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Article

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Thermal, Catalytic Conversion of Alkanes to Linear Aldehydes and Linear Amines

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ABSTRACT: Alkanes, the main constituents of petroleum, are attractive feedstocks for producing value-added chemicals. Linear aldehydes and amines are two of the most important building blocks in the chemical industry. To date, there have been no effective methods for directly converting *n*-alkanes to linear aldehydes and linear amines. Here, we report a molecular dual-catalyst system for production of linear aldehydes via regioselective carbonylation of *n*-alkanes. The system is comprised of a pincer iridium catalyst for transfer-dehydrogenation of the alkane using *t*-butylethylene or ethylene as a hydrogen acceptor working sequentially with a rhodium catalyst for olefin isomerization-hydroformylation with syngas. The system exhibits high regioselectivity for linear aldehydes and gives high catalytic turnover numbers when using ethylene as the acceptor. In addition, the direct conversion of light alkanes, *n*-pentane and *n*-hexane, to siloxy-terminated alkyl aldehydes through a sequence of Ir/Fe catalyzed alkane silylation and Ir/Rh catalyzed alkane carbonylation, is described. Finally, the Ir/Rh dual-catalyst strategy has been successfully applied to regioselective alkane aminomethylation to form linear alkyl amines.

INTRODUCTION

The mild, selective catalytic conversion of low-value alkanes to value-added chemicals has the potential to be a revolutionary technology in the chemical industry, given the vast quantities of underutilized saturated hydrocarbons.[1] Alkanes are among the most inert organic molecules which is reflected by the forcing conditions employed in the few alkane transformations performed industrially (e.g., hydrocracking or reforming processes typically operate at >450 °C).[2] Moreover, the selective functionalization of a specific C–H bond of an alkane is challenging in the absence of a directing or activating group. Alkanes do react with highly reactive species such as free radicals[3] and carbene or nitrene intermediates[4] under mild conditions, but the reactions typically exhibit low regioselectivity. Although several enzymatic systems are known to selectively catalyze alkane oxidations, the use of such enzymes poses a challenge for large-scale industrial alkane transformations.[5]

Selective alkane activation reactions have been a major goal of research in organometallic chemistry since the discovery that some d8 transition-metal complexes can react selectively at the terminal position of alkanes to form *n*-alkyl complexes.[6] Nevertheless, there have been only a few catalytic methods for selective functionalization of primary C–H bonds of alkanes. One landmark example is rhodium-catalyzed alkane borylation to form linear alkyl boronate esters.[7] Pincer-ligated iridium complexes effect transfer-dehydrogenations of linear alkanes to generate α-olefins selectively at early stages, but the kinetic products isomerize rapidly under reaction conditions to internal olefins.[8] Very recently, Goldman showed that the use of ethylene or propylene as the hydrogen acceptor could significantly improve the selectivity for α-olefins.[9,10]

Linear alkyl aldehydes and amines are high-value intermediates for production of a range of important commodity chemicals. For example, the annual production of oxo chemicals derived from aldehydes exceeds 10 million metric tons.[11] The current technology for synthesis of linear aldehydes relies on transition metal-catalyzed α-olefin hydroformylation, which is one of the largest volume reactions conducted with homogeneous catalysts.[12] Since alkanes are far more abundant and diverse than α-olefins, the direct conversion of alkanes to linear alkyl aldehydes is a transformation with considerable potential. Photoinduced carbonylation of *n*-pentane catalyzed by $RhCl(CO)(PMe_3)_2$ forms *n*-hexanal as the major product, but with low efficiency due to facile catalyst decomposition (turnover number (TON) = 28).[13] Under the UV irradiation conditions, aldehydes readily undergo secondary photoreactions (Norrish Type II) to give side products including olefins, acetaldehyde, and ethanol (Fig. 1A).[14] A purely radical-based process involving the polyoxotungstate-photocatalyzed carbonylation of *n*-hexane with CO to yield branched aldehydes has also been described (Fig. 1A).[15]

During the past decade, several dehydrogenation-based reactions, such as alkane metathesis[16] and alkane dehydroaromatization,[17] have been reported for alkane transformations.[18] However, examples of dehydrogenation-based alkane functionalizations (i.e., the incorporation of

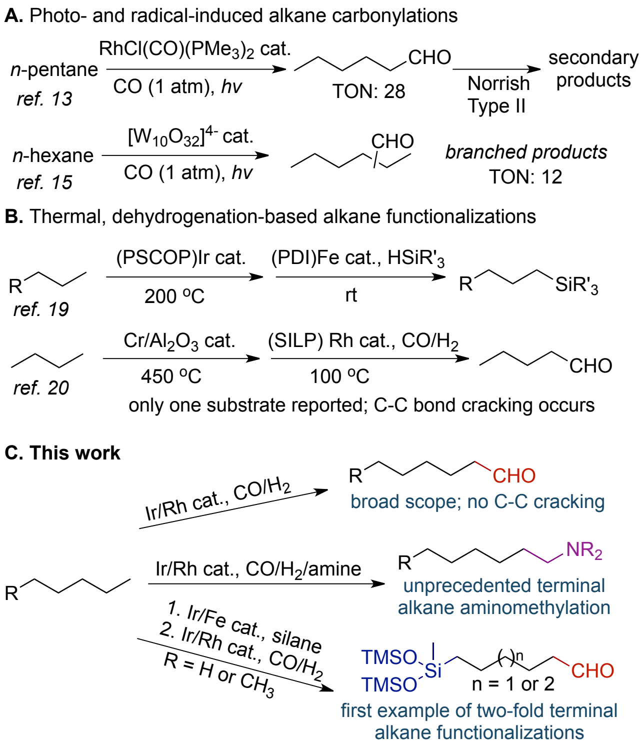
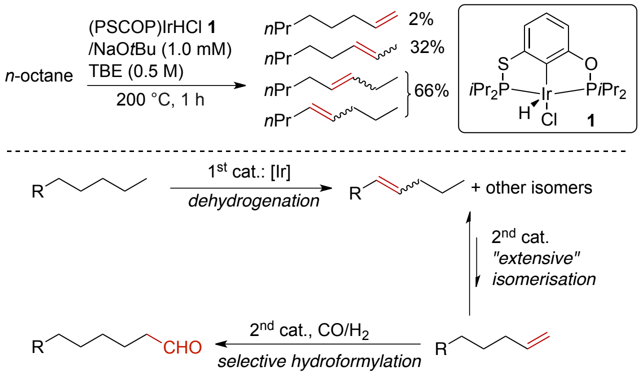


Figure 1. A. Photo- and radical-induced alkane carbonylations. **B.** Dehydrogenation-based alkane functionalizations. **C.** This work: regioselective conversion of *n*-alkanes to linear aldehydes and amines, and alkane two-fold functionalizations.

a functional group into an alkane) are very limited. Fig. 1B depicts the few known examples to date. Our group reported a dual-catalyst system for terminally selective alkane silylations using a (PSCOP)Ir-catalyzed alkane dehydrogenation (AD) process coupled to an Fe-catalyzed olefin isomerization-hydrosilylation (ISO-HSi).[19] Haumann, Hahn, and co-workers reported the conversion of *n*-butane to *n*-pentanal via a continuous gas-phase process consisting of *n*-butane dehydrogenation over Cr/Al_2O_3 and hydroformylation of the resulting butenes by a supported ionic liquid phase (SILP) Rh catalyst of biphephos ligand.[20] Although the SILP Rh catalyst was found to be active for both isomerization and hydroformylation, the conversion of 2-butenes (the major dehydrogenation products) to the desired *n*-pentanal was low (~15%).[20] Moreover, using the heterogeneous dehydrogenation catalyst under harsh conditions (450 °C) invariably led to cracking products (e.g., ethylene and propylene) (Fig. 1B). An additional condensation step was thus required to separate the volatile cracking products from butenes, prior to the hydroformylation. The facile C–C bond cracking makes the heterogeneous process ill-suited to carbonylation of higher alkanes.

Here we report a homogeneous dual-catalyst system for thermal alkane carbonylation through iridium-catalyzed dehydrogenation and rhodium-catalyzed tandem olefin isomerization-hydroformylation (ISO-HF) (Fig. 1C). This sequential methodology using two molecular catalysts[21] exhibits a broad substrate scope and excellent site selectivity for linear aldehydes. In addition, we describe the conversion of simple alkanes to high-value siloxy-terminated linear aldehydes via a sequence of alkane silylation and carbonylation, an unprecedented transformation for two-fold catalytic alkane functionalizations. Moreover, this dual-catalyst system was successfully applied to alkane aminomethylations, which represent the first example of regioselective conversion of *n*-alkanes to linear amines (Fig. 1C).[22]

Scheme 1. Conversion of linear alkanes to linear aldehydes via dehydrogenation and olefin-isomerization-hydroformylation.

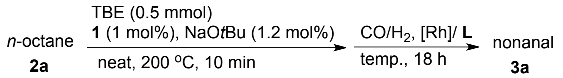


RESULTS AND DISCUSSION

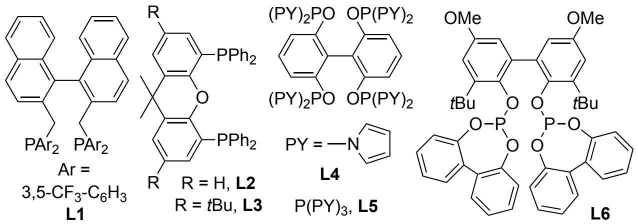
Design of a molecular dual-catalyst system for terminally selective alkane carbonylation. The formal carbonylation scheme (Scheme 1) involves two molecular catalysts – one catalyzes AD and the other catalyzes the hydroformylation of the resulting olefin(s). Among various known homogeneous AD catalysts,[23] pincer-ligated iridium complexes are the most effective catalysts for transfer-dehydrogenation of alkanes, operating at temperatures (typically 150-200 °C) much lower than those used for the heterogeneous dehydrogenations.[24] No C–C bond cleavage[25] occurs using these molecular catalyst, but the dehydrogenation of linear alkanes yields predominantly internal olefins at high conversions.[18a-c] To produce linear aldehydes from the internal olefin mixtures, the hydroformylation catalyst should not only enable selective anti-Markovnikov hydroformylation of α-olefins, but also effect rapid olefin isomerization. Earlier studies showed that the pincer Ir-catalyzed dehydrogenation of medium low-carbon number *n*-alkanes (e.g., *n*-octane) yielded olefins with double bonds remote from the terminal position at high conversions. For instance, the dehydrogenation of *n*-octane gave primarily 3- and 4-octenes as the major products, rather than 2-octenes and 1-octene (Scheme 1).[26] Thus, the selective formation of linear aldehydes requires a catalyst with the capability to effect isomerization of the remote internal olefins (“extensive” isomerization) to the terminal olefin followed by selective hydroformylation (Scheme 1). The whole process is operated in a one-pot, two-step fashion because the iridium AD catalyst is likely subject to inhibition by CO and the phosphine ligand used in the ISO-HF reaction, and the ISO-HF catalyst may not tolerate the high reaction temperatures required for the AD reaction. Although performed sequentially, the ISO-HF catalyst must tolerate the AD catalyst because the second step will be performed without product purification.

Development of iridium-catalyzed transfer-dehydrogenation and rhodium-catalyzed olefin ISO-HF. Initial efforts were focused on the search for two molecular catalysts for AD-ISO-HF. Considering its superior catalytic activity, the *i*Pr-substituted phosphinothious-phosphinite iridium complex (PSCOP)IrHCl **1** (cf. Scheme 1) developed by this group was selected as the dehydrogenation catalyst.[26] The transfer-dehydrogenation of *n*-octane (6.2 M) with *t*-butylethylene (TBE, 0.25 M) catalyzed by the active species generated from **1** (1 mol% relative to TBE) and NaO*t*Bu (1.2 mol%) resulted in nearly quantitative conversion (>99%) of TBE to *t*-butylethane (TBA) after 10 min at 200 °C, with the formation of internal octenes as the major products. Next we screened homogeneous Rh catalysts for the ISO-HF of olefin mixtures derived from the AD. Note that we did not need to separate the Ir catalyst for the ISO-HF step. The results are summarized in Table 1. Beller's Iphos ligand (**L1**) was previously reported to be highly selective for the Rh-catalyzed hydroformylation of 2-alkenes to form linear aldehydes.[27] Unfortunately, using the Iphos ligand for the Ir/Rh-catalyzed (0.8 mol% Rh) AD-ISO-HF under optimized conditions (5/5 bar CO/H_2 at 120 °C) gave only 24% GC yield of aldehydes after 18 h with a low regioselectivity (*n:i* = 1.0, entry 1); three branched aldehydes were detected by GC analysis (see Supporting Information). Reactions with Xantphos (**L2**) and its *t*Bu-substituted variant (**L3**) resulted in similar yields, but even lower linear selectivity (entries 2, 3). Switching the ligand to Zhang's pyrrole-based tetraphosphorus ligand (**L4**), which proved to be the most selective ligand for the ISO-HF of 2-alkenes to linear aldehydes,[28] afforded a high linear selectivity (*n:i* = 17.9), but an unsatisfactory yield (36%, entry 4). Performing the reaction with a monophosphine ligand, tripyrrolylphosphine (**L5**), resulted in a low site selectivity (entry 5).

Table 1. Catalyst development for selective formation of *n*-nonanal via AD-ISO-HF of *n*-octane[a]



Entry	Rh (mol%)	L	temp. (°C)	CO/H_2 (bar)	Yield (%)	*n:i*
1	0.8	**L1**	120	5/5	24	1.0
2	0.8	**L2**	120	5/5	28	0.5
3	0.8	**L3**	120	5/5	26	0.7
4	0.8	**L4**	120	5/5	36	17.9
5[b]	0.8	**L5**	120	5/5	22	1.0
6	0.8	**L6**	120	5/5	80	13.6
7	0.8	**L6**	100	5/5	58	17.0
8	0.8	**L6**	140	5/5	30	10.9
9[c]	0.8	**L6**	120	5/5	60	16.2
10[d]	0.8	**L6**	120	5/5	76	15.0
11	0.8	**L6**	120	2/2	58	17.8
12	0.8	**L6**	120	10/10	69	9.0
13	0.8	**L6**	120	5/25	46	16.0
14	1.2	**L6**	120	5/5	81	13.9

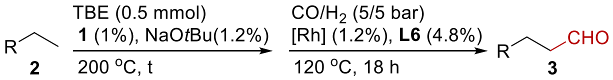


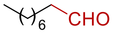
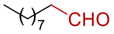
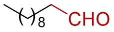
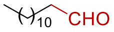
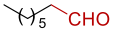
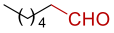
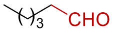
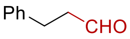
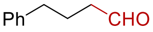
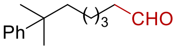
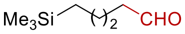
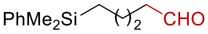
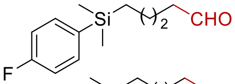
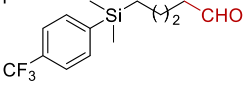
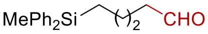
[a]Conditions: **1** (1 mol% relative to TBE), NaO*t*Bu (1.2 mol%), alkane (2 mL), [Rh] = $Rh(acac)(CO)_2$ (0.8 mol%), **L**:[Rh] = 4:1. Yields and *n:i* ratios were determined by GC. Yields are relative to TBE. [b]**L5**:[Rh] = 20:1. [c]5 h for ISO-HF. [d]10 h for ISO-HF.

The poor conversion to the desired linear product demonstrated in the reactions using **L1**-**L5** can in part be attributed to the slow isomerization of the remote internal olefins (e.g., 3- and 4-octenes) to 1-octene, which is consistent with the low yield of *n*-nonanal obtained for the ISO-HF of 4-octene by using **L1**.[27b] Encouragingly, using the biphephos ligand **L6** developed by Union Carbide,[29] extensive isomerization of the internal olefins and selective anti-Markovnikov hydroformylation of the terminal olefin was achieved. The AD-ISO-HF reaction using **L6**, offered aldehydes in 80% yield with a 13.6:1 *n:i* ratio (entry 6). Conducting the ISO-HF step at a lower temperature (100 °C) resulted in an improved selectivity, but a moderate yield (entry 7), while increasing the temperature (140 °C) had a detrimental effect on the yield and the selectivity (entry 8). Shortening the reaction time from 18 h to 10 h and 5 h led to enhanced *n:i* ratios, albeit with slightly reduced yields (entries 9, 10). The pressure of CO and H_2 did show a significant impact on the product distributions.[21g] The reaction at a lower pressure of CO/H_2 (2 /2 bar) offered a higher selectivity, while the run at a higher pressure (10/10 bar CO/H_2) gave a lower selectivity for the linear product (entries 11 and 12). Increasing the pressure of H_2 (25 bar) relative to that of CO (5 bar) resulted in an improved selectivity (*n:i* = 16.0), but a lower yield (46%) compared to that obtained for the run at 5/5 bar CO/H_2 (entry 13 versus 6). Comparison of the outcomes at different pressures revealed that the run at 5/5 bar CO/H_2 gave the optimal results with respect to both the yield and the selectivity. Finally, when the Rh catalyst was increased to 1.2%, the AD-ISO-HF reaction provided aldehydes in 81% yield with a 13.9:1 *n:i* selectivity (entry 14).

Carbonylations of linear *n*-alkanes (C_5-C_{10} and C_{12}). Having established an Ir/Rh dual-catalyst system for the selective and high-yielding conversion of *n*-octane to *n*-nonanal, we applied this reaction to various linear alkanes, from low-molecular weight (MW), low-carbon number (C_5-C_7) to medium low MW *n*-alkanes (C_9, C_{10}, C_{12}). The results are summarized in Table 2. All of these reactions produced good-to-high yields relative to TBE, which was the limiting reagent, and the products with relative high boiling point were isolated in useful yields.

Table 2. Catalytic carbonylation of various alkanes[a]



Entry	t (min)	Product	Yield (%)	*n:i*
1	10	 **3a**	81(70)	13.9
2	10	 **3b**	82(71)	12.5
3	10	 **3c**	87(78)	11.6
4	10	 **3d**	75(66)	8.5
5	30	 **3e**	70(55)	19.6
6	30	 **3f**	67	23.3
7[b]	30	 **3g**	84	48.9
8[c,d]	300	 **3h**	48	1.8
9[c,d]	300	 **3i**	82	1.0
10[c,e]	180	 **3j**	64(60)	10.6
11[c,e]	180	 **3k**	82(67)	17.1
12[c,e]	180	 **3l**	86(72)	18.3
13[c,e]	180	 **3m**	64(54)	10.4
14[c,e]	180	 **3n**	63(55)	11.3
15[c,e]	180	 **3o**	78(73)	16.5

[a]Conditions: **1** (1% relative to TBE), NaO*t*Bu (1.2%), alkane (2 mL), [Rh] (1.2%), **L6**:[Rh] = 4:1. Yields and *n:i* ratios were determined by GC. Numbers in parentheses are isolated yields. Yields are relative to TBE. [b]At 190 °C for AD. [c]**1** (2 mol% relative to TBE), NaO*t*Bu (2.4 mol%), [d]Rh(acac)(CO)$_2$ (0.8 mol%) and **L6** (3.2 mol%), [e]Alkane (1.5 mmol), *p*-xylene (1.5 mL).

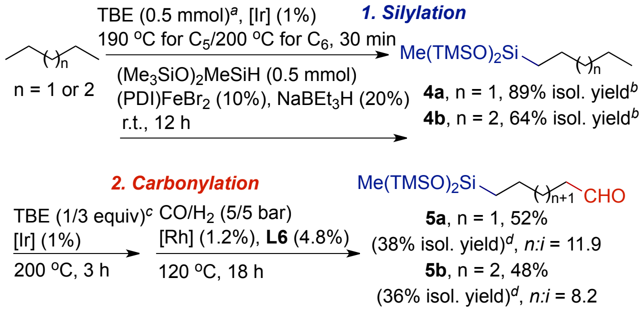
Notably, analysis of the product distributions established a clear correlation between the terminal selectivity and the length of alkane. The terminal selectivity observed for the reaction of *n*-nonane (C_9, *n:i* = 12.5) is slightly lower than that for *n*-octane (C_8) (entry 2 versus entry 1). Two longer alkanes, *n*-decane (C_{10}) and *n*-dodecane (C_{12}), produced the corresponding aldehydes with further reduced site selectivity (*n:i* = 11.6 for C_{10}, and 8.5 for C_{12}, entries 3, 4). The data imply that the terminal selectivity decreases as the carbon number increases. Consistent with this trend, the reactions of lower-carbon number *n*-alkanes, C_7 and C_6, gave the linear products with enhanced selectivity (*n:i* = 19.6 for C_7, and 23.3 for C_6, entries 5, 6). Furthermore, the carbonylation of *n*-pentane gave *n*-hexanal with an excellent selectivity (*n:i* = 48.9, entry 7). The isomerization of the internal olefins derived from the short alkanes to the terminal olefin is expected to be faster than for the heavier hydrocarbons, which may account for the higher terminal selectivity obtained for the reactions of C_5-C_7 compared to those of C_8-C_{10}, C_{12}. A second possibility is that isomerization is fast relative to hydroformylation and at steady state the terminal olefin will be present in lower concentrations relative to the internal olefins in the higher hydrocarbons.

Carbonylations of aryl-substituted alkanes. Given the fact that linear alkylbenzenes are produced on a million ton per year scale,[30] the carbonylation of the alkyl chains is of interest. The Ir-catalyzed dehydrogenation of ethylbenzene occurred in moderate yield, and the subsequent hydroformylation of the resulting styrene gave a 1.8:1 *n:i* selectivity favoring the anti-Markovnikov product (entry 8). The carbonylation of *n*-propylbenzene resulted in a lower terminal selectivity (*n:i* = 1.0), albeit with higher yield (entry 9). The dehydrogenation yielded *β*-methylstyrene as the major product. Such a conjugated internal olefin is thermodynamically far more stable than the terminal olefin, rendering the isomerization of the former to the latter particularly challenging. On the basis of these results, we envisaged that the installation of a quaternary carbon center at alpha to the ring might lead to a terminal selectivity. Indeed, the reaction of (2-methylheptan-2-yl)benzene containing two Me groups at the benzyl position exhibited a high level of site selectivity for the linear aldehyde **3j** (*n:i* = 10.6, entry 10).

Carbonylations of silyl-substituted alkanes. In addition to the carbonylation of simple hydrocarbons, the Ir/Rh dual-catalyst system can effect the carbonylation of silyl-terminated linear alkanes.[31] These reactions proceed effectively in a *p*-xylene solution without requiring a large excess of substrate. With alkane:TBE ratios of 3:1, the *n*-alkyl chain of trimethylbutylsilane (entry 11), 1-(dimethylphenylsilyl)butane (entry 12), and 1-(diphenylmethylsilyl)butane (entry 15) underwent selective carbonylation to form the corresponding aldehydes in moderate-to-good isolated yields with high terminal selectivity. The fluoro and trifluoromethyl groups on the aryl rings were tolerated, as demonstrated by the isolation of the aldehydes (**3m** and **3n**) in useful yields. It should be noted that the aryl groups on Si can be readily substituted with alkoxy groups upon alcoholysis to form silyl ethers, while the terminal aldehyde group of these products is readily transformed to hydroxyl or amine functionalities, making them potential precursors for silicone surfactants[32] or reagents for preparation of silicone-modified polymers.[33]

Direct two-fold functionalizations of simple alkanes: synthesis of siloxy-terminated linear aldehydes. Moreover, we describe an approach to dual-functionalizations of simple linear alkanes regioselectively at the terminal positions to generate α,ω-siloxy aldehydes (Scheme 2). This process first involves the installation of a bis(trimethylsiloxy)methylsilyl group at one terminal position of an alkane using an (PSCOP)Ir-catalyzed dehydrogenation and (PDI)Fe-catalyzed ISO-HSi sequence (PDI = bis(imino)pyridine), a protocol previously developed by our group.[19] As shown in Scheme 2, the silylations of *n*-pentane and *n*-hexane with (TMSO)$_2$MeSiH gave the corresponding linear alkyl silanes (**4a** and **4b**) in 89% and 64% isolated yield with exclusive linear selectivity. Submission of the silylation products to the standard carbonylation conditions with alkyl silane:TBE ratios of 3:1 furnished the siloxy-functionalized aldehydes (**5a** and **5b**) in moderate yields, with good terminal selectivity. To the best of our knowledge, this represents the first example of two-fold functionalizations, leading to the incorporation of two different functionalities into simple alkanes, both at the terminal positions.

Scheme 2. Regioselective synthesis of α,ω-siloxy aldehydes by two-fold alkane functionalizations.



[a] *n*-Pentane:TBE = 35:1, *n*-hexane:TBE = 31:1, alkane (2 mL). [b] Yields are relative to TBE. [c] Alkyl silane:TBE = 3:1. [d] Yields are relative to TBE added in the carbonylation step.

Alkane carbonylations via transfer-dehydrogenation using ethylene as the hydrogen acceptor. Ethylene is more abundant and less expensive than TBE. Inspired by the recent work of Goldman on gas-solid (PCP)Ir-catalyzed transfer-dehydrogenation of alkanes with ethylene,[9] we show here that the AD-ISO-HF process can employ ethylene as the acceptor (Table 3). The (PSCOP)Ir-catalyzed alkane dehydrogenation reaction was carried out in an autoclave charged with ethylene (2-4 bar). The optimum dehydrogenation temperature (180 °C) was found to be lower than that used for the catalysis with TBE (200 °C). The transfer-dehydrogenation of *n*-octane with 2 bar ethylene catalyzed by **1** (2.5 mM) at 180 °C for 8 h, followed by the ISO-HF reaction catalyzed by the Rh complex (1.3 mM) at 5/5 bar CO/H_2 at 120 °C for 24 h, provided 0.67 g of isolated aldehyde (**3a**, 1.39 M) with a 11.1:1 *n*:*i* selectivity, corresponding to a TON of 577 for Ir and 1110 for Rh (entry 1). Performing the reaction at a lower concentration of **1** and/or at a higher pressure of ethylene gave a higher selectivity for the linear product, but with lower overall TONs (entries 2, 3). Similarly, the reactions of *n*-decane and *n*-dodecane using ethylene provided the desired linear products with high selectivity and isolated yields, producing >400 TONs relative to Ir and >800 TONs relative to Rh (entries 4, 5).

Table 3. Catalytic carbonylation of alkanes using ethylene as the hydrogen acceptor[a]

$$\underset{\mathbf{2}}{\text{alkane}} \xrightarrow[180\ ^{\circ}\mathrm{C},\ 8\ \mathrm{h}]{\text{ethylene (2-4 bar)}\ [\mathrm{Ir}]\ (2.5\ \mathrm{mM})} \xrightarrow[120\ ^{\circ}\mathrm{C},\ 24\ \mathrm{h}]{\mathrm{CO/H_2}\ (5/5\ \mathrm{bar})\ [\mathrm{Rh}]\ (1.3\ \mathrm{mM}),\ \mathbf{L6}\ (5.2\ \mathrm{mM})} \text{linear aldehyde}\ \mathbf{3}$$

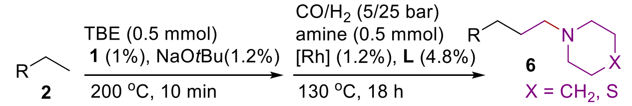
Entry	Alkane	Product concentration	*n*:*i*	TON for Ir	TON for Rh
1	*n*-octane	**3a**, 1.39 M, 0.67 g	11.1	577	1110
2[b]	*n*-octane	**3a**, 0.60 M	18.0	480	462
3[b,c]	*n*-octane	**3a**, 0.24 M	22.0	192	185
4[d]	*n*-decane	**3c**, 1.19 M, 0.72 g	12.5	474	912
5[e]	*n*-dodecane	**3d**, 1.06 M, 0.72 g	11.0	422	812

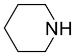
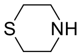
[a] Conditions: [Ir] = **1** (2.5 mM)/NaO*t*Bu (3.0 mM), alkane (4 mL), ethylene (2 bar). [Rh] (1.3 mM), **L6** (5.2 mM), 120 °C for 24 h. Product concentration and *n*:*i* ratios were determined by GC. [b] [Ir] (1.25 mM). [c] ethylene (4 bar). [d] AD time 15 h. [e] AD time 20 h.

Terminally selective aminomethylation of alkanes. Finally, we developed a protocol for alkane aminomethylations using Ir-catalyzed alkane dehydrogenation and Rh-catalyzed isomerization-hydroaminomethylation (AD-ISO-HAM) (Table 4). Optimization of the reaction conditions revealed that the pressure of CO/H_2, and the ligand have an important impact on the yield and selectivity of the product (see Supporting Information for details). **L6** is the optimal one among the ligands investigated for the carbonylation, but the aminomethylation reaction using **L6** at 10/50 bar CO/H_2 with one equiv piperidine at 120 °C gave a low yield (22% combined yields) with moderate selectivity for amine (substantial amounts of side products including aldehyde, enamine and imine were observed), although the regioselectivity for the linear amine (**6**) was high (*n*:*i* = 10.4, entry 1). The pyrrole-based tetraphosphorus ligand **L4** was ineffective for the ISO-HAM (entry 2), while the run with tripyrrolylphosphine **L5** afforded a moderate yield with high selectivity for amine, but low terminal selectivity (entry 3). The reaction with Xantphos **L2** resulted in a low yield and low selectivity (entry 4). Among the series ligands explored, Iphos **L1** proved to be most effective,[27a] furnishing the product in 58% yield with 96% amine selectivity, and moderate regioselectivity favoring the linear product (*n*:*i* = 1.6, entry 5). Conducting the reaction at 130 °C at a lower pressure (5/25 bar CO/H_2) offered the products in higher yield (85%) with almost exclusive amine selectivity (99%), albeit with lightly reduced regioselectivity (*n*:*i* = 1.3, entry 6). The regioselectivity was significantly improved when thiomorpholine was used as the amine source (*n*:*i* = 4.0, 36% yield, entry 7).

Similar to the carbonylation reactions described above, the regioselectivity for the linear amines (**6**) increases as the carbon number of the alkane substrate decreases. The reactions of *n*-heptane with piperidine and thiomorpholine gave the linear amines in good yield with satisfactory regioselectivity (entries 8 and 9). Moreover, the aminomethylations of *n*-pentane gave *n*-hexanamines with excellent selectivity for amines and high regioselectivity (entries 10 and 11). The reaction of *n*-pentane and thiomorpholine gave a particularly high level of regiocontrol (*n*:*i* = 24.0, entry 11). In general, the terminal selectivity observed for the reactions with thiomorpholine is higher than that with piperidine.

Table 4. Catalytic aminomethylation of alkanes[a]



Entry	Alkane	L	Amine	Yield (%)	Amine selectivity (%)	*n:i*
1[b]	*n*-octane	**L6**	 (PP)	22	47	10.4
2[b]	*n*-octane	**L4**	PP	trace	-	-
3[c]	*n*-octane	**L5**	PP	59	93	0.4
4[c]	*n*-octane	**L2**	PP	20	22	0.3
5[b]	*n*-octane	**L1**	PP	58	96	1.6
6	*n*-octane	**L1**	PP	85	99	1.3
7	*n*-octane	**L1**	 (TP)	36	93	4.0
8[d]	*n*-heptane	**L1**	PP	75	99	3.3
9[d]	*n*-heptane	**L1**	TP	71	97	4.6
10[e]	*n*-pentane	**L1**	PP	95	98	6.1
11[e]	*n*-pentane	**L1**	TP	60	99	24.0

[a] Conditions: **1** (1 mol% relative to TBE), NaO*t*Bu (1.2 mol%), alkane (2 mL), [Rh] = Rh(acac)$(CO)_2$ (1.2 mol%), **L**:[Rh] = 4:1. Amine (0.5 mmol). Yields, amine selectivities, and *n:i* ratios were determined by GC. Yields are relative to TBE. [b] 120 °C, CO/H_2 (10/50 bar) for ISO-HAM. [c] 120 °C, CO/H_2 (5/33 bar) for ISO-HAM. [d] AD 200 °C, 30 min. [e] AD 190 °C, 30 min.

CONCLUSIONS

An unprecedented thermal carbonylation of alkane feedstocks to valuable linear alkyl aldehydes using a dual molecular catalyst system has been described. This one-pot process consists of a pincer (PSCOP)Ir catalyst for the transfer dehydrogenation of the alkane to an olefin and a rhodium catalyst for the olefin-isomerization-hydroformylation. These two molecular catalysts operate with up to 577/1110 (Ir/Rh) turnovers in the carbonylation of alkane using abundant ethylene as the hydrogen acceptor. The Ir/Rh dual-catalyst system can be further employed in AD-ISO-HAM, to provide value-added linear alkyl amines, for the first time, directly from *n*-alkanes. A novel two-fold functionalization of alkane has also been developed using a sequential alkane silylation and carbonylation process, enabling the installation of siloxy and aldehyde groups into the two terminal positions of *n*-pentane or *n*-hexane to furnish potential precursors for silicone surfactants.

The protocols directly using alkane feedstocks offer advantages in terms of accessibility and diversity of the starting materials, considering that the industrial synthesis of linear aldehydes mainly relies on the use of even-numbered linear α-olefins, which are commonly produced by ethylene oligomerization with a Schulz–Flory distribution.[34] However, the atom economy for these dehydrogenation-based methods remains to be improved because of the need to use a sacrificial hydrogen acceptor. To address such a limitation, further studies will focus on the development of new catalysts for highly efficient thermal acceptorless dehydrogenation,[35] and new dual-catalyst systems that allow for the concurrent catalytic AD-ISO-HF reactions, thus enabling the effective use of hydrogen derived from the AD.

EXPERIMENTAL SECTION

Materials and Methods. All manipulations were carried out using standard Schlenk, high-vacuum and glovebox techniques. Tetrahydrofuran (THF), *p*-xylene, toluene, *t*-butylethlene (TBE) and alkanes were dried with $LiAlH_4$ and distilled under argon prior to use. H_2 (99.999%) and CO (99.9%) were used without further purification. Ethylene (99.995%) was dried and deoxidized prior to use. NMR spectra were recorded on Varian Mercury 400 MHz and Agilent 400 MHz spectrometers at ambient temperature. The residual peak of deuterated solvent was used as a reference for ^1H and ^{13}C chemical shifts.

General procedure for carbonylation of alkanes with TBE as the hydrogen acceptor. In an argon-filled glovebox, a thick-wall Kontes flask (5 mL) was charged with (PSCOP)IrHCl (**1**) (1.0 mol%), NaO*t*Bu (1.2 mol%), alkane (2.0 mL) and TBE (0.50 mmol). The flask was sealed with a Teflon plug under an argon atmosphere, and the solution was stirred in a 200 °C oil bath for allotted time. After that, the flask was cooled to room temperature. A 5-mL vial with a magnetic stirring bar was charged with Rh(acac)$(CO)_2$ (20 mM solution in toluene) and **L6** in the glove box. The mixture was stirred for 5 min. The solution derived from alkane dehydrogenation was then added to the 5-mL vial. The vial was transfer to a 50 mL autoclave. The autoclave was purged with H_2 three times and then charged with CO (5 bar) and H_2 (5 bar). The autoclave was heated for 18 h and cooled in an icy bath. The gases were carefully released in a well-ventilated hood. After adding mesitylene (50 μL) as an internal standard, the reaction mixture was analyzed by GC.

General procedure for carbonylation of alkanes with ethylene as the hydrogen acceptor. An oven dried autoclave (130 mL) was charged with (PSCOP)IrHCl (**1**) NaO*t*Bu, *n*-alkane (4.0 mL) and stirred for 2 mins in a glovebox. The autoclave was then purged with ethylene three times and charged with ethylene. Then the autoclave was heated in a 180 °C oil bath for allotted time. After that, the autoclave was cooled to room temperature and the gas pressure was carefully released. The solution derived from alkane dehydrogenation was then added to a 20-mL vial, which was equipped with Rh(acac)$(CO)_2$ (1.3 mM) and **L6** (5.2 mM). The vial was transferred into a 250 mL autoclave. Then the autoclave was purged with H_2 three times and charged with CO (5 bar) and H_2 (5 bar). The autoclave was heated at 120 °C for 24 h and then cooled in an icy bath. The gases were carefully released in a well-ventilated hood. After adding mesitylene (100 μL) as an internal standard, the reaction mixture was analyzed by GC. The products were isolated by flash column chromatography on silica gel (PE:EA = 50:1).

General procedure for two-fold functionalization of alkanes. In an argon-filled glovebox, a thick-wall Kontes flask (10 mL) was charged with (PSCOP)IrHCl (**1**) (1.0 mol%), NaO*t*Bu (1.2 mol%), alkane (2.0 mL) and TBE (0.50 mmol). The flask was sealed and stirred in a heated oil bath for allotted time. After cooling to room temperature, (^{Et}PDI)FeBr$_2$ (10.0 mol%), NaBHEt$_3$ (20.0 mol%), (TMSO)$_2$MeSiH (0.5 mmol) were added to the solution and the solution was stirred at room temperature for 12 h. The reaction mixture then passed through a silica gel plug with *n*-pentane as the eluent to give the pure product. The silylation product then underwent the carbonylation following the general procedure described above. The crude final product was analyzed by GC with 50 μL mesitylene as an internal standard. The product was then further isolated through a silica gel plug (*n*-hexane:EA = 50:1).

General procedure for aminomethylation of alkanes. In an argon-filled glovebox, a thick-wall Kontes flask (5 mL) was charged with (PSCOP)IrHCl (**1**) (1.0 mol%), NaO*t*Bu (1.2 mol%), alkane (2.0 mL) and TBE (0.50 mmol). The flask was sealed with a Teflon plug under an argon atmosphere, and the solution was stirred in a 200 °C or 190 °C oil bath for allotted min. After that, the flask was cooled to room temperature. A 5-mL vial with a magnetic stirring bar was charged with Rh(acac)(CO)$_2$ (20 mM solution in toluene) and **L1** in the glove box. The mixture was stirred for 5 min, followed by the addition of amine (1 equiv relative to TBE). The solution derived from alkane dehydrogenation was then added to the 5-mL vial. The vial was transfer to a 50 mL autoclave. The autoclave was purged with H$_2$ three times and then charged with CO (5 bar) and H$_2$ (25 bar). The autoclave was heated for allotted time and cooled in an icy bath. The gases were carefully released in a well-ventilated hood. After adding mesitylene (50 μL) as an internal standard, the reaction mixture was analyzed by GC.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications web site at DOI:

■ AUTHOR INFORMATION

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Labinger, J. A.; Bercaw, J. E. *Nature* **2002,** *417*, 507. (b) Bergman, R. G. *Nature* **2007,** *446,* 391. (c) Hartwig, J. F. *J. Am. Chem. Soc.* **2016,** *138*, 2. (d) Goldberg, K. I.; Goldman, A. S. *Acc. Chem. Res.* **2017,** 50, 620.

(2) Weissermel, K., Arpel, H.-J. *Industrial Organic Chemistry*, Wiley-VCH, Weinheim, Germany, **2003**; pp 59-89.

(3) (a) Liu, W.; Groves, J. T. *Acc. Chem. Res.* **2015,** *48*, 1727. (b) Tse, C.-W.; Chow, T. W.-S.; Guo, Z.; Lee, H. K.; Huang, J.-S.; Che, C.-M. *Angew. Chem. Int. Ed.* **2014,** 53, 798. (c) Hartwig, J. F.; Larsen, M. A. *ACS Cent. Sci.* **2016,** *2*, 281.

(4) (a) Díaz-Requejo, M. M.; Pérez, P. J. *Chem. Rev.* **2008,** *108*, 3379. (b) Thu, H.-Y.; Tong, S.-M.; Huang, J.-S.; Chan, L.-F.; Deng, Q.-H.; Che, C.-M. *Angew. Chem. Int. Ed.* **2008,** *47*, 9747. (c) Caballero, A.; Despagnet-Ayoub, E.; Mar Díaz-Requejo, M.; Díaz-Rodríguez, A.; González-Núñez, M. E.; Mello, R.; Muñoz, B. K.; Ojo, W.-S.; Asensio, G.; Etienne, M.; Pérez, P. J. *Science* **2011,** 332, 835. (d) Liao, K.; Negretti, S.; Musaev, D. G.; Bacsa, J.; Davies, H. M. L. *Nature* **2016,** 533, 230.

(5) (a) Meunier, B.; de Visser, S. P.; Shaik, S. *Chem. Rev.* **2004,** *104*, 3947. (b) Ortiz de Montellano, P. R. *Chem. Rev.* **2010,** *110*, 932.

(6) (a) Wenzel, T. T.; Bergman, R. G. *J. Am. Chem. Soc.* **1986,** *108*, 4856. (b) Jones, W. D.; Feher, F. J. *Organometallics* **1983,** *2*, 562.

(7) (a) Chen, H.; Schlecht, S.; Semple, T. C.; Hartwig, J. F. *Science* **2000,** *287*, 1995. (b) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010,** *110*, 890.

(8) Liu, F.; Pak, E. B.; Singh, B.; Jensen, C. M.; Goldman, A. S. *J. Am. Chem. Soc.* **1999,** *121*, 4086.

(9) Kumar, A.; Zhou, T.; Emge, T. J.; Mironov, O.; Saxton, R. J.; Krogh-Jespersen, K.; Goldman, A. S. *J. Am. Chem. Soc.* **2015,** *137*, 9894.

(10) Mindiola and Baik reported a terminally selective alkane dehydrogenation catalyzed by a pincer titanium complex, albeit with low TONs. See: (a) Solowey, D. P.; Mane, M. V.; Kurogi, T.; Carroll, P. J.; Manor, B. C.; Baik, M.-H.; Mindiola, D. J. *Nat. Chem.* **2017,** *9*, 1126. Photocatalytic alkane dehydrogenation using RhCl(CO)(PMe$_3$)$_2$ was shown to give improved terminal selectivity. See: (b) Chowdhury, A. D.; Weding, N.; Julis, J.; Franke, R.; Jackstell, R.; Beller, M. *Angew. Chem. Int. Ed.* **2014,** *53*, 6477.

(11) Franke, R.; Selent, D.; Börner, A. *Chem. Rev.* **2012,** *112*, 5675.

(12) van Leeuwen, P. W. N. M., In *Rhodium Catalyzed Hydroformylation*; van Leeuwen, P. W. N. M.; Claver, C., Ed.; Springer: Dordrecht, Netherlands, 2002, pp 1-13.

(13) Sakakura, T.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1987,** 758.

(14) (a) Sakakura, T.; Sodeyama, T.; Sasaki, K.; Wada, K.; Tanaka, M. *J. Am. Chem. Soc.* **1990,** *112*, 7221. (b) Boese, W. T.; Goldman, A. S. *J. Am. Chem. Soc.* **1992,** *114*, 350.

(15) Jaynes, B. S.; Hill, C. L. *J. Am. Chem. Soc.* **1995,** *117*, 4704.

(16) (a) Goldman, A. S.; Roy, A. H.; Huang, Z.; Ahuja, R.; Schinski, W.; Brookhart, M. *Science* **2006,** *312*,257. (b) Dobereiner, G. E.; Yuan, J.; Schrock, R. R.; Goldman, A. S.; Hackenberg, J. D. *J. Am. Chem. Soc.* **2013,** *135*, 12572. (c) Jia, X.; Qin, C.; Friedberger, T.; Guan, Z.; Huang, Z. *Sci. Adv.* **2016,** *2*, e1501591.

(17) Ahuja, R.; Punji, B.; Findlater, M.; Supplee, C.; Schinski, W.; Brookhart, M.; Goldman, A. S. *Nat. Chem.* **2011,** 3, 167.

(18) (a) Choi, J.; MacArthur, A. H. R.; Brookhart, M.; Goldman, A. S. *Chem. Rev.* **2011,** *111*, 1761. (b) Haibach, M. C.; Kundu, S.; Brookhart, M.; Goldman, A. S. *Acc. Chem. Res.* **2012,** *45*, 947. (c) Tang, X.; Jia, X.; Huang, Z. *Chem. Sci.* **2018,** *9*, 288. (d) Leitch, D. C.; Lam, Y. C.; Labinger, J. A.; Bercaw, J. E. *J. Am. Chem. Soc.* **2013,** *135*, 10302.

(19) Jia, X.; Huang, Z. *Nat. Chem.* **2016,** *8*, 157.

(20) (a) Walter, S.; Haumann, M.; Wasserscheid, P.; Hahn, H.; Franke, R. *AlChE J.* **2015,** *61*, 893. A combination of photocatalytic dehydrogenation of *n*-butane using RhCl(CO)(PMe$_3$)$_2$ and SILP Rh-catalyzed hydroformylation of butenes with CO$_2$ has also been reported. The substrate scope disclosed in that work was limited to n-butane. See: (b) Fritschi, S.; Korth, W.; Julis, J.; Kruse, D.; Hahn, H.; Franke, R.; Fleischer, I.; Chowdhury, A. D.; Weding, N.; Jackstell, R.; Beller, M.; Jess, A. *Chem. Ing. Tech.* **2015,** *87*, 1313.

(21) (a) Wasilke, J.-C.; Obrey, S. J.; Baker, R. T.; Bazan, G. C. *Chem. Rev.* **2005,** *105*, 1001. (b) van der Veen, L. A.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Angew. Chem. Int. Ed.* **1999,** *38*, 336. (c) Selent, D.; Hess, D.; Wiese, K.-D.; Röttger, D.; Kunze, C.; Börner, A. *Angew. Chem. Int. Ed.* **2001,** *40*, 1696. (d) Bronger, R. P. J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Organometallics* **2003,** *22*, 5358. (e) Bronger, R. P. J.; Bermon, J. P.; Herwig, J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Adv. Synth. Catal.* **2004,** *346*, 789. (f) Behr, A.; Obst, D.; Westfechtel, A. *Eur. J. Lipid Sci. Technol.* **2005,** *107*, 213. (g) Klein, H.; Jackstell, R.; Beller, M. *Chem. Commun.* **2005,** 2283. (h) Yu, S.; Chie, Y.-m.; Guan, Z.-h.; Zhang, X. *Org. Lett.* **2008,** *10*, 3469. (i) Yuki, Y.; Takahashi, K.; Tanaka, Y.; Nozaki, K. *J. Am. Chem. Soc.* **2013,** *135*, 17393.

(22) Alkane aminations via carbenium intermediate yield branched products. See: Wnuk, T. A.; Chaudhary, S. S.; Kovacic, P. *J. Am. Chem. Soc.* **1976,** *98*, 5678.

(23) For pioneering works on AD with molecular catalysts, see: (a) Burk, M. J.; Crabtree, R. H.; Parnell, C. P.; Uriarte, R. J. *Organometallics* **1984,** *3*, 816. (b) Felkin, H.; Fillebeen-Khan, T.; Gault, Y.; Holmes-Smith, R.; Zakrzewski, J. *Tetrahedron Lett.* **1984,** *25*, 1279.

(24) (a) Gupta, M.; Hagen, C.; Flesher, R. J.; Kaska, W. C.; Jensen, C. M. *Chem. Commun.* **1996,** 2083. (b) Xu, W.-w.; P. Rosini, G.; Krogh-Jespersen, K.; S. Goldman, A.; Gupta, M.; M. Jensen, C.; C. Kaska, W. *Chem. Commun.* **1997,** 2273. (c) Göttker-Schnetmann, I.; White, P.; Brookhart, M. *J. Am. Chem. Soc.* **2004,** *126*, 1804.

(25) Crabtree, R. H. *Chem. Rev.* **1985,** *85*, 245.

(26) Yao, W.; Zhang, Y.; Jia, X.; Huang, Z. *Angew. Chem. Int. Ed.* **2014,** 53, 1390.

(27) (a) Seayad, A.; Ahmed, M.; Klein, H.; Jackstell, R.; Gross, T.; Beller, M. *Science* **2002,** *297*, 1676. (b) Klein, H.; Jackstell, R.; Wiese, K.-D.; Borgmann, C.; Beller, M. *Angew. Chem. Int. Ed.* **2001,** *40*, 3408.

(28) Yan, Y.; Zhang, X.; Zhang, X. *J. Am. Chem. Soc.* **2006,** *128*, 16058.

(29) (a) Billig, E.; Abatjoglou, A. G.; Bryant, D. R. (UCC). U.S. Patent 4748261, 1988. (b) Behr, A.; Obst, D.; Schulte, C.; Schosser, T. *J. Mol. Catal. A: Chem.* **2003,** *206*, 179.

(30) Kocal, J. A.; Vora, B. V.; Imai, T. *Appl. Catal. A: Gen.* **2001,** *221*, 295.

(31) (a) Ohmura, T.; Torigoe, T.; Suginome, M. *J. Am. Chem. Soc.* **2012,** *134*, 17416. (b) Ohmura, T.; Torigoe, T.; Suginome, M. *Organometallics* **2013,** *32*, 6170.

(32) (a) (a) Liu, H.-J.; Lin, L.-H.; Chen, K.-M. *Colloids and Surf. A: Physicochem. Eng. Aspects* **2003,** *215*, 213. (b) Kekevi, B.; Berber, H.; Yıldırım, H. *J. Surfact. Deterg.* **2012,** *15*, 73.

(33) (a) Verdejo, R.; Barroso-Bujans, F.; Rodriguez-Perez, M. A.; Antonio de Saja, J.; Lopez-Manchado, M. A. *J. Mater. Chem.* **2008,** *18*, 2221. (b) Purohit, P. S.; Kulkarni, R.; Somasundaran, P. *J. Colloid Interface Sci.* **2012,** *383*, 49.

(34) Keim, W. *Angew. Chem. Int. Ed.* **2013,** 52, 12492.

(35) The existing systems for acceptorless AD exhibit much lower efficiency in comparison to the catalytic systems in the presence of a hydrogen acceptor. For example, see ref. 24b

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