



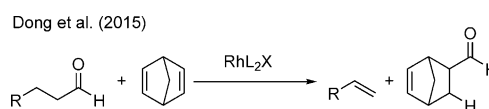
The Retro-Hydroformylation Reaction**

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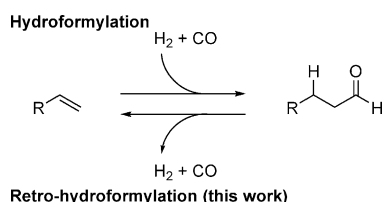
Abstract: Hydroformylation, a reaction that adds carbon monoxide and dihydrogen across an unsaturated carbon–carbon multiple bond, has been widely employed in the chemical industry since its discovery in 1938. In contrast, the reverse reaction, retro-hydroformylation, has seldom been studied. The retro-hydroformylation reaction of an aldehyde into an alkene and synthesis gas (a mixture of carbon monoxide and dihydrogen) in the presence of a cyclopentadienyl iridium catalyst is now reported. Aliphatic aldehydes were converted into the corresponding alkenes in up to 91 % yield with concomitant release of carbon monoxide and dihydrogen. Mechanistic control experiments indicated that the reaction proceeds by retro-hydroformylation and not by a sequential decarbonylation–dehydrogenation or dehydrogenation–decarbonylation process.

For more than 75 years since its discovery, hydroformylation, that is, the addition of carbon monoxide and dihydrogen to an unsaturated carbon–carbon multiple bond, has been widely employed in the chemical industry for the synthesis of aliphatic aldehydes from olefins.^[1] Thus, among the reactions that utilize synthesis gas (a mixture of carbon monoxide and dihydrogen), such as the Fischer–Tropsch process,^[2] methanol synthesis,^[3] and others,^[4] hydroformylation has long been a subject of most intensive studies both from industry and academia. On the other hand, the reverse reaction, retro-hydroformylation, has rarely been studied thus far (Scheme 1). The examples have been limited to stoichiomet-

ric reactions mediated by ruthenium or rhodium complexes^[5] and iron porphyrin complexes,^[6,7] transformations of steroidal aldehydes catalyzed by heterogeneous rhodium or palladium catalysts,^[8] and side reactions in decarbonylation reactions catalyzed by rhodium or iridium complexes.^[9,10] Some related reactions, such as a catalytic transfer of a formyl group from 1-heptanal to cyclohexene with a ruthenium complex^[11] and the migration of a formyl group to isomerize a linear aldehyde into its branched isomer with a rhodium catalyst^[12] have also been reported. We envisioned that the efficient elimination of synthesis gas from the reaction system would enable the formation of alkenes from aldehydes without any formyl-group acceptors if appropriate catalysts were applied. Earlier this year, while our studies were in progress, Dong and co-workers reported a transfer hydroformylation reaction catalyzed by a rhodium/Xantphos system for the conversion of aliphatic aldehydes into the corresponding alkenes by transferring a hydrogen atom and a formyl group to a strained alkene.^[13] In this process, the key for the reaction to proceed was proposed to be the use of strained alkenes, such as norbornadiene, as effective hydrogen and formyl-group acceptors (Scheme 2). However, a retro-hydroformylation



Scheme 2. Transfer hydroformylation.



Scheme 1. Hydroformylation and retro-hydroformylation.

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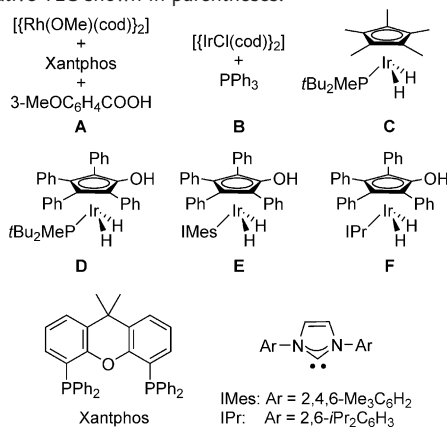
reaction, that is, the conversion of an aldehyde into an alkene with concomitant release of carbon monoxide and dihydrogen, has previously not been reported. Herein, we report the first retro-hydroformylation reaction, an acceptor-free dehydroformylation process that is catalyzed by cyclopentadienyl iridium complexes.

The retro-hydroformylation of cyclododecanecarbaldehyde was accomplished in up to 91 % yield with cyclopentadienyl iridium complexes **C–F**. Representative results of the optimization of the catalyst and the reaction conditions are summarized in Table 1. In all reactions, cyclododecanecarbaldehyde (0.50 mmol) was treated with 10 μ mol of a catalyst at 160 °C (except for entries 12–14) in an open glass tube for 20 hours, and then the reaction mixture was analyzed by GC and ¹H NMR spectroscopy. The three main products were the retro-hydroformylation product cyclododecene (**1**), the decarbonylation product cyclododecane (**2**), and cyclododecylmethanol (**3**), which results from hydrogenation of the starting aldehyde. First, the indispensability of the metal catalysts was confirmed by a control reaction without any catalyst (entry 1).^[14] Rhodium complex **A**, which was used for the transfer hydroformylation reported by Dong

Table 1: Retro-hydroformylation of cyclododecanecarbaldehyde.^[a]

Entry	Cat.	Solvent	Conv. [%]	1	2	3
1	—	mesitylene	19	0.0	6.6	0.71
2	A	mesitylene	95	44	2.1	33
3	B	mesitylene	42	11	20	1.1
4	C	mesitylene	51	33	2.4	11
5	D	mesitylene	98	67	12	8.0
6	E	mesitylene	98	85	4.5	5.4
7	F	mesitylene	100	91	0.0	9.5
8 ^[b]	F	mesitylene	99	58	11	24
9	F	DMSO	84	66	2.7	12
10	F	1,2-Cl ₂ C ₆ H ₄	87	60	11	9.7
11	F	diglyme	99	77 (55) ^[g]	8.0	14
12 ^[c]	F	mesitylene	34	14	0.25	0.85
13 ^[c]	A	mesitylene	96	37	0.37	34
14 ^[d]	A	mesitylene	39	15	2.8	4.0
15 ^[e]	A	mesitylene	58	23	8.7	0.48

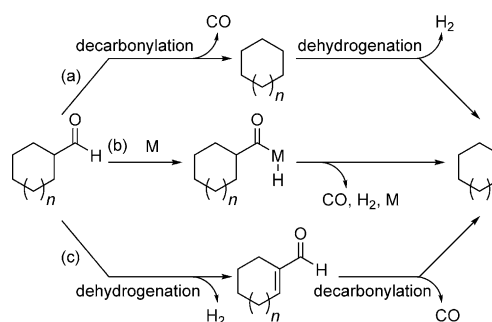
[a] Cyclododecanecarbaldehyde (ca. 0.1 mL, 0.5 mmol) was added to a 3 mL glass tube containing the catalyst (10 μ mol). After stirring at 160 °C for 20 h, dodecane (ca. 45 μ mol) and 1,1,2,2-tetrachloroethane (ca. 95 μ mol) were added, and the reaction mixture was analyzed by GC and ¹H NMR spectroscopy. [b] The reaction was conducted in a glass tube connected to a water tank to collect the evolved gases by downward displacement of water. The release of 29 % of H₂ and 63 % of CO was detected by GC and gas-detecting tube analysis. [c] 120 °C. [d] 80 °C, 72 h. [e] Reaction conducted with continuous Ar bubbling. [f] The yields of products **1** and **2** were determined by ¹H NMR spectroscopy and GC with 1,1,2,2-tetrachloroethane and dodecane as internal standards. The yield of **3** was determined by GC analysis with dodecane as an internal standard. [g] Yield of isolated product after bromination and purification by preparative TLC shown in parentheses.



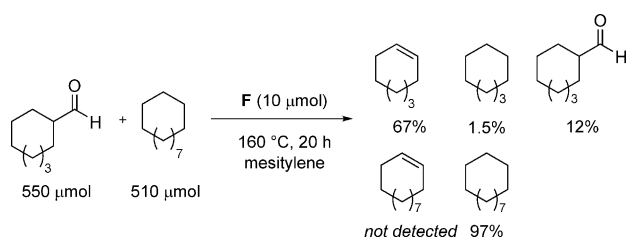
et al.,^[13] also mediated retro-hydroformylation to give **1** in 44 % yield; however, this process was accompanied by dihydrogen transfer to the starting aldehyde, which afforded side product **3** in 33 % yield (entry 2). Iridium complex **B**, which was reported to be effective for the decarbonylation of aldehydes,^[10] showed low activity and low selectivity for **1** (11 %) over **2** (20 %; entry 3). On the other hand, iridium complexes bearing a cyclopentadienyl ligand afforded retro-hydroformylation product **1** as the major product (entries 4–7). Pentamethylcyclopentadienyl complex **C** showed moder-

ate reactivity and high selectivity for the formation of **1** (33 % yield) while the yield of **2** was as low as 2.4 % (entry 4). The activity was remarkably improved by replacing the pentamethylcyclopentadienyl ligand with hydroxytetraphenylcyclopentadienyl,^[15,16] but this resulted in a slightly lower selectivity for **1** over **2** (entry 5).^[17] The yield of **1** was further improved by employing N-heterocyclic carbene ligands, such as *N,N*-bis(2,4,6-trimethylphenyl)imidazolyliene (IMes) or *N,N*-bis(2,6-diisopropylphenyl)imidazolyliene (IPr), instead of a phosphine ligand. With complex **E**, which bears one IMes ligand, the desired product **1** was obtained in 85 % yield with 4.5 % of **2** (entry 6). With IPr bearing complex **F**, the yield of **1** was further improved to 91 % with only a trace amount of **2** (entry 7). When the gas was collected by water displacement, the yields of carbon monoxide and dihydrogen evolution were determined to be 63 % and 29 %, respectively, which are in good agreement with the theoretical values calculated from the product yields (entry 8).^[18,19] It should be noted that this is the first example of a retro-hydroformylation reaction. As the yields of **1** with catalyst **F** were slightly lower in other solvents, such as DMSO, 1,2-dichlorobenzene, and diglyme (entries 9–11), mesitylene was used for all other experiments. Whereas isolation of alkene **1** from its mixture with alkane **2** was unsuccessful, we could transform **1** into 1,2-dibromocyclododecane, which was isolated in 55 % overall yield for the two steps (entry 11). The retro-hydroformylation of cyclododecanecarbaldehyde proceeded even at reduced temperature (120 °C, entry 12) but a significant drop in yield occurred. With rhodium catalyst **A**, the relative yield of alkene **1** compared to **2** or **3** remained low under various reaction conditions, such as at lower temperatures (entries 13 and 14) or with removal of dihydrogen by bubbling argon through the reaction solution (entry 15).

Possible reaction pathways for the formation of alkene **1** from the aldehyde are shown in Scheme 3: Path a corre-

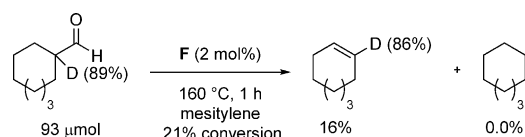

Scheme 3. Possible reaction pathways.

sponds to a sequential process consisting of decarbonylation followed by a dehydrogenation reaction, path b describes the retro-hydroformylation reaction that proceeds without forming a free cycloalkane or an α,β -unsaturated aldehyde as an intermediate, and path c corresponds to a dehydrogenation reaction to form an α,β -unsaturated aldehyde followed by decarbonylation. Based on the control experiments illustrated in Schemes 4 and 5, we concluded that path b is the dominant pathway operating under these reaction conditions. In one



Scheme 4. Retro-hydroformylation in the presence of an alkane.

control experiment, the retro-hydroformylation of cyclooctanecarbaldehyde was conducted in the presence of cyclooctadecane (Scheme 4). The possibility of path a, which involves the intermediacy of a free cycloalkane, was excluded because cyclooctadecane was not dehydrogenated while cyclooctanecarbaldehyde was converted into cyclooctene. The intermediacy of the α,β -unsaturated aldehyde was also disproved by the deuterium labelling experiment shown in Scheme 5. When cyclooctanecarbaldehyde with deuterium



Scheme 5. Deuterium labelling experiment.

(89 %) at the α -position was treated with catalyst **F**, an almost quantitative amount of deuterium was incorporated into the cyclooctene product, as confirmed by ^1H and ^2H NMR spectroscopy and GC and GC-MS analysis (86 % in the alkenyl position; Scheme 5). If the reaction had proceeded via path c, the deuterium would have been eliminated in the first dehydrogenation step. Accordingly, this retro-hydroformylation reaction is suggested to proceed along path b and not along paths a or c. The most probable mechanism for path b involves oxidative addition of the aldehyde C–H bond to the iridium catalyst followed by decarbonylation and β -hydride elimination.^[20,21]

The substrate scope of the reaction is not limited to cycloalkanecarbaldehydes. In additional experiments, acyclic secondary and primary alkyl aldehydes were also tested (Table 2). As the acyclic alkenes produced by retro-hydroformylation are more susceptible to hydrogenation than cyclic alkenes, argon gas was continuously bubbled through the reaction mixture in these experiments to remove the evolved dihydrogen. When 3-(4-*tert*-butylphenyl)-2-methylpropanal was employed as the starting material, an *E/Z* mixture of 4-*tert*-butyl- β -methylstyrene was obtained in either 73 or 74 % yield in the presence of catalyst **E** and **F**, respectively (entries 1 and 2). A linear primary alkyl aldehyde, tridecanal, was converted into a mixture of dodecenes in a total yield of 64 and 68 % with catalysts **E**

and **F** (entries 3 and 4). The product mixtures consisted of internal dodecene isomers varying in the position of the C=C bond probably owing to facile isomerization by olefin insertion into a metal–hydride bond and subsequent β -hydride elimination. In these reactions, the formation of dodecadiene was not observed, and dodecane formation was limited to 20 and 30 % yield (entries 3 and 4). The formation of dodecane could be largely attributed to the hydrogenation of dodecenes by the evolved dihydrogen rather than a simple decarbonylation reaction. This was supported by an experiment confirming that 1-dodecene was hydrogenated when it was present in the reaction mixture of the cyclooctanecarbaldehyde retro-hydroformylation (see the Supporting Information). An ester moiety was found to be compatible with these reaction conditions. Specifically, methyl 9-formylnonanoate was converted into methyl nonenoate (68 % and 67 %, entries 5 and 6, respectively).^[22]

In summary, the retro-hydroformylation for the degradation of aliphatic aldehydes into the corresponding alkenes and synthesis gas has been accomplished with hydroxycyclopentadienyl iridium complexes as the catalysts. The reaction was indicated to proceed by simultaneous retro-hydroformylation rather than a sequential decarbonylation–dehydrogenation or dehydrogenation–decarbonylation pathway. Further developments of the retro-hydroformylation might open the door for the future utilization of renewable oxygen-containing bulk resources, such as sugars, glycerin, and possibly cellulose, as feedstocks of synthesis gas, providing a mild process for the gasification of biomass materials.

Table 2: Substrate scope.^[a]

Entry	Substrate	Cat.	Conv. [%]	Product ^[e]	Yield ^[e] [%]
1		E	100 ^[b]		73 (<i>E/Z</i> = 66:6.6) ^[c] (27) ^[b]
2		F	100 ^[b]		74 (<i>E/Z</i> = 66:8.0) ^[c] (26) ^[b]
3		E	100 ^[c]		64 ^[c] (20) ^[d]
4		F	99 ^[c]		68 ^[c] (30) ^[d]
5		E	99 ^[c]		68 ^[c] (19) ^[d]
6		F	100 ^[c]		67 ^[c] (12) ^[d]

[a] The aldehyde (ca. 0.5 mmol) was added to a Schlenk tube containing the catalyst (10 μmol). After stirring at 160 °C for 20 h with continuous Ar bubbling, undecane (ca. 0.1 mmol) or dodecane (ca. 0.1 mmol) and pyrazine (ca. 0.2 mmol) were added, and the reaction mixture was analyzed by GC and ^1H NMR spectroscopy.

[b] Yield and conversion determined by GC analysis with dodecane as an internal standard. [c] Yield and conversion determined by ^1H NMR spectroscopy with pyrazine as an internal standard. [d] Yield determined by ^1H NMR spectroscopy and GC analysis with pyrazine and undecane as internal standards. [e] Side products and their yields are shown in parentheses.

Experimental Section

General procedure for retro-hydroformylation without Ar bubbling (Table 1): Substrate (ca. 0.5 mmol) and solvent (200 μ L) were added to a 3 mL glass tube containing the catalyst (10 μ mol; Supporting Information, Figure S1 a). After the reaction mixture had been stirred at the temperature and for the period of time indicated in Table 1, it was cooled to 0°C. The indicated internal standards for ^1H NMR spectroscopy and GC analysis were added to the reaction mixture, which was then analyzed by ^1H NMR spectroscopy and GC and GC-MS analysis.

Keywords: aldehydes · homogeneous catalysis · iridium · retro-hydroformylation · synthesis gas

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- [17] Although the catalyst with a tetraphenylhydroxycyclopentadienyl ligand gave higher activity, the role of the hydroxy group is not clear at this moment.
- [18] The theoretical value for carbon monoxide evolution is 69% (sum of the yields for products **1** and **2**). The theoretical value for hydrogen evolution is 34% (the yield of **1** minus the yield of **3**).
- [19] The low selectivity for cyclododecene formation in Table 1, entry 8 might be due to contaminated moisture in the system.
- [20] Although the retro-hydroformylation catalysts that were employed in this study were anticipated to mediate the hydroformylation of alkenes, the hydrogenation of alkenes to alkanes was the major pathway under standard hydroformylation conditions with complex **F**. (see the Supporting Information).
- [21] After the reaction for 20 h, the catalysts could be recycled, but catalyzed subsequent reactions with lower activity (see the Supporting Information).
- [22] The functional group tolerance was further examined by adding various additives to the retro-hydroformylation of cyclododecanecarbaldehyde with complex **F**. Aryl methyl ethers, aryl chlorides, and aryl amides were reasonably compatible with the reaction conditions whereas phenolic hydroxy group significantly decelerated the retro-hydroformylation, and 4-phenylphenol was recovered in rather low yield (see the Supporting Information, Table S3).

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