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Transfer Dehydrogenations of Alkanes and Related Reactions Using Iridium Pincer Complexes

David Bézier and Maurice Brookhart

Abstract This chapter covers advances during the past 5 years in using iridium pincer complexes for transfer dehydrogenations of alkanes as well as related reactions which couple dehydrogenation with other transformations. Several new pincer complexes are described which have emerged during this period and which have added not only to the scope of available catalysts but also to the range of substrates and products generated. Transfer dehydrogenation has been linked with other reactions to produce catalytic systems that carry out alkane metatheses, generate benzene bearing a long-chain linear alkyl group from ethyl benzene and linear alkanes, couple alkanes with alkenes, and use transfer dehydrogenation in combination with Diels–Alder chemistry to produce *para*-xylene from ethylene as the sole feedstock.

Keywords Alkane functionalization · C–H activation · Dehydrogenation · Iridium pincer catalysts

Contents

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1 Introduction

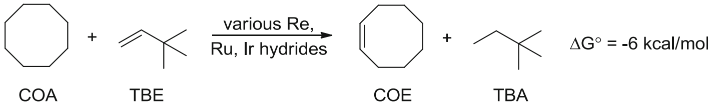
Alkanes are the primary feedstock from which the majority of the world's chemicals are derived. They are the primary constituents of petroleum and natural gas and the associated low boiling components of natural gas. Coal, natural gas, and biomass are also sources of alkanes produced via gasification of these materials to syngas (CO/H_2) followed by Fischer–Tropsch catalysis resulting in a stochastic distribution of linear hydrocarbons.

Alkenes as well as aromatics are derived from alkanes through dehydrogenation. Alkenes and aromatics are highly versatile intermediates which can be converted to a wide array of value-added chemicals and materials including detergents, pharmaceutical intermediates, and polymers. Alkenes are primarily produced via "cracking" alkanes over heterogeneous dehydrogenation catalysts at very high temperatures (500–900°C) [1]. Such "acceptorless" dehydrogenations are endothermic (ca. 28–30 kcal/mol), but the large positive entropy gained from loss of H_2 renders these processes exergonic at such high temperatures. Additionally, aromatics are also made by heterogeneous dehydrogenations of various hydrocarbon feedstocks. Such high-temperature processes often result in low selectivities and generation of by-products.

There has been growing interest in homogeneous alkane dehydrogenations due to the possibility of obtaining higher selectivities and the prospects for production of functionalized alkenes via dehydrogenation of functionalized alkanes. Homogeneous dehydrogenations are normally carried out at much lower temperatures which require the use of a hydrogen acceptor to render the reactions thermodynamically feasible [Eq. (1)]. In the majority of the cases examined to date, the acceptor molecule has been an alkene, rendering the overall reaction close to thermoneutral.

$$\begin{array}{c} R\text{-}CH_2\text{-}CH_2\text{-}R' + A \longrightarrow R\text{-}CH{=}CH\text{-}R' + AH_2 \\ A = \text{alkene} \end{array} \tag{1}$$

Early studies of catalytic intermolecular dehydrogenations were reported independently by Felkin and Crabtree. In a series of papers [2–4], Felkin employed phosphine-stabilized polyhydrides of rhenium, ruthenium, and iridium as catalysts. Conditions were generally mild (25–150°C), but turnover numbers were low (2–70). The primary screening reaction employed both by Felkin and Crabtree, which has become standard today for screening transfer dehydrogenations, used *t*-butylethylene (TBE) as acceptor to dehydrogenate cyclooctane (COA) [Eq. (2)]. The favorable ΔG° of -6 kcal/mol avoids reversibility issues, and the bulky *t*-butylethylene acceptor binds weakly to metal centers and possesses no allylic hydrogens, thus avoiding potential catalyst deactivation through strong binding or formation of a π-allyl species.



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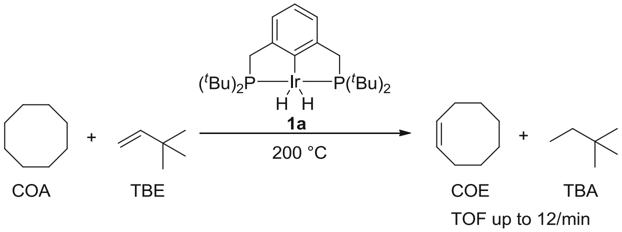
Crabtree started his investigations by using the cationic Ir(III) complex $IrH_2(acetone)_2(PPh_3)_2^+$ followed by neutral Ir(III) carboxylates $(PR_3)_2IrH_2(\eta^2\text{-}O_2CCF_3)$ (R = cyclohexyl, p-C_6H_5) as catalysts for thermal and photochemical dehydrogenations [5–7]. As with the case for Felkin's polyhydride studies, turnover numbers were generally low, but driving the reaction with light allowed acceptorless dehydrogenation of cyclooctane to be achieved [8]. In related studies, the groups of Saito [9], Tanaka [10], and Goldman [11] independently showed that photolysis of $Rh(Cl)(CO)(PMe_3)_2$ in linear and cyclic alkanes resulted in conversion to alkenes with high turnover numbers. Goldman showed a related system, $Rh(Cl)(L)(PMe_3)_2$ (L = PCy_3 or $P(^iPr)_3$), as well as the dimer, $[ClRh(PMe_3)_2]_2$, could be activated with H_2 in the presence of an acceptor to generate the active species $Rh(Cl)(PMe_3)_2$ which could achieve rapid transfer dehydrogenation [12–15]. A drawback of the system is that under H_2, alkene hydrogenation competes with alkane dehydrogenation. A thorough mechanistic study was reported.

A major breakthrough in transfer dehydrogenation of alkanes was achieved in 1996 by Jensen, Kaska, and coworkers [16, 17]. They reported that the iridium pincer complex $(^{tBu4}PCP)IrH_2$, **1a**, was highly reactive and exceptionally thermally stable for transfer dehydrogenation of COA employing TBE as the acceptor [Eq. (3)]. For example, at 200°C the turnover frequency was reported to be 12/min with no noticeable catalyst decomposition over 7 days.



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The report by Jensen and Kaska stimulated extensive work using various iridium pincer complexes for alkane transfer dehydrogenations and related chemistry. Indeed, iridium pincer complexes have dominated this area of research. Some of the highlights during the period 1996–2010 include the modification of the complex $(^{tBu4}PCP)IrH_2$, **1a**, by changing substituents on the phosphine (**1b**–**1c**) [18–20], adding functional groups to the aromatic backbone (**1d**–**1f**) [21–24], replacing the phosphines by phosphinite groups (**2a**–**2d**) [25–28], and incorporating an anthracenyl group in the backbone (**3a**) (Fig. 1) [29]. The mechanism of the alkane dehydrogenation reaction using **1a** [22, 30–33] and **2a** [22, 25, 26] was thoroughly investigated.

The above work has been extensively reviewed [34–37]; the reader is directed to these publications for an in-depth coverage. This chapter will be devoted to more

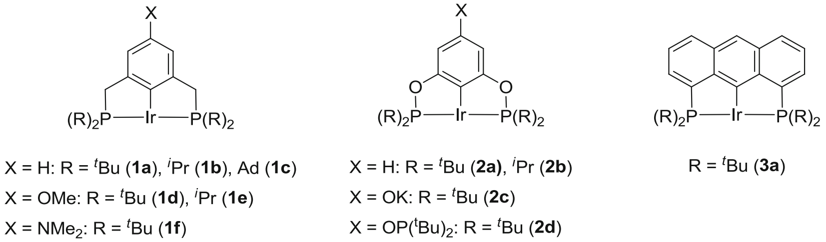

Fig. 1 Examples of active PCP iridium pincer complexes for alkane dehydrogenation

recent advances employing iridium pincer complexes in transfer dehydrogenation reactions and closely related chemistry.

2 Alkane Dehydrogenation

It has been shown that iridium pincer complexes containing electron-rich alkylphosphines are highly efficient catalysts for alkane dehydrogenation reactions. However, the Roddick group demonstrated that iridium complexes bearing electron poor phosphines can also efficiently catalyze the dehydrogenation of alkanes [38]. The iridium complex containing bis(trifluoromethyl)phosphine groups (^{CF3}PCP)Ir(η^4-COD), **4** (Fig. 2), was shown to catalyze the transfer dehydrogenation of COA with TBE (1:1) giving TONs up to 660 after 58 h (initial TOF = 40 h^{-1}) at 200°C. Due to inhibition by TBE, by using a 5:1 COA/TBE ratio, higher initial activities (TOF = 155 h^{-1}) and TONs (2,580 after 24 h) were obtained. This catalyst showed relatively minor inhibition by cyclooctene (COE), and no inhibition was detected with N_2 or H_2O. Using the same catalyst, very low activity was observed for the dehydrogenation of linear alkanes with TBE at 150°C (TONs = 81 after 48 h), and moderate TONs were obtained for the acceptorless dehydrogenation of cyclodecane (TONs = 92 after 24 h).

The Yamamoto group reported the use of 7-6-7 fused-ring PCP iridium catalysts (7–6–7-^{R}PCP)Ir(H)(Cl), **5a**, (R = *i*Pr) and **5b** (R = Ph) for alkane transfer dehydrogenation (Fig. 3) [39]. After activation with NaO^{t}Bu, TONs up to 3,510 and 4,140 were obtained with catalysts **5a** and **5b**, respectively, after 36 h at 200°C when using a COA/TBE ratio of 1.5:1. While both catalysts **5a** and **5b** showed no inhibition by product formation, the latter allowed highest TONs (4,821 at 230°C after 24 h) due to its higher stability. The catalyst **5a** is also an active catalyst for the transfer dehydrogenation of linear alkanes. By using a ratio *n*-octane/norbornene of 1.5:1, TONs up to 1,100 were obtained at 200°C after 12 h. However, due to its low solubility in *n*-octane, the catalyst **5b** showed no activity under similar conditions.

Huang and coworkers synthesized a new phosphinothious/phosphinite (^{iPr4}PSCOP)Ir pincer complex, **6** (Fig. 4) [40]. Upon activation with NaO^{t}Bu, this complex exhibits exceptionally high activity for transfer dehydrogenation of COA

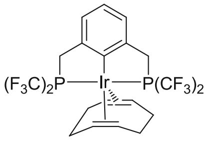

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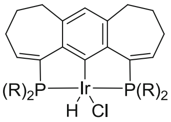
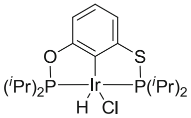
Fig. 2 (^{CF3}PCP)Ir(η^4-COD) complex reported by Roddick [38]



R = ^{i}Pr (**5a**), R = Ph (**5b**)

Fig. 3 (7–6–7-^{R}PCP)Ir complexes reported by Yamamoto [39]



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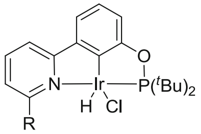


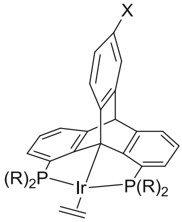
R = H (**7a**), R = Me (**7b**), R = ^{t}Bu (**7c**)

Fig. 4 Iridium complexes reported by Huang [40, 41]

with TBE as the hydrogen acceptor. By using a COA/TBE ratio of 1:1, TONs up to 5,900 were achieved after 15 h at 200°C with an initial rate of 2,910 TO h^{-1}. Due to slight inhibition with TBE, this rate was increased to 5,600 TO h^{-1} by using a COA/TBE ratio of 4.8:1. This catalytic system also demonstrated high efficiency for the transfer dehydrogenation of *n*-octane with TOF up to 1,400 h^{-1} when the reaction was carried out at 200°C with TBE (0.5 M). Under these conditions, a selectivity of 33% for the formation of 1-octene was observed after 5 min due to fast isomerization of the terminal olefin. The olefin isomerization mechanism by iridium pincer catalysts was shown by Goldman and Brookhart to proceed via a π-allyl mechanism involving a η^3-allyl iridium hydride intermediate [42]. At the same temperature, by increasing the TBE concentration to 3 M, TONs up to 1,200 were obtained.

The Huang group also reported iridium complexes of novel NCP pincer ligands containing pyridine and phosphinite arms (^{R}NCOP^{tBu})Ir(H)(Cl), **7a**–**7c** (Fig. 4) [41]. While complexes **7b** (R = Me) and **7c** (R = ^{t}Bu) after activation with NaO^{t}Bu showed quite low catalytic activity for the cyclooctane transfer dehydrogenation (TONs up to 6), the less sterically hindered complex **7a** (R = H) activated with NaO^{t}Bu exhibited TONs up to 466 with initial rates of 1,010 TO h^{-1} when using a COA/TBE ratio of 14:1 at 150°C. TONs of 78, 28, and 19 were obtained for the dehydrogenation of *n*-octane with TBE (0.5 M) at 150°C when using the catalytic systems NaO^{t}Bu plus **7a**, **7b**, and **7c**, respectively. Due to a fast isomerization process, the selectivity for the formation of 1-octene was low (7% after 5 min with **7a**).

The Brookhart group reported the use of PC(sp^3)P–Ir(ethylene) pincer complexes, **8a**–**8d**, based on the triptycene ligand (Fig. 5) [43] (for earlier reports of similar iridium triptycene complexes, see [44–47]). The complex **8a** (R = *i*Pr)



R = ^{i}Pr, X = H (**8a**); R = ^{i}Pr, X = NMe_2 (**8b**)
R = Cy, X = H (**8c**), R = Cp, X = H (**8d**)

Fig. 5 PC(sp^3)P–Ir (ethylene) complexes reported by Brookhart [43]

showed high activity for the dehydrogenation of COA with TBE (1:1) giving TONs of 910, 2,590, and 2,820 after 0.5, 4, and 24 h, respectively. The higher TONs obtained with **8a** compared to (^{tBu4}POCOP)IrH_2, **2a**, were explained by the difference of binding affinities of these two complexes for TBE and COE. The complex **8a** has a similar affinity for these two alkenes, in contrast to **2a** which favors COE over TBE, thus inhibiting the catalytic activity by the product formation (COE) as the reaction proceeds. Surprisingly, very low activities (TONs ≈40) were observed when using catalysts **8c** (R = Cy) and **8d** (R = Cp). The complex **8a** also exhibited high catalytic activity (TOF up to 2,400 h^{-1}) and stability (TON = 6,000 after 10 h) for the dehydrogenation of *n*-octane with TBE (6M) at 200°C. By decreasing the reaction temperature to 100°C with 0.5 M of TBE, 1-octene represented up to 27% of all the octenes after 1 h of reaction (TON = 34). Under these conditions, full conversion of TBE to TBA (TON = 500) was obtained after 29 h. The complex **8b** bearing a NMe_2CH_2 substituent on the triptycene backbone was synthesized and successfully supported on alumina by following a previously reported strategy [24]. Modest catalytic activity was observed for the transfer dehydrogenation of COA with TBE when using this supported catalyst due to a fast decomposition of the catalytic system, most likely due to the reaction between the alumina support and the iridium center.

By replacing the phenyl backbone of the PCP ligand by a cyclohexyl backbone, the Wendt group succeeded in the synthesis of the aliphatic iridium complex (PCyP)Ir(H)(Cl), **9** (Fig. 6) [48]. The catalytic activity of this complex activated with NaO^{t}Bu was found to be very low (TONs up to 50) for the transfer dehydrogenation of COA by TBE (1:1) at 200°C due to fast decomposition of the active species. By decreasing the temperature to 120°C with the use of a ratio COA/TBE of 24:1 at 120°C, TONs up to 200 have been achieved. The acceptorless dehydrogenation of COA was also carried out at 150°C giving low TONs (≈5).

The most active iridium dehydrogenation catalysts are based on pincer ligands bearing phoshine or phosphinite groups. However, non-phosphine-based iridium pincer catalysts were also recently developed. The Braunstein group synthesized iridium complexes based on pincer ligands bearing *N*-heterocylic carbenes (NHCs) (Fig. 7). After activation with NaO^{t}Bu, the species generated from the bis(NHC) complex **10** was inactive for alkane transfer dehydrogenation [49]. Similarly, the active catalyst generated from the complex **11** bearing one normal and one

Fig. 6 (PCyP)Ir(H)(Cl) complex reported by Wendt [48]

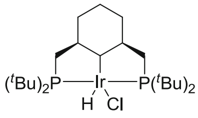


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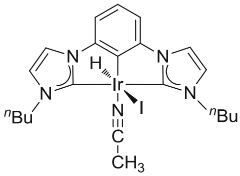
Fig. 7 CCC iridium complexes reported by Braunstein [49, 50]



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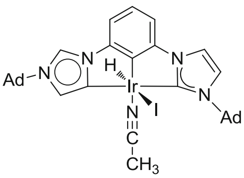

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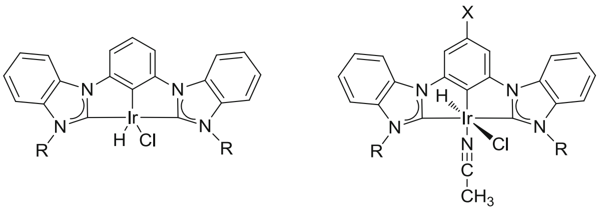
abnormal NHC ligand showed very low activity for the dehydrogenation of COA with TBE (8:1) at 200°C (TONs = 4 after 10 h) due to its low stability and low solubility in the reaction media [50].

The Chianese group synthesized more rigid bis(NHC) iridium complexes, **12a**–**12f**, which were shown to be active pre-catalysts for the acceptorless dehydrogenation of alkanes (Fig. 8) [51, 52]. For the acceptorless dehydrogenation of COA, the catalytic systems generated in situ from **12c**, **12d**, and **12e** with NaO^{t}Bu gave TONs of 103, 84, and 35, respectively, after 12 h at reflux of COA (bp = 150°C). The catalytic activity of **12c** appears to exhibit no inhibition in the presence of COE or N_2. By using the higher-boiling cyclodecane, TONs up to 102 were achieved with the pre-catalyst **12c** after 22 h. Acceptorless dehydrogenation of linear alkanes was also carried out. TONs up to 97 were obtained when using the pre-catalyst with *n*-undecane, which is comparable to the results obtained from the most active iridium PCP catalysts. Under similar conditions, pre-catalysts **12c** and **12d** showed lower reactivity (TON = 50).

Other non-phosphine-based catalysts active for alkane dehydrogenation were developed by the Jensen group [53]. The complex ($^{t\mathrm{Bu}4}$AsOCOAs)IrHCl, **13** (Fig. 9), combined with NaO^{t}Bu catalyzed the transfer dehydrogenation of COA with TBE (1:1) giving TONs of up to 930 after 24 h with initial rates of 600 TO h^{-1} at 200°C. The leveling off in catalytic activity was explained by inhibition by the COE product, as well as thermal decomposition of the catalyst over time.

3 Applications to the Synthesis of Aromatics

As the global demand for chemicals grows, so does that for aromatics, which constitute a significant fraction of the major building blocks of the chemical industry. As petroleum is displaced by natural gas, and as decreased gasoline refining (in favor of diesel [54]) limits production of aromatic by-products, the



R = ^{t}Bu (**12a**), R = Ad (**12b**)

R = Mesityl, X = H (**12c**), R = Mesityl, X = CF_3 (**12d**)
R = 3,5-di-*t*-Butylphenyl, X = H (**12e**)
R = 2,6-diisopropylphenyl, X = H (**12f**)

Fig. 8 CCC iridium complexes reported by Chianese [51, 52]

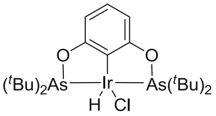


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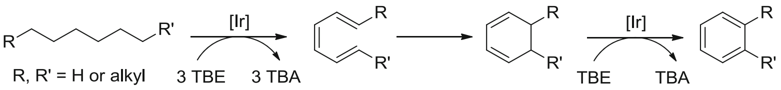
Fig. 9 (^{tBu4}AsOCOAs)IrHCl complex reported by Jensen [53]

synthesis of aromatics from alkanes becomes increasingly attractive. Heterogeneously catalyzed dehydroaromatization of *n*-alkanes is known to occur at very high temperatures (>500°C) but with low yields and low selectivity [55–60].

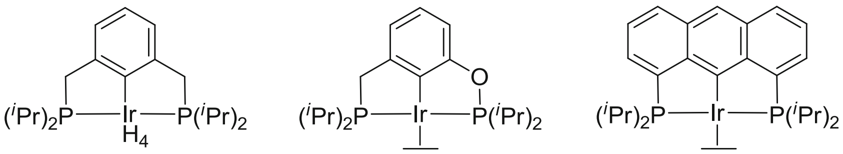
By using iridium pincer catalysts, Goldman and Brookhart developed the dehydroaromatization of *n*-alkanes which allows the formation of alkylaromatics in the presence of an excess of hydrogen acceptors [61]. This reaction occurs via sequential dehydrogenation of alkanes generating conjugated trienes which undergo electrocyclization to give cyclohexadienes which are then further dehydrogenated to yield the aromatic products [Eq. (4)].



(4)

Through the screening of numerous iridium pincer catalysts, high activities were obtained when using the complexes **1b**, **14a**, and **3b** with 4 equiv. of TBE (relative to the *n*-alkane) (Fig. 10). The newly reported hybrid phosphine/phosphinite (^{iPr4}PCOP)Ir, **14a**, emerged as the most effective catalyst allowing the conversion of *n*-hexane to benzene with a yield of 44% (670 mM) after heating a solution of 6.13 M TBE with 1.53 M *n*-hexane for 120 h at 165°C. The dehydroaromatization of *n*-octane was achieved even more efficiently generating aromatics with a yield of 86% including *o*-xylene and ethylbenzene with a 7:1 ratio. Propene was able to replace the expensive TBE as hydrogen acceptor albeit with lower yields (38%).

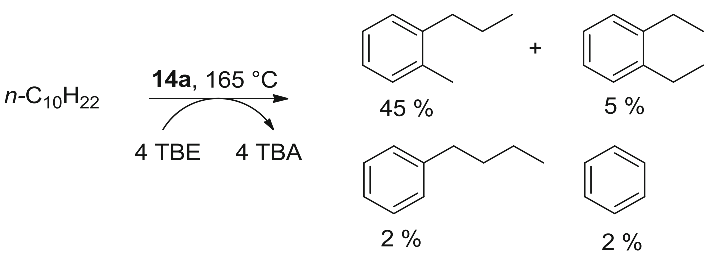
Moreover, starting from *n*-decane or *n*-dodecane, this protocol resulted in the formation of non-branched *n*-alkylarenes which are not accessible via the classical industrial route involving Friedel–Crafts alkylation of arenes with linear olefins. For example, when the dehydroaromatization of *n*-decane was catalyzed by **14a**,



1b **14a** **3b**

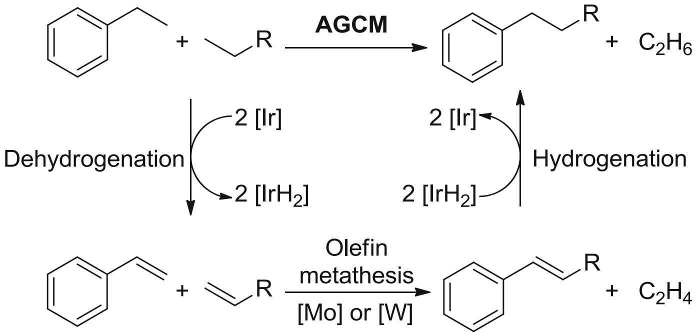
Fig. 10 Active catalysts for *n*-alkane dehydroaromatization [61]

o-propyltoluene was the major product along with *n*-butylbenzene, 1,2-diethylbenzene, and benzene [Eq. (5)].



(5)

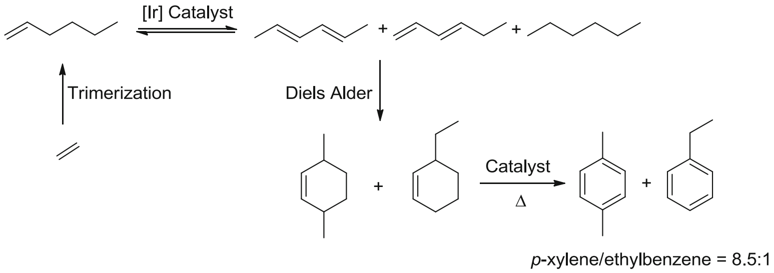
Another protocol for the synthesis of *n*-alkylarenes was recently developed by Schrock, Goldman, and coworkers [Eq. (6)] [62]. This process combines a Schrock-type olefin metathesis catalyst (Mo or W) with an iridium pincer dehydrogenation catalyst and results in the conversion of ethylbenzene and *n*-alkanes to long-chain *n*-alkyl arenes via the reaction sequence shown in Eq. (6). This reaction termed “Alkyl Group Cross-Metathesis” (AGCM) was carried out at 180°C, and best results were obtained with the use of W(NAr′)(C_3H_6)(pyr)(OHIPT) (Ar′ = 2,6-$Me_2C_6H_3$, OHIPT = 2,6-(2,4,6-$^iPr_3C_6H_2$)$_2C_6H_3O$) as the olefin metathesis catalyst and (^{tBu4}PCP)IrH_2, **1a**, as the dehydrogenation/hydrogenation catalyst. For example, the reaction between *n*-octane and ethylbenzene after 24 h yielded a mixture of 1-phenyloctane (240 mM), 1-phenylheptane (60 mM), and tetradecane (20 mM).



(6)

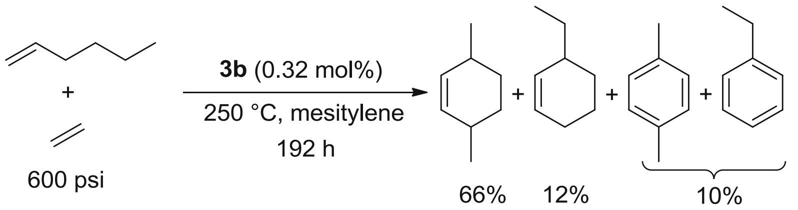
An alternative route to the most valuable constituent of the BTX (benzene, toluene, xylene) mixture, *p*-xylene, has been reported by Brookhart and coworkers

[63]. *p*-Xylene is one of the highest volume chemical intermediates derived from petroleum. Its primary use is for the production of the dimethyl ester of terephthalic acid, which is copolymerized with ethylene glycol to produce polyethylene terephthalate (PET). Traditionally, *p*-xylene is produced by catalytic reforming of various crude oil streams, followed by a difficult separation of the mixture containing benzene, toluene, *o*-xylene, *m*-xylene, and *p*-xylene. Taking advantage of the abundance of ethane in the USA via the recent shale gas boom, the use of ethylene (obtained from cracking of ethane) [64] has drawn growing interest as a feedstock. By using ethylene as the sole feedstock, the Brookhart group developed the synthesis of *p*-xylene, uncontaminated by the *ortho* and *meta* isomers [Eq. (7)]. The stepwise synthesis relies on the disproportionation of 1-hexene (which can be obtained from the trimerization of ethylene) to 2,4-hexadiene catalyzed by an iridium pincer complex (0.04 mol%) at 180°C. Through a catalyst screening, best results were obtained when using the catalyst ($^{i\text{Pr}4}$Anthraphos)Ir(C_2H_4), **3b** (TON = 777 after 3.5 h), with moderate activities observed with $^{i\text{Pr}4}$PC(sp^3)P–Ir (ethylene), **8a** (TON = 506 after 3.5 h) [43], and ($^{i\text{Pr}4}$PCOP)Ir(ethylene), **14** (TON = 214 after 3.5 h). The mixture was subjected to a Diels–Alder cyclization at 250°C with ethylene (600 psi) resulting in the complete formation of 3,6-dimethylcyclohexene and 3-ethylcyclohexene (ratio 8:1). The dehydrogenation of these two compounds was carried out at 400°C over Pt/Al_2O_3 giving a mixture of *p*-xylene and ethylbenzene (ratio 8.5:1) in 93% and 88% yields, respectively.



(7)

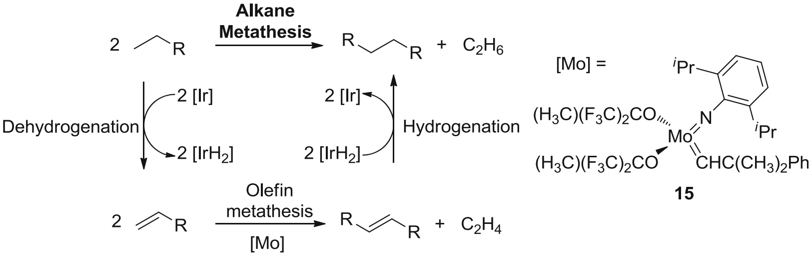
A one-pot procedure was also developed [Eq. (8)]. Heating 1-hexene at 250°C with 600 psi of ethylene for 24 h in the presence of 0.32 mol% of **3b** after 192 h resulted in nearly complete conversion with respect to hexenes (93%) yielding 3,6-dimethylcyclohexene (66%), ethylcyclohexene (12%), and aromatics (10%). This mixture is readily converted to *p*-xylene and ethyl benzene using classical heterogeneous catalysts such as Pt on alumina. This was the first example of ethylene serving as a hydrogen acceptor in alkane dehydrogenation. The yield of hexadienes (and ultimately *p*-xylene) is no longer limited by the equilibrium disproportionation of 1-hexene to hexadienes and *n*-hexane, making this one-pot approach to 3,6-dimethylcyclohexene a more attractive route for *p*-xylene synthesis from ethylene. A similar strategy was used for the synthesis of piperylene and toluene via the tandem transfer dehydrogenation of pentane or pentene followed by a Diels–Alder reaction with ethylene [65].



(8)

4 Applications to the Synthesis of Long-Chain Alkanes

Alkane metathesis has potential applications on an enormous scale. Most notably, it would allow the "upgrading" of low carbon number *n*-alkanes (C_3–C_8) to chains with higher carbon number which are ideal for diesel and jet fuel. Lighter *n*-alkanes can be obtained via Fischer–Tropsch chemistry from syngas [66–69], from direct biomass reduction, or even from CO_2 reduction with the use of sustainable energy sources. Moreover, light alkanes are found in vast amounts in natural gas and petroleum reserves, equivalent to >10% of current world oil reserves. While heterogeneous alkane metathesis catalysts have been reported [70–73], the first homogeneous alkane metathesis catalytic system was developed by Goldman, Brookhart, and coworkers in 2006 based on tandem transfer dehydrogenation and olefin metathesis [Eq. (9)] [74, 75]. The system exhibits high efficiency with overall product concentrations of 1.25 and 2.05 M obtained from 7.6 M *n*-hexane using 10 mM (^{tBu4}PCP)IrH$_2$, **1a**, and (^{tBu4}POCOP)IrH$_2$, **2a**, respectively, in combination with the Mo catalyst, **15** (16 mM), after 1 day at 125°C. In addition to decane and ethane, *n*-alkanes of intermediate chain lengths are formed and represent a large fraction of the total alkene product. Due to the low stability of the Mo catalyst, **15**, the overall yield was limited.

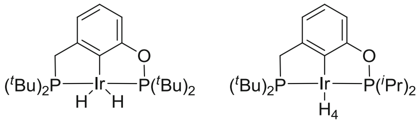


15

(9)

Other catalysts have been used to increase the substrate scope, yield, and selectivity of this reaction [19, 76–78]. Particularly, the Goldman group investigated the use of the mixed phosphine/phosphinite catalyst (^{tBu4}PCOP)Ir(H$_2$), **14b**, which was found to be four times faster than (^{tBu4}PCP)IrH$_2$, **1a**, and eight times faster than (^{tBu4}POCOP)IrH$_2$, **2a** [79] (Fig. 11). More interestingly, the less sterically hindered (^{tBu2}PCOP^{iPr2})Ir(ethylene), **14c**, was found to be even more active

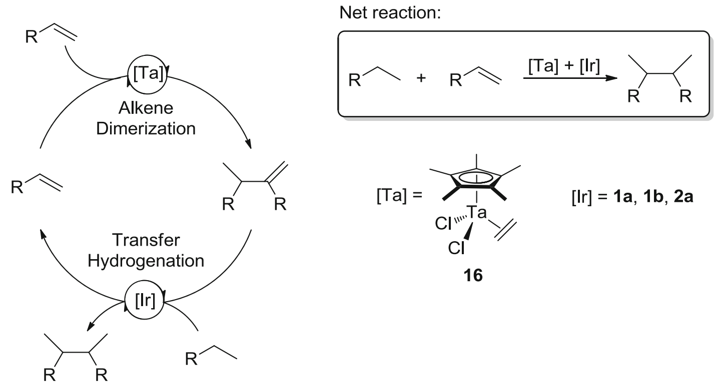
Fig. 11 Active co-catalysts in tandem alkane metathesis [79]



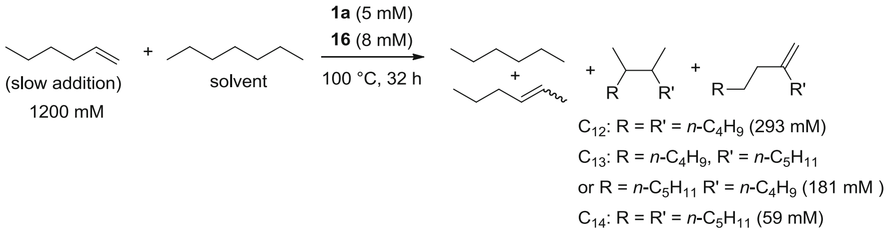
14b **14c**

with rates four times greater than (${}^{t\mathrm{Bu}4}$PCOP)Ir(ethylene), **14b**. However, (${}^{i\mathrm{Pr}4}$PCOP)Ir(H_2), **14a**, was not as productive as the two other catalysts presumably due to lower stability.

Alkane–alkene coupling, another strategy to upgrade light hydrocarbons, was recently reported by Bercaw and Labinger [80–82]. This process takes advantage of the mixed nature of many light by-product streams which contain both alkanes and alkenes as substrates. The ideal reaction [Eq. (10)] involves a tantalum-based catalyst to dimerize the alkene component of the mixed feedstock to afford the C_{2n} alkene. Subsequent transfer hydrogenation by an iridium pincer catalyst allows the conversion of the alkane component to the 1-alkene while hydrogenating the C_{2n} product to an alkane. The 1-alkene is next catalytically dimerized with a second equivalent of 1-alkene, and the cycle can continue. The net reaction corresponds to the coupling of the alkane and alkene to give the higher alkane without the formation of any lighter by-products. This process involves alkane dehydrogenation by a pincer-ligated iridium complex (**1a**, **1b**, or **2a**) and alkene dimerization by Cp*TaCl_2(ethylene), **16**, which is inert to internal olefins. Best results were obtained by slowly adding 1-hexene (1,200 mM) to a mixture containing (${}^{t\mathrm{Bu}4}$PCP)Ir(H_2), **1a** (5 mM), and Cp*TaCl_2(ethylene), **16** (8 mM), in *n*-heptane (solvent) which resulted in the generation of C_{13} alkenes (obtained from hexane/heptene coupling) and C_{14} alkenes with a yield of 40% (C_{13}+C_{14}) and a cooperativity of 91% [Eq. (11)]. The "cooperativity" was defined by Bercaw and Labinger as the amount of 1-heptene generated by dehydrogenation that is incorporated into C_{13} and C_{14} alkenes. The absence of C_{13}/C_{14} alkanes indicates that the last step of the catalytic cycle (hydrogenation of the long-chain alkene) cannot be completed. When using (${}^{t\mathrm{Bu}4}$POCOP)Ir(H_2) **2a** as the co-catalyst, no desired products (C_{13}/C_{14}) were detected due to the fast isomerization of 1-heptene to internal heptenes which are inert to coupling by **16**. Moreover, this tandem catalytic system can be applied to the dimerization of *n*-heptane with TBE (which is inert to dimerization). The use of (${}^{i\mathrm{Pr}4}$PCP)Ir(H_2) **1b** (2 mM) with **16** (8 mM) and 250 mM of TBE in *n*-heptane at 100°C for 18 h resulted in ~50% conversion and the generation of C_{14} alkenes in 18% yield. Styrene was also investigated as an alternate hydrogen acceptor. The conversion of styrene/heptane mixtures by the Ta/Ir tandem system led to the formation of heptene dimers, with up to 58% overall yield of heptane-derived products.



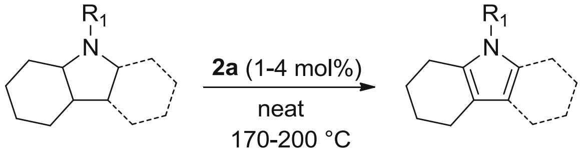
(10)



(11)

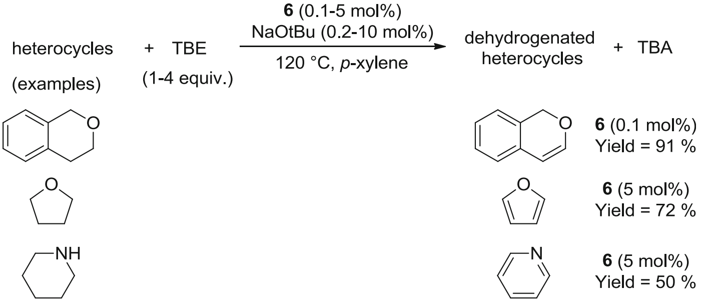
5 Dehydrogenation of Functionalized Organic Molecules

Despite the large number of highly active catalysts for alkane dehydrogenation, surprisingly little work has been extended to functionalized substrates. An early report by Jensen and Kaska showed modest reactivity (~57 TONs) for the dehydrogenation of tetrahydrofuran with TBE by using ($^{t\mathrm{Bu}4}$PCP)Ir(H_2), **1a**, as the catalyst at 150°C [83]. Using the same catalyst, the dehydrogenation of tertiary amines to form enamines in the presence of TBE at 90°C was reported by Goldman, again with modest TONs (≈10) [84]. A similar reaction developed by the Wendt group with (PCyP)Ir(H)(Cl), **9**, as catalyst required higher temperatures (120°C) to obtain comparable activity [48]. In the context of hydrogen storage, acceptorless dehydrogenation of *N*-ethylperhydrocarbazole by ($^{t\mathrm{Bu}4}$PCP)Ir(H_2), **1a**, ($^{i\mathrm{Pr}4}$PCP)Ir (H_2), **1b**, and ($^{t\mathrm{Bu}4}$POCOP)Ir(H_2), **2a**, was developed by Jensen [85]. They later found that ($^{t\mathrm{Bu}4}$POCOP)Ir(H_2), **2a**, was able to selectively dehydrogenate the heterocycle ring of various indolic and carbazolic molecules [Eq. (12)] [86].



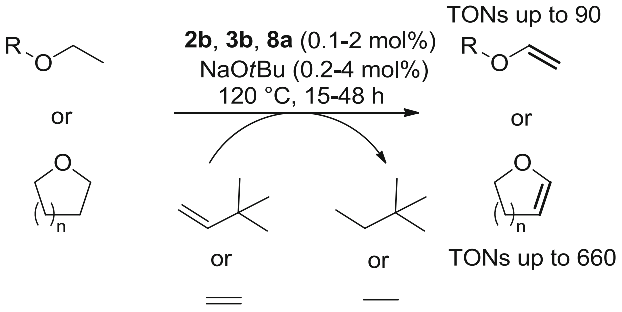
(12)

Recently, Huang demonstrated a much broader scope of heterocycle dehydrogenations using the hybrid phosphinothious/phosphinite ($^{i\text{Pr}4}$PSCOP)Ir(H)(Cl) pincer complex **6** activated with NaO^{t}Bu [40]. A large variety of O- and N-containing heterocycles were successfully dehydrogenated at 120°C in the presence of TBE [Eq. (13)]. For example, 2,3-dihydrobenzofuran gives benzofuran in high yield with low catalyst loading (0.1 mol%). Higher catalyst loading (5 mol%) was required to dehydrogenate tetrahydrofuran to furan and piperidine to pyridine.

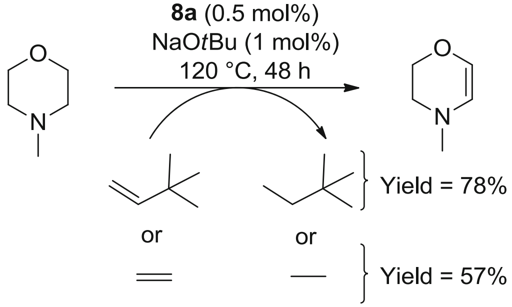


(13)

Brookhart and coworkers recently showed that catalysts ($^{i\text{Pr}4}$Anthraphos)Ir(H)(Cl), **3b**, $^{i\text{Pr}4}$PC(sp^3)P–Ir(H)(Cl), **8a**, and ($^{i\text{Pr}4}$POCOP)Ir(H)(Cl), **2b**, were effective for the dehydrogenation of cyclic and acyclic ethers using TBE as a hydrogen acceptor at 120°C after activation with NaO^{t}Bu [Eq. (14)] [87]. For example, THF and *N*-methylmorpholine were converted to furan and 2,3-dehydro-*N*-methylmorpholine with TONs of 660 and 325, respectively, using the pre-catalyst **3b**. Acyclic ethers represent a more challenging class of substrates. The small, electron-rich alkene products are strong ligands for Ir(I) complexes and thus readily inhibit catalysis. However, it was observed that diethyl ether was dehydrogenated with all three catalysts, though pre-catalyst **8a** gave the best result providing 90 TONs with 0.2 mol% loading. The dehydrogenation of cyclic and acyclic ether substrates using ethylene as the hydrogen acceptor was demonstrated for the first time. Under mild conditions at 120°C, a series of ether heterocycles can be dehydrogenated with up to 375 TONs producing ethane as the hydrogenated product. The pre-catalyst **8a** was particularly active in this protocol, producing good yields for all the substrates surveyed. For example, the reaction of *N*-methylmorpholine with ethylene catalyzed by **8a** (0.5 mol%)/NaO^{t}Bu (1 mol%) selectively formed 2,3-dehydro-*N*-methylmorpholine in 57 % yield, lower than the 78% yield obtained with TBE [Eq. (15)].



(14)



(15)

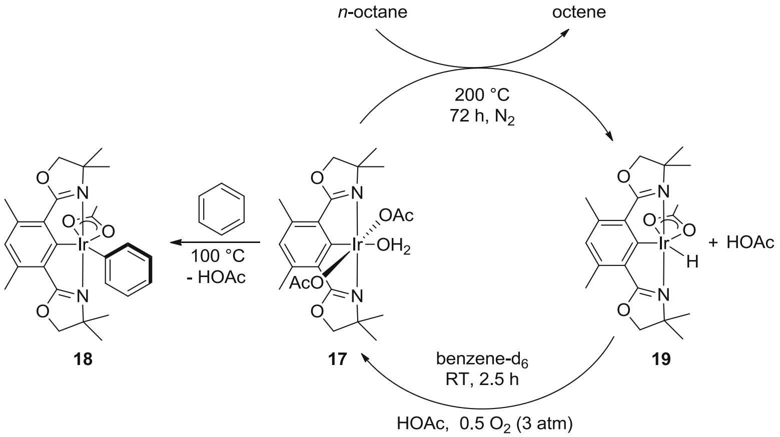
6 Moving Forward by Using O_2 as Hydrogen Acceptor

Oxidative dehydrogenation of light alkanes offers a potentially attractive route to alkenes, since the reaction is exothermic and avoids the thermodynamic constraints of non-oxidative routes by forming water as a by-product [Eq. (16)]. This methodology has been intensively studied for the conversion of ethane to ethylene and propane to propene via the use of heterogeneous catalysts [88, 89]. Homogeneous systems for such reactions have not yet been reported, but they could complement heterogeneous catalysts via the use of milder conditions and application to a larger substrate scope including longer-chain alkanes.

$$C_nH_{2n+2} + 0.5\ O_2 \xrightarrow[\Delta H° \approx -28\ \text{kcal.mol}^{-1}]{} C_nH_{2n} + H_2O \qquad (16)$$

Goldberg, Heinekey, Goldman, and coworkers have recently made progress towards achieving this goal. They found that the Ir(III) bis-acetate complex (^{dm}phebox)Ir(OAc)$_2$(OH$_2$) (^{dm}phebox = 2,6-bis(4,4-dimethyloxazolinyl)-3,5-dimethylphenyl), **17**, can achieve stoichiometric C–H activation of arenes and alkanes [Eq. (17)] [90]. With benzene, C–H activation takes place to form (^{dm}phebox)Ir(OAc)(Ph), **18**, at 100°C, and with *n*-octane, an aliphatic C–H bond is activated followed by a β-hydride elimination to give (^{dm}phebox)Ir(OAc)(H), **19**, and octene after 72 h at 200°C. The dehydrogenation mediated by **17** results from C–H activation at an Ir(III) center via a concerted metalation–deprotonation pathway [91], in contrast with the reactions of phosphine-based pincer iridium systems.

A fast isomerization of the kinetic product 1-octene to internal octenes has been observed. The stoichiometric alkane dehydrogenation mediated by **17** is not inhibited by the presence of N_2 and α-olefins, and the rate of the reaction seems to be accelerated by the presence of water. Complex **17** can be regenerated from **19** by reacting with O_2 and HOAc [92]. This suggests that a catalytic cycle involving O_2 as hydrogen acceptor is plausible. However, preliminary attempts to make this reaction catalytic have been thwarted by catalytic instability towards O_2 at the temperature required for alkane dehydrogenation.



(17)

7 Summary and Future Challenges

The period 2011–2015 has seen continued development of a wide variety of new iridium pincer complexes active for transfer dehydrogenations of alkanes. These include iridium complexes which have incorporated, for example, electron-deficient PCP ligands, CCC pincer ligands bearing NHC carbene arms, $PC_{sp3}P$ ligands exhibiting a cyclohexyl or triptycene unit in the backbone, $PC_{sp2}P$ ligands based on an anthracene and a rigid fused 7-6-7 ring structure, hybrid PCP systems bearing mixed phosphine/phosphinite (PCOP) and phosphinothious/phosphinite (PSCOP) arms, and a pincer ligand, AsOCOAs, in which phosphorus atoms have been replaced by arsenic. Several of these systems have shown improved thermal stabilities and/or turnover numbers with respect to alkane transfer dehydrogenations. A major unsolved problem in simple transfer dehydrogenations is the selective generation of valuable α-olefins from linear alkanes. While several iridium pincer systems show kinetic selectivity for formation of α-olefins, subsequent olefin isomerization results in loss of selectivity at high conversion. While *t*-butyl ethylene and to a lesser extent norbornene have been used as efficient acceptors, for practical applications less expensive, more readily available acceptors need to be developed. Use of ethylene and propylene as acceptors has recently seen success and will likely be a focus of future studies. The ideal acceptor would of course be dioxygen, and recent results from Goldberg, Goldman, and Heinekey suggest this is plausible. There has been increasing interest and advances in catalyst development for dehydrogenations of functionalized systems, in particular dehydrogenations of heterocyclic amines and ethers. Applications to more complex molecules and late stage functionalizations of pharmaceuticals represent attractive future endeavors in this area.

This period has also seen numerous advances in coupling transfer dehydrogenation with a second transformation. Increased efficiency in homogeneous alkane metathesis has been reported, but achieving high selectivity for converting the C_n alkane to ethane and the C_{2n-2} alkane has proved elusive. The high temperatures required for pincer iridium-catalyzed dehydrogenation result in short lifetimes of the olefin metathesis catalysts, so a challenge to be addressed is to develop a highly thermally stable olefin metathesis catalyst or a homogeneous dehydrogenation catalyst that functions efficiently at much lower temperatures. Other attractive processes which likely will see more development include alkyl group cross-metathesis whereby ethyl benzene plus a linear alkane can be converted to benzene bearing a linear long-chain alkyl group, alkane–alkene coupling employing tandem iridium and tantalum catalysts, and combining Diels–Alder reactions of dienes produced through hydrogen transfer reactions to ultimately lead to valuable aromatics such as *p*-xylene and toluene. Coupling other catalytic reactions involving olefins to their generation via dehydrogenation is also an area ripe for further exploitation.

Acknowledgments We gratefully acknowledge the financial support of the National Science Foundation as part of the Center for Enabling New Technologies through Catalysis (CENTC), Phase II Renewal, CHE-1205189.

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