxylic acids using continuous distillation protocol at 190 °C (not shown).¹⁶ In their approach, cheap and weakly coordinating PPh₃ was shown to promote decarbonylation in similar yields and selectivity as bidentate Xantphos and DPEPhos, while the catalyst loading could be lowered to 0.005 mol% without a significant decrease in the reaction efficiency.

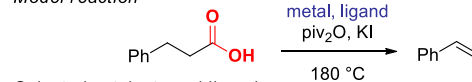
In 2016, Tolman and co-workers reported a major breakthrough in finding that catalysts based on inexpensive and abundant 3d transition metal, nickel, effectively promote decarbonylation of carboxylic acids (Scheme 4).¹⁷ Using high-throughput experimentation techniques, a combination of

Ni(0) or Ni(II) precatalysts (NiI₂, Ni(PPh₃)₄) and bidentate phosphine ligands (DPPB, DPEPhos) under a continuous distillation process at 180 °C was identified as the best catalytic system for the reaction. Interestingly, a 2:1 ligand:nickel ratio gave optimum results. As expected, the reaction was inhibited when the process was performed under the atmosphere of CO. DFT studies suggested that a rate-determining step may involve regeneration of the active monoligated Ni(0) species via CO dissociation. Furthermore, the proposed catalytic cycle involving the acyl-Ni intermediate mirrored the previous mechanistic studies on using palladium-



B: Selected metal catalysts and ligands in combinatorial screening

Model reaction



Selected catalysts and ligands

FeCl ₂	Fe(OAc) ₂	PPh ₃	PhBI
CoCl ₂	Co(OAc) ₂	PCy ₃	pyrBI
NiBr ₂ (DME)	Pd(OAc) ₂	P(OPh) ₃	ADI
CuCl	Fe(OTf) ₂	pyridine	IMes
ZnCl ₂	CuOTf	BIMP	IPr
PdCl ₂	Ni(OTf) ₂	Salph	bipy
Co(acac) ₃	Zn(OTf) ₂	POI	TMEDA
Ni(acac) ₂	CoCl(PPh ₃) ₄		
Mn(OAc) ₂	Pd(MeCN) ₄ (BF ₄) ₂		

Scheme 4 Ni-catalyzed decarbonylation of carboxylic acids by Tolman: A) α -linear olefins; B) high-throughput screening.

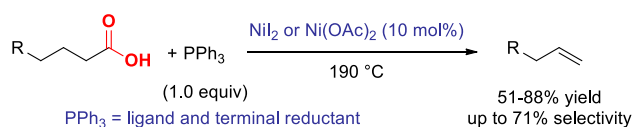
based catalysts for decarbonylation of hydrocinnamic acid.¹⁸ Given the recent interest in nickel-catalyzed cross-couplings, the facile decarbonylation of acyl-nickel species demonstrated by Tolman and co-workers opens the door for a plethora of decarbonylative processes of carboxylic acids by nickel-catalysis.¹⁹

In 2017, Tolman and co-workers reported another important contribution to the direct dehydrative deoxygenation of carboxylic acids by developing a solvent-free Ni/PPh₃-catalyzed deoxygenation of carboxylic acids to olefins without the use of activating additives (Scheme 5).²⁰ For the vast majority of decarbonylative reactions of carboxylic acids, the use of sacrificial anhydride is essential to generate the acyl-metal species.^{2,4,8} However, they found that when PPh₃ is used in combination with Ni(II) salts, the phosphine acts as both ligand and reductant, resulting in the production of α -olefins in high yields and with good selectivity. Notably, the reaction is catalytic in PPh₃ by using TMDS (1,1,3,3-tetramethyldisiloxane) and Cu(OTf)₂ that can regenerate PPh₃ from the phosphine oxide. Without Cu(OTf)₂/TMDS additives the reaction is stoichiometric in PPh₃. The impressive results of Tolman considerably extend the scope of decarbonylative processes of carboxylic acids by incorporating two complementary catalytic cycles to effect catalysis.

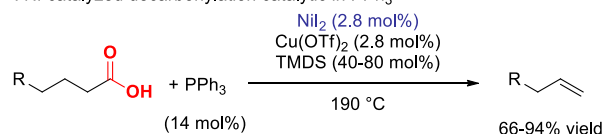
A very significant recent development by Tolman and co-workers involves a highly selective Pd-catalyzed decarbony-

lation of *p*-nitrophenylesters of fatty acids to linear α -olefins with a mixed phosphine/NHC (NHC = N-heterocyclic carbene) ligand system (Scheme 6).²¹ After extensive screening of various ligands, they found that a combination of bidentate phosphine (Xantphos)²² and sterically-bulky NHC ligand (IPr)²³ was optimal for the decarbonylation process (>98% selectivity, >90% conversion). DFT calculations showed that in the mixed phosphine-NHC ligand system the steric bias of IPr (buried volume of 45.4%)²⁴ and the coordination of XantPhos in both mono- and bidentate mode promoted a rapid and irreversible de-coordination of the product olefin, thus preventing the

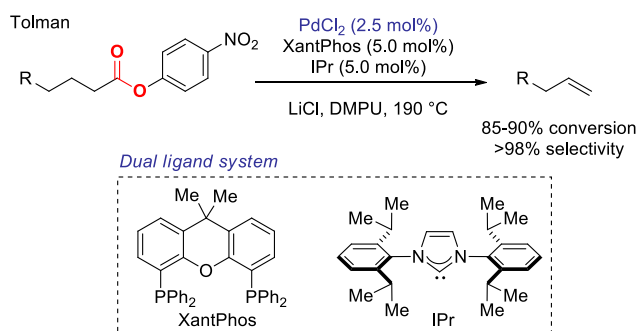
A: Tolman



B: Ni-catalyzed decarbonylation catalytic in PPh₃



Scheme 5 Anhydride-free Ni-catalyzed decarbonylation of carboxylic acids by Tolman: A) stoichiometric PPh₃; B) catalytic PPh₃.



Scheme 6 Pd-catalyzed decarbonylation of carboxylic acid esters using a dual ligand system by Tolman.

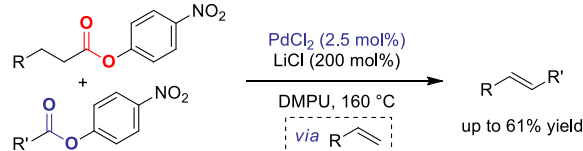
isomerization pathway. Collectively, the finding that ligands from two different classes act cooperatively to improve the reaction efficiency will undoubtedly find numerous applications in decarbonylative processes of acyl electrophiles.

In addition to direct decarbonylation of carboxylic acids and derivatives to olefins, the Tolman group has also studied the development of tandem protocols based on the in situ generation of olefin precursors (Scheme 7). In 2015, they reported a tandem double decarbonylation of *p*-nitrophenylesters/Heck reaction, which was catalyzed by PdCl₂ in the presence of LiCl.²⁵ The reaction sets an important precedent for rapidly building-up molecular complexity from biomass-derived fatty acids.²⁶

Jensen and co-workers independently described another strategy to promote decarbonylative dehydration of fatty acids with high efficiency (Scheme 8A).²⁷ They developed a well-defined Pd(II) precatalyst, [Pd(DPEPhos)(cin)Cl], as a new catalyst for decarbonylation of fatty acids with high α -olefin selectivity. Impressively, the precatalyst was found to operate

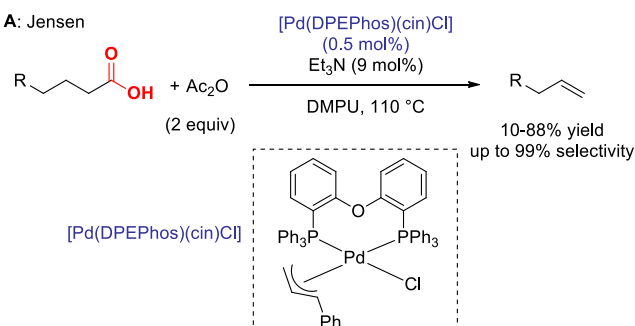
with more than 8 times higher TOF than standard in situ protocols. High functional group tolerance and operational-simplicity²⁸ are other noteworthy features of this approach. Subsequently, the Jensen group reported an improved protocol for the decarbonylation of fatty acids based on a heterogeneous Pd catalyst, Pd/C, in the presence of DPEPhos (Scheme 8B).²⁹ The catalyst could be recycled up to three times without any loss in activity and olefin selectivity. The work by Jensen opens new avenues for exploring decarbonylation of carboxylic acids by heterogeneous Pd catalysis.³⁰

Tolman

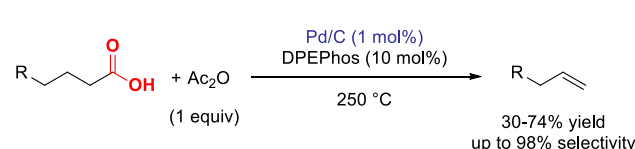


Scheme 7 Pd-catalyzed tandem decarbonylative Heck reaction of carboxylic acid esters by Tolman.

A: Jensen



B: Decarbonylation of carboxylic acids under heterogeneous conditions

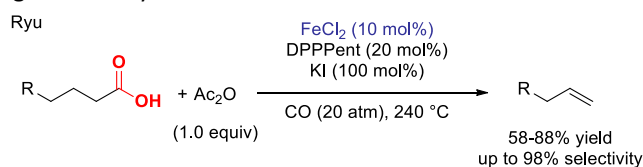


Scheme 8 Decarbonylation of carboxylic acids by Jensen: A) well-defined Pd(II) precatalyst; B) heterogeneous conditions.

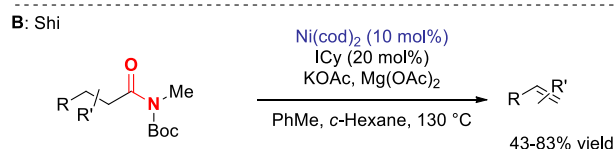
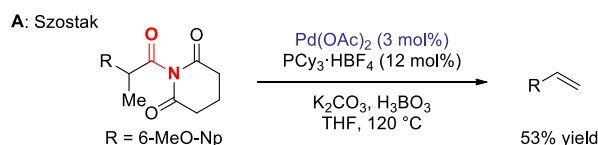
In another approach to improve efficiency of the decarbonylation of carboxylic acids, the Ryu group reported highly selective decarbonylation of aliphatic carboxylic acids to α -olefins using iron catalysis (Scheme 9).³¹ High yields and high selectivity were achieved by using FeCl₂ as catalyst, DPPent as ligand, and KI and Ac₂O as additives. While the current drawback involves the need for pressurized CO to improve catalyst performance and α -olefin selectivity, likely due to generation of a catalytically-active iron-carbonyl species, this research shows that cheap, non-toxic and sustainable iron³² represents an effective tool to perform catalytic decarbonylation of carboxylic acids.

Two other recent developments in this area are noteworthy. In 2015, we reported the first decarbonylation of amides to olefins using Pd-catalysis (Scheme 10A).³³ Not only are the reaction conditions mild, but equally important is the finding that decarbonylation of carboxylic acid derivatives by N–C cleavage³⁴ provides an alternative pathway to

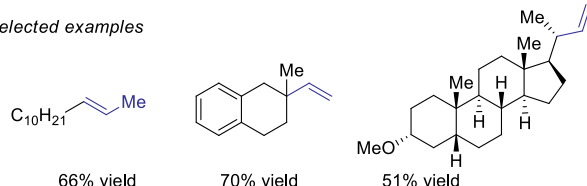
decarbonylative dehydration by C–O scission. This process was subsequently expanded to Ni-catalysis by the Shi group (Scheme 10B).³⁵ A particularly attractive feature of this catalytic method is the ability to engage complex amide precursors to furnish congested olefins that would otherwise be difficult to prepare. More recently, Glorius and co-workers reported an impressive example³⁶ of merging photoredox/Cu(II) catalysis with redox active N-hydroxyphthalimide esters³⁷ to produce olefins from fatty acid derivatives via a decarboxylative pathway (Scheme 11). The method results in high selectivity for the formation of terminal olefins. The



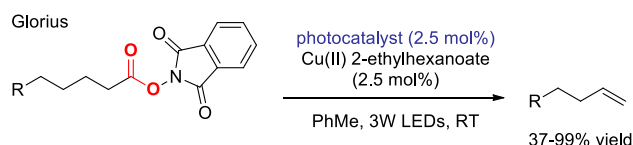
Scheme 9 Fe-catalyzed decarbonylation of carboxylic acids by Ryu. DPPent = 1,5-Bis(diphenylphosphino)pentane.



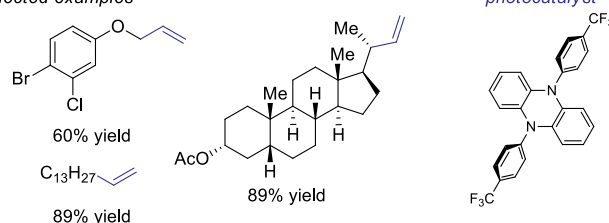
Selected examples



Scheme 10 Pd- and Ni-catalyzed decarbonylation of amides by N–C cleavage: A) Szostak; B) Shi.

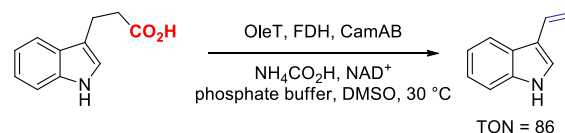


Selected examples

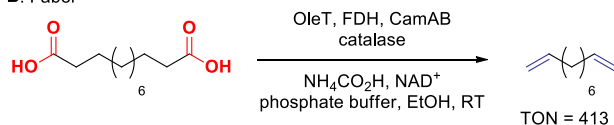


Scheme 11 Photoredox/Cu(II)-catalyzed decarboxylative olefination of redox-active carboxylic acid esters by Glorius.

A: Reetz



B: Faber



Scheme 12 Oxidative decarboxylation catalyzed by the P450 monooxygenase OleT: A) Reetz; B) Faber. OleT = P450 monooxygenase OleT; CamA = putidaredoxin reductase; CamB = putidaredoxin.

photoredox catalysis may not only enable more efficient decarboxylative olefination of carboxylic acid derivatives, but also open new vistas for oxidative decarboxylative methods by single electron transfer.³⁸

Toward the development of efficient approaches for the synthesis of olefins from carboxylic acid derivatives, bio-enzymatic methods should also be mentioned in passing. In particular, recent advances in oxidative decarboxylation of fatty acids by the p450 monooxygenase OleT provide a convincing illustration that bioenzymatic processes can lead to the development of practical methods for the synthesis of olefins from biomass resources (Scheme 12).³⁹ Ultimately, it can be expected that further improvements to enhance olefin complexity by tandem chemoenzymatic transformations⁴⁰ will be realized.

Conclusions

In summary, recently impressive advances in the transition metal-catalyzed decarbonylative reactions of carboxylic acids and derivatives to olefins have been accomplished. These methods provide efficient and straightforward synthetic solution to obtain high value linear alpha-olefins from bio-renewable resources. Several powerful strategies have emerged, thus improving the yield, selectivity, and practicality of this class of reactions. The development of inexpensive base-metal catalysts, improved catalyst systems and new carboxylic acid precursors are undoubtedly a major step forward. In addition to providing the much-needed biomass alternative to petrochemical feedstock, the synthesis of densely-functionalized fine chemicals⁴¹ illustrate the power of this class of reactions. With recently developed isomerization methods of linear olefins,⁴² organic chemists are now well-equipped to fully exploit abundant carboxylic acids as key precursors in a broad range of chemical transformations.

Acknowledgements

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Notes and references

- (a) S. D. Ittel, L. K. Johnson and M. Brookhart, *Chem. Rev.*, 2000, **100**, 1169; (b) R. Franke, D. Selent and A. Börner, *Chem. Rev.*, 2012, **112**, 5675; (c) D. S. McGuinness, *Chem. Rev.*, 2011, **111**, 2321.
- (a) G. J. S. Dawes, E. L. Scott, J. Le Notre, J. P. M. Sanders and J. H. Bitter, *Green Chem.*, 2015, **17**, 3231; (b) P. N. R. Vennestrøm, C. M. Osmundsen, C. H. Christensen and E. Taarning, *Angew. Chem. Int. Ed.*, 2011, **50**, 10502; (c) P. Y. Dapsens, C. Mondelli and J. Perez-Ramirez, *ACS Catal.*, 2012, **2**, 1487; (d) R. W. Gosselink, S. A. W. Hollak, S. W. Chang, J. van Haveren, K. P. De Jong, J. H. Bitter and D. S. van Es, *ChemSusChem*, 2013, **6**, 1576; (e) E. Santillan-Jimenez, M. Crocker, *J. Chem. Technol. Biotechnol.*, 2012, **87**, 1041.
- A. Gollwitzer, T. Dietel, W. P. Kretschmer and R. Kempe, *Nat. Commun.*, 2017, **8**, 1226.
- (a) H. L. Bos and K. P. M. Sanders, *Biofuels, Bioprod. Bioref.*, 2013, **7**, 246; (b) T. N. Pham, T. Sooknoi, S. P. Crossley and D. E. Resasco, *ACS Catal.*, 2013, **3**, 2456; (c) G. Knothe, K. R. Steidley, B. R. Moser and K. M. Doll, *ACS Omega*, 2017, **2**, 6473; (d) T. J. Benson, P. R. Dagglou, R. A. Hernandez, S. Liu and M. G. White, *Adv. Catal.*, 2013, **56**, 187.
- D. R. Dodds and R. A. Gross, *Science*, 2007, **318**, 1250.
- For an early example of C–O activation in carboxylic acid derivatives, see: Y. Yamamoto, J. Ishizu, T. Kohara, S. Komiya and A. Yamamoto, *J. Am. Chem. Soc.*, 1980, **102**, 3758.
- For a recent example of cross-coupling by C–O activation in carboxylic acid derivatives, see: P. Lei, G. Meng, S. Shi, Y. Ling, J. An, R. Szostak and M. Szostak, *Chem. Sci.*, 2017, **8**, 6525.
- For early examples of decarbonylation of carboxylic acids and derivatives, see: (a) J. Tsuji and K. Ohno, *Synthesis*, 1969, **4**, 157; (b) T. A. Foglia and P. A. Barr, *J. Am. Oil Chem. Soc.*, 1976, **53**, 737; (c) J. A. Miller, J. A. Nelson and M. P. Byrne, *J. Org. Chem.*, 1993, **58**, 18; (d) L. J. Gooßen and N. Rodriguez, *Chem. Commun.*, 2004, 724; (e) G. A. Kraus and S. Riley, *Synthesis*, 2012, **44**, 3003; (f) For additional examples, see: A. de Meijere, S. Bräse and M. Oestreich, *Metal-Catalyzed Cross-Coupling Reactions and More*, Wiley, New York, 2014.
- For an excellent review on the use of carboxylic acids as substrates in catalysis, see: L. J. Gooßen, N. Rodriguez and K. Gooßen, *Angew. Chem. Int. Ed.*, 2008, **47**, 3100.
- J. Le Notre, E. L. Scott, M. C. R. Franssen and J. P. M. Sanders, *Tetrahedron Lett.*, 2010, **51**, 3712.
- A. Sen and T. W. Lai, *Inorg. Chem.*, 1984, **23**, 3257.
- (a) S. Maetani, T. Fukuyama, N. Suzuki, D. Ishihara and I. Ryu, *Organometallics*, 2011, **30**, 1389; For related decarbonylative C–H arylation methods, see: (b) S. Maetani, T. Fukuyama and I. Ryu, *Org. Lett.*, 2013, **15**, 2754; (c) T. Fukuyama, S. Maetani, K. Miyagawa and I. Ryu, *Org. Lett.*, 2014, **16**, 3216.
- J. Ternel, T. Lebarbe, E. Monflier and F. Hapiot, *ChemSusChem*, 2015, **8**, 1585.
- Y. Liu, K. E. Kim, M. B. Herbert, A. Fedorov, R. H. Grubbs and B. M. Stoltz, *Adv. Synth. Catal.*, 2014, **356**, 130.
- Y. Liu, S. C. Virgil, R. H. Grubbs and B. M. Stoltz, *Angew. Chem. Int. Ed.*, 2015, **54**, 11800.
- M. O. Miranda, A. Pietrangelo, M. A. Hillmyer and W. B. Tolman, *Green Chem.*, 2012, **14**, 490.
- A. John, M. O. Miranda, K. Ding, B. Dereli, M. A. Ortuno, A. M. LaPointe, G. W. Coates, C. J. Cramer and W. B. Tolman, *Organometallics*, 2016, **35**, 2391.
- M. A. Ortuno, B. Dereli and C. J. Cramer, *Inorg. Chem.*, 2016, **55**, 4124.
- (a) S. Z. Tasker, E. A. Standley and T. F. Jamison, *Nature*, 2014, **509**, 299; (b) V. P. Ananikov, *ACS Catal.*, 2015, **5**, 1964.
- A. John, M. A. Hillmyer and W. B. Tolman, *Organometallics*, 2017, **36**, 506.
- A. John, B. Dereli, M. A. Ortuno, H. E. Johnson, M. A. Hillmyer, C. J. Cramer and W. B. Tolman, *Organometallics*, 2017, **36**, 2956.
- M. N. Birkholz (nee Gensow), Z. Freixa and P. W. N. M. van Leeuwen, *Chem. Soc. Rev.*, 2009, **38**, 1099.
- S. P. Nolan and C. S. J. Cazin, *Science of Synthesis: N-Heterocyclic Carbenes in Catalytic Organic Synthesis*, Thieme, Stuttgart, 2017.
- G. C. Fortman and S. P. Nolan, *Chem. Soc. Rev.*, 2011, **40**, 5151.
- (a) A. John, L. T. Hogan, M. A. Hillmyer and W. B. Tolman, *Chem. Commun.*, 2015, **51**, 2731; For decarbonylative Heck reactions of carboxylic acid derivatives, see: (b) L. J. Gooßen and J. Paetzold, *Angew. Chem. Int. Ed.*, 2002, **41**, 1237; (c) G. Meng and M. Szostak, *Angew. Chem. Int. Ed.*, 2015, **54**, 14518.
- A. Behr, A. J. Vorholt, K. A. Ostrowski and T. Seidensticker, *Green Chem.*, 2014, **16**, 982.
- A. Chatterjee, S. H. H. Eliasson, K. W. Törnroos and V. R. Jensen, *ACS Catal.*, 2016, **6**, 7784.
- For an excellent review on Pd(II)-precatalysts, see: P. G. Gildner and T. J. Colacot, *Organometallics*, 2015, **34**, 5497.
- A. Chatterjee and V. Jensen, *ACS Catal.*, 2017, **7**, 2543.
- L. Yin and J. Liebscher, *Chem. Rev.*, 2007, **107**, 133.
- S. Maetani, T. Fukuyama, N. Suzuki, D. Ishihara and I. Ryu, *Chem. Commun.*, 2012, **48**, 2552.
- For reviews, see: (a) I. Bauer and H. J. Knölker, *Chem. Rev.*, 2015, **115**, 3170; (b) A. Fürstner, *ACS Cent. Sci.*, 2016, **2**, 778; For a pertinent review on iron-catalyzed C–O cross-coupling, see: (c) E. Bisz and M. Szostak, *ChemSusChem*, 2017, **10**, 3964.
- G. Meng and M. Szostak, *Org. Lett.*, 2015, **17**, 4364.
- For reviews on C–N activation in amides, see: (a) G. Meng, S. Shi and M. Szostak, *Synlett*, 2016, **27**, 2530; (b) C. Liu and M. Szostak, *Chem. Eur. J.*, 2017, **23**, 7157.
- J. Hu, M. Wang, X. Pu and Z. Shi, *Nat. Commun.*, 2017, **8**, 14993.
- A. Tlahuext-Aca, L. Candishi, R. A. Garza-Sanchez and F. Glorius, *ACS Catal.*, 2018, **8**, 1715.
- T. Qin, J. Cornella, C. Li, L. R. Malins, J. T. Edwards, S. Kawamura, B. D. Maxwell, M. D. Eastgate and P. S. Baran, *Science*, 2016, **352**, 801.
- J. Twilton, C. C. Le, P. Zhang, M. H. Shaw, R. W. Evans and D. W. C. MacMillan, *Nat. Rev. Chem.*, 2017, **1**, 0052.
- Selected examples: (a) J. B. Wang, R. Lonsdale and M. T. Reetz, *Chem. Commun.*, 2016, **52**, 8131; (b) A. Dennig, S. Kurakin, M. Kuhn, A. Dordic, M. Hall and K. Faber, *Eur. J. Org. Chem.*, 2016, 3474; (c) C. Lu, F. Shen, S. Wang, Y. Wang, J. Liu, W. J. Bai and X. Wang, *ACS Catal.*, 2018, **8**, 5794; For leading mechanistic studies, see: (d) J. L. Grant, C. H. Hsieh and T. M. Makris, *J. Am. Chem. Soc.*, 2015, **137**, 4940; (e) C. H. Hsieh, X. Huang, J. A. Amaya, C. D. Rutland, C. L. Keys, J. T. Groves, R. N. Austin and T. M. Makris, *Biochemistry*, 2017, **56**, 3347; (f) J. A. Amaya, C. D. Rutland, N. Leschinsky and T. M. Makris, *Biochemistry*, 2018, **57**, 344; For selected reviews, see: (g) J. H. Schrittwieser, S. Velikogne, M. Hall and W. Kroutil, *Chem. Rev.*, 2018, **118**, 270; (h) J. Dong, E. Fernandez-Fueyo, F. Hollmann, C. Paul, M. Pasic, S. Schmidt, Y. Wang, S. Younes and W. Zhang, *Angew. Chem. Int. Ed.*, 2018, DOI: 10.1002/anie.201800343.
- H. Gröger and W. Hummel, *Curr. Opin. Chem. Biol.*, 2014, **19**, 171.
- M. Beller and H. U. Blaser, *Top. Organomet. Chem.*, Vol. 42, Springer, Berlin, 2012.
- (a) F. Julia-Hernandez, T. Moragas, J. Cornella and R. Martin, *Nature*, 2017, **545**, 84; (b) A. L. Kocen, M. Brookhart and O. Daugulis, *Chem. Commun.*, 2017, **53**, 10010; (c) X. Liu, W. Zhang, Y. Wang, Z. X. Zhang, L. Jiao and Q. Liu, *J. Am. Chem.*

Soc., 2018, **140**, 6873; (d) C. Romano and C. Mazet, *J. Am. Chem. Soc.*, 2018, **140**, 4743; (e) D. P. Ojha, K. Gadde and K. R. Prabhu, *J. Org. Chem.*, 2017, **82**, 4859.