One-Pot Carbon Monoxide-Free Hydroformylation of Internal Olefins to Terminal Aldehydes

David R. Edwards, Cathleen M. Crudden,* Katherine Yam

Department of Chemistry, Queen's University, 90 Bader Lane, Kingston, ON K7L 3N6, Canada
Fax: (+1)-613-533-6669, e-mail: cruddenc@chem.queensu.ca

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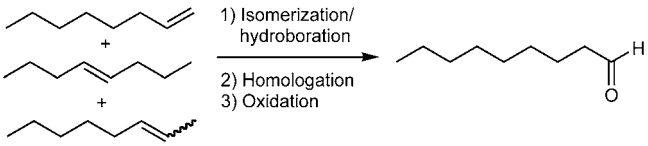
Abstract: A one-step hydroformylation of mixtures of internal and terminal olefins yielding terminal aldehydes without the need for carbon monoxide has been developed. Treatment of the olefin mixtures with Rh catalysts and pinacolborane leads to isomerization and hydroboration in one step. Homologation and subsequent oxidation regiospecifically afford the terminal aldehyde. Good overall yields are obtained for all substrates examined.

Keywords: aldehydes; boronates; homologation; hydroboration; hydroformylation

The hydroformylation of olefins is the oldest and largest chemical process currently in use employing homogenous transition metal catalysts.[1] A major limitation of this process is the requirement for terminal olefin feedstocks in order to access the terminal aldehyde, which is desired for most applications.[2] Innovations geared towards the use of economically more feasible olefin mixtures, such as raffinate II containing a mixture of butene isomers, are highly desirable. Cobalt-based catalytic systems have the dual problem of high temperature and pressure requirements as well as low regioselectivity towards terminal aldehydes.[2] Greater advances have been made with rhodium-based catalysts. For example, van Leeuwen et al. have described a series of diphosphine ligands that catalyze the isomerization/hydroformylation of internal octenes to the linear aldehyde in excellent yields.[3] Similarly, Beller et al. have reported an Rh/NAPHOS system that affects the same transformation as well as the related hydroaminomethylation reaction.[4] Both these synthetic processes share a common limitation of decreased activity and selectivity when internal olefins, such as 4-octene, are employed.

For this reason, we were intrigued by a report of Srebnik et al. in which 1-octene and *trans*-4-octene were both hydroborated with complete regioselectivity to the linear boronate **1** using pinacolborane (HBPin).[5] Combined with our recently reported homologation chemistry,[6] we felt this would provide an interesting possibility of performing a CO-free hydroformylation[7] in which internal olefins are converted into terminal aldehydes. In fact, after some optimization of the individual steps, we have been able to accomplish this transformation in high yield, as illustrated in Scheme 1.



Scheme 1.

Since the hydroboration was reported to proceed smoothly with dichloromethane as solvent, we set out to develop a one-pot procedure with the solvent of the first transformation functioning as the reagent in the homologation step. After homologation, oxidation would give the product of hydroformylation without the need for carbon monoxide. The homologation has precedent in the work of Matteson[8] on boronic esters in general and by us specifically with the homologation of substituted phen-1-ethylpinacol boronate during the asymmetric synthesis of Ibuprofen and Naproxen.[6] Thus, we report herein a one-pot carbon monoxide-free hydroformylation procedure for mixtures of olefins, which produces linear aldehydes in high yields.

Our initial efforts focused on hydroborating 1-octene with Wilkinson's catalyst according to the reported procedure of Srebnik et al. [Eq. (1)].[5] We found the reaction to be quite sluggish. Even after 120 minutes, conversion to **1** was only 6%. Freshly prepared and recrystallized catalyst gave identical results.[9] Catalyst that had been stored outside the glove box and showed signs of phosphine oxide in its ^{31}P NMR gave significantly better results. In fact, GC *yields of up to 92% could be obtained when a stream of air was passed through a solution of* $RhCl(PPh_3)_3$ in dichloromethane. Since this method gave variable yields, a more predictable procedure was sought.

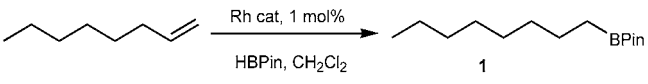


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Table 1. Catalyst screening for hydroboration/isomerization of 1-octene.[a]

Entry	Catalyst	Additive (Phosphine:Rh)[b]	Yield[c] [%]	Time [h]
1	$RhCl(PPh_3)_3$	–	6	2
2	$RhCl(PPh_3)_3$	–	31–92[d]	2
3	$[RhCl(PPh_3)_2]_2$	–	88[e]	3
4	$[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$	PPh_3 (1:1)	71	0.5
5	$[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$	PPh_3 (1.25:1)	98	0.5
6	$[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$	PPh_3 (1.5:1)	83	0.5
7	$[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$	PPh_3 (2:1)	79	0.5
8	$[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$	DPPB[f] (1.25:1)	28	0.5
9	$[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$	$P(OPh)_3$ (1.25:1)	83	0.5
10	$[Rh(COD)_2]_2BF_4$	PPh_3 (1.25:1)	77	0.5

[a] Reactions were run on a 1 mmol scale, 1.0 M in dichloromethane under nitrogen with 1% catalyst in entries 1–3 and 10, and 2% catalyst for entries 4–9.
[b] Molar ratio of phosphine to Rh (in the monomeric form for entries 4–9).
[c] GC yield using decane as internal standard.
[d] Air was bubbled through the reaction mixture until the color changed from pale yellow to black.
[e] Isolated yield.
[f] DPPB = 1,4-bis(diphenylphosphino)butane.

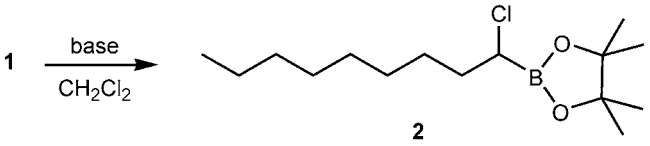
Table 2. Optimization of homologation reaction conditions.

Entry	Base (equivs.)	Temperature [°C]	Additive	Conversion[a] [%]
1	*n*-BuLi (2)	–100	$ZnCl_2$	82
2	*n*-BuLi (3)	–100	$ZnCl_2$	89
3	*n*-BuLi (3)	–100	–	89
4	*n*-BuLi (3)	–78	–	88
5	LDA[b] (2)	–40	–	100

[a] Conversion was determined by ^1H NMR assay of the ratio of starting material to α-chloropinacol boronate.
[b] LDA = lithium diisopropylamide.

$[RhCl(PPh_3)_2]_2$ was examined as a catalyst precursor because of its latent free coordination site and decreased phosphine to Rh ratio compared to Wilkinson's catalyst. Gratifyingly, hydroboration of 1-octene proceeded with a 90% conversion to **1** after 3 hours reaction time. In an effort to further optimize the Rh:phosphine ratio, $[RhCl(C_2H_2)_2]_2/PPh_3$ combinations were examined (Table 1). It was determined that a ratio of 1.25 phosphine to 1 Rh was optimal. Use of 1–2 mole percent of catalyst precursor resulted in near quantitative isolated and GC yields of linear boronate **1**. Attempts to decrease catalyst loading below this resulted in observation of the isomerization product 2-octene. Triphenyl phosphite and DPPB were also examined in the reaction. Neither of these phosphines nor even the use of a cationic Rh species gave improved results *vs.* the Rh dimer and PPh_3. Results are summarized in Table 1.

Having established a suitable protocol for the regioselective and nearly quantitative conversion of 1-octene to the corresponding linear pinacol boronates, our attention turned to the task of converting **1** to the α-chloropinacol boronate **2** [Eq. (2)]. Invariably, the crude reaction mixture resulting from the first transformation was diluted to a 0.1 M concentration in dry THF. The reaction flask was then cooled to the desired temperature and base was added slowly according to the Matteson protocol.[10] The resulting homologated product was then worked up and examined for conversion of **1** to **2** by ^1H NMR, see Table 2.



(2)

Matteson has demonstrated that the addition of $ZnCl_2$ aids in the breakdown of the borate complex and permits the reaction to take place with high diastereoselectivity when the boronate ester is derived from a chiral diol.[11] Since our reaction employs an achiral boronate ester and is not diastereoselective, $ZnCl_2$ was unnecessary. Entries two and three reveal that omission of the zinc additive made no difference to the reaction. The slightly milder temperature of –78 °C could also be employed using this *in situ* homologation procedure, entry 4. LDA (lithium diisopropylamide) was able to affect

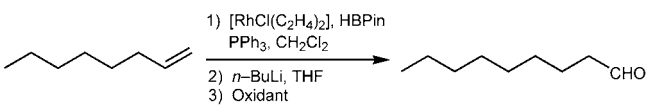
Table 3. Optimization of oxidation reaction conditions.

Entry	Oxidant (equivs.)	Conditions	Overall Yield[a] [%]
1	TMANO[b] (3.0)	PhH, 60 °C, 9 h	74–76
2	NMO[c] (3.0)	PhH, 60 °C, 24 h	0
3	$Me_2N(O)C_{11}H_{24}$ (3.0)	PhH, 60 °C, 9 h	0
4	$NaBO_3$ (1.2)	H_2O[d], 25 °C, 2 h	42
5	H_2O_2/NaOH (1.2)	H_2O[d], 25 °C, 2 h	<20
6	Na_2CO_3/1.5 H_2O_2 (1.2)	H_2O[d], 25 °C, 2 h	65
7	Na_2CO_3/1.5 H_2O_2 (2.0)	H_2O[d], 25 °C, 2 h	80

[a] GC yield over all three steps using decane as internal standard.
[b] Trimethylamine *N*-oxide.
[c] *N*-Methylmorpholine *N*-oxide.
[d] Crude reaction mixture was further diluted to a 0.2 M concentration in water.

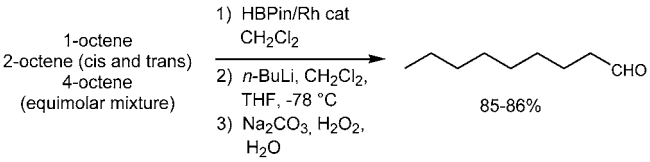
this transformation with quantitative conversion of **1** to **2** at the more desirable temperature of −40 °C, entry 5. Nonetheless, attempts to oxidize **2** in the presence of the resulting two equivalents of diisopropylamine failed. Carrying out a simple extractive work-up procedure to remove the amine allowed the oxidation to proceed, however, this did not fit with our initial goal of developing a one-pot procedure so the procedure described in entry 4 was adopted.

The crude reaction mixture containing **2** was treated with various oxidizing reagents to complete the sequence. Reactions were monitored by GC and the *overall yield* of aldehyde from 1-octene was calculated. Amine oxides have previously been employed for oxidation in organoborane chemistry and we tested three such reagents, trimethylamine *N*-oxide (TMANO), *N*-methylmorpholine *N*-oxide (NMO), *N,N*-dimethylundecylamine *N*-oxide, entries 1, 2, 3 of Table 3.[12] Unfortunately none of these reagents was soluble in THF. TMANO could only be employed following a solvent switch, in which THF was partially removed and benzene subsequently added to the crude reaction flask. Reflux for 9 h furnished nonyl aldehyde in an overall yield of 74–76% over the three steps. Other amine oxides tested showed no conversion to the aldehyde. Since the solvent switch is cumbersome, we examined other oxidants that would be soluble in THF/CH_2Cl_2. Neither Kabalka's perborate[13] nor basic hydroperoxide[14] led to sufficient amounts of aldehyde, entries 4 and 5. However, we were delighted to see that sodium percarbonate, a very inexpensive oxidant, cleanly furnished nonyl aldehyde in good overall yield, entry 6.[15] The oxidation could be carried out without switching solvents, requiring only the addition of water as a co-solvent. The reaction proceeded faster and with better conversion using two equivalents of the reagent, entry 7.



(3)

Having identified a suitable protocol for the conversion of 1-octene, a linear olefin, to nonyl aldehyde, it remained to be shown that the same procedure could be applied to mixtures of octene isomers. This requires that the olefin isomerization be faster than hydroboration.[16] A stock solution consisting of equimolar amounts of 1-, *cis*-2-, *trans*-2-, and *trans*-4-octene was subjected the one-pot hydroboration/homologation/oxidation reaction [Eq. (4)]. In order to further optimize the procedure, we carried out the hydroboration with a slight increase in dichloromethane (0.5 M instead of 1.0 M in dichloromethane). This simple switch allowed us to decrease the amount of base in the following homologation step, and did not adversely affect the hydroboration reaction itself. Presumably the addition of extra dichloromethane was sufficient to drive the homologation reaction to high conversion without the requirement for three equivalents of base. Employing the new protocol, the overall yield of the one-pot reaction was 85–86% [Eq. (4)].



(4)

To further probe the scope of the reaction and demonstrate its potential as a viable option for the production of aldehydes from olefin mixtures, a series of internal olefins of varying carbon length were subjected to the optimized protocol, Table 4. In all substrates examined, good overall yields of the linear aldehyde were obtained. Most gratifying were the results obtained for 2-hexene, in which an excellent yield of 90–95% was observed over the three steps.

In conclusion, a one-pot protocol for the conversion of olefins to linear aldehydes without the need for carbon monoxide has been developed. A highlight of the de-

Table 4. Hydroformylation of various internal olefins.

Entry	Olefin	Yield of Aldehyde [%][a]
1	2-hexene	90–95
2	2-heptene	79–83
3	octenes[b]	85–86
4	3-nonene	60–64

[a] GC yield using decane as internal standard except for entry 2, where octane was used.
[b] Equimolar mixture of 1-octene, 2-octene and *trans*-4-octene.

vised methodology is the ability to convert mixtures of olefins to the more desirable linear aldehyde in up to 95% yield. This represents a significant step towards the development of hydroformylation procedures capable of functioning on cheaper feedstocks comprised of internal as well as terminal carbon-carbon double bonds. Although our method does require cryogenic temperatures for the homologation step and one full equivalent of hydroborating reagent, it provides a significantly safer and easier method to carry out hydroformylations. Thus regular synthetic laboratories not equipped to handle CO can use our method to affect hydroformylations without the need for high pressure vessels and special safety equipment. The reaction also works best with simple, easily handled catalysts such as $[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$ and triphenylphosphine.

Experimental Section

General Remarks

$[RhCl(C_2H_2)_2]_2$ was prepared from commercial rhodium chloride trihydrate by the reported procedure.[17] *n*-BuLi was freshly titrated against *N*-benzylbenzamide to the deep blue endpoint. All other reagents were commercially available and were purified according to Perrin and Perrin techniques prior to use.[18] Hydroborations took place in the oxygen-free environment of a glove box. Yields of all aldehydes were obtained *via* an Agilent 6850 GC referenced to a commercially available authentic sample. Calibration curves were constructed by running a series of samples containing the aldehyde and internal standard, decane, at four different concentrations. All attempts to obtain isolated yields of **2** led to partial decomposition of the *alpha*-chloropinacol boronates. Conversion of **1** to **2** was calculated based on crude ^{1}H NMR integration ratios for proton signals *alpha* to boron.

Nonyl Aldehyde

$[RhCl(C_2H_4)_2]_2$ [0.01 mmoles, 3.9 mg, 2% (per Rh)] was weighed into a 50-mL two-necked round-bottomed flask inside a glove box. To this PPh_3 (0.025 mmoles, 6.6 mg, 2.5%) was added followed by 2 mL of deoxygenated and dry dichloromethane. The reddish-yellow solution was stirred for five minutes and then 1-octene (1.02 mmol, 160 μL) was added by syringe followed immediately by pinacolborane (1.2 mmol, 175 μL). The clear reddish-yellow solution went dark within five minutes and reactions were left in the glove box for a further 30 minutes. The reaction flask was then removed from the glove box, the mixture was diluted with 10 mL dry THF and cooled to −78 °C. Freshly titrated *n*-BuLi (2 equivs.) was then added slowly down the side of the flask. Reactions were then left to slowly warm to room temperature overnight. The following morning the reaction mixture was further diluted with 5 mL distilled water and 2 equivalents of sodium percarbonate (2.04 mmol, 320 mg) were added at 0 °C and the reaction was left to warm to room temperature over 2 hours. Decane was added as internal standard and a small aliquot removed for yield determination by GC.

Acknowledgements

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References and Notes

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