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Toward the Rhodium-Catalyzed Bis-Hydroformylation of 1,3-Butadiene to Adipic Aldehyde

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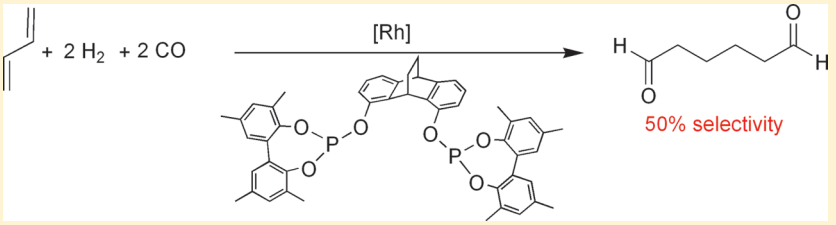
Supporting Information

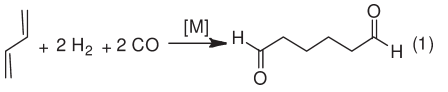
ABSTRACT:



The effects of the ligand to metal ratio, temperature, syngas pressure, partial pressures of H_2 and CO, and new ligand structures have been examined on 12 of the most reasonable products resulting from the rhodium-catalyzed low-pressure hydroformylation of 1,3-butadiene. The selectivity for the desired linear dihydroformylation product, 1,6-hexanedial (adipic aldehyde), is essentially independent of all of these reaction parameters, except for ligand structure. However, the reaction parameters do have a substantial effect on the selectivity for the products, resulting from the branched addition of the rhodium hydride to the carbon−carbon double bond. The optimum reaction parameters and ligand have resulted in a so far unprecedented maximum selectivity of 50% for adipic aldehyde.

INTRODUCTION

Hydroformylation (the "oxo reaction") is one of the largest homogeneous transition-metal-catalyzed processes operated industrially. The substrates commonly employed in these processes are nonconjugated terminal or internal alkenes. Typically, linear aldehydes are the desired products,[1] which are then subsequently converted to more valuable downstream compounds (e.g., carboxylic acids, alcohols, ...).[1] Despite the importance and atom economy of the oxo process, the dihydroformylation of conjugated dienes is not a standard reaction. Arguably, the reason stems from the lack of regioselectivity in these reactions. For instance, the simplest diene, 1,3-butadiene, typically obtained from large industrial steam-cracking units, can yield up to 14 different aldehyde products.[2] These numerous products result from *n* and *i* addition of the intermediate metal hydride to the metal-coordinated diene, a step that is alternatively often viewed as double-bond *n* or *i* insertion into the metal−hydride bond. Frequently, *i* addition is favored both kinetically and thermodynamically because the barrier to hydride addition is decreased as a result of conjugation so that a stable η^3-methallyl complex is produced.[3,4] Once this occurs, the formation of the linear dialdehyde is prevented, provided that rapid double-bond isomerization and hydroformylation of the terminal position of the carbon−carbon double bond does not occur. If a solution to these problems of regioselectivity were found, an attractive commercial process would be the dihydroformylation of 1,3-butadiene to form 1,6-hexanedial (adipic aldehyde; eq 1). This product is an attractive precursor to the synthesis of other more valuable C6 compounds (e.g., adipic acid, hexamethylenediamine, ε-caprolactone, and 1,6-hexanediol).[5−10] Of course, the hydroformylation of 1,3-butadiene has been investigated by quite a number of research groups since Roelen's discovery of Co-catalyzed hydroformylation in 1938,[5,6,8−19] but the selectivity for adipic aldehyde has always been much too low to make a technical process viable. To our knowledge, the best results with respect to the yield of adipic aldehyde (up to 31%) were claimed by Ohgomori et al.[8] These authors used $Rh_4(CO)_{12}$ as the Rh source and DIOP as the ligand. This paper presents our work on the rhodium-catalyzed low-pressure hydroformylation of 1,3-butadiene to form adipic aldehyde utilizing a new ligand family.



Previous work in our group has established that a new family of chelating P-based bidentate ligands (phosphines, phosphonites, phosphites, phosphoramidites) are capable of producing very high *n*:*i* ratios for monoaldehydes from nonconjugated terminal olefins.[20−26] These ligands generally feature a doubly

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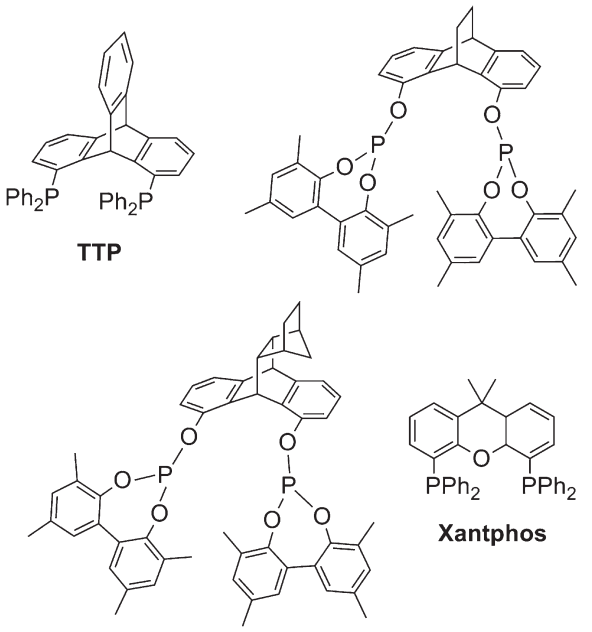
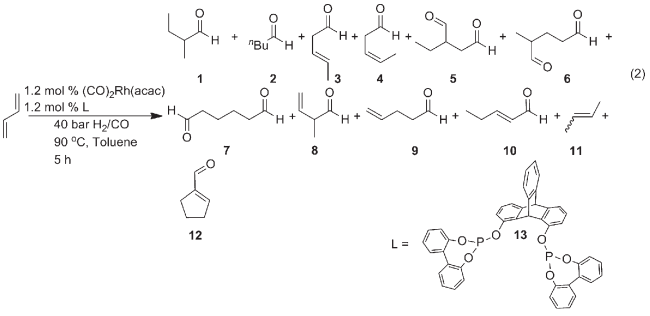


Figure 1. TTP, typical TTP-derived bisphosphite chelate ligand systems (entries 11 and 12 in Table 5, vide infra), and Xantphos.

P-functionalized 9,10-C_2-bridged 9,10-dihydroanthracene scaffold. They are derived from the parent system Triptyphos (TTP; Figure 1) and are easily accessible in broad structural variety by Diels–Alder reactions of properly prefunctionalized anthracenes. TTP and two representative structures of bisphosphites are displayed in Figure 1. Their synthesis has been described elsewhere.[21,24−26] Essentially the choice and development of this new ligand family was based upon the published knowledge about ligand structures, coordination chemistry, reactivity patterns, and catalytic performance of van Leeuwen's xantphos ligand (Figure 1) and its congeners, originally with the intention to approach a rational ligand design strategy in order to boost activity, catalyst stability, and in particular *n* selectivity of Rh-catalyzed low-pressure hydroformylation of terminal monoolefins.[20,21] Bisphosphines such as TTP and related C_2-bridged analogues have indeed produced *n*:*i* ratios of up to 60:1 and are considerably faster than xanthphos-based bisphosphines. In particular, rhodium complexes of bisphosphites such as the ones shown in Figure 1 have turned out not only to be highly active (as fast as triphenylphosphine) but also lead to full conversion to *n*-aldehydes (*n*:*i* above 300:1), practically without side products. Experimental and theoretical (DFT) mechanistic work has shown that the high regioselectivity in these systems has both kinetic and thermodynamic origins, which will be reported separately.

RESULTS AND DISCUSSION

Hydroformylation of 1,3-Butadiene at 90 °C and 40 bar Syngas. Due to our previous experience with 1-alkenes, we focused our attention on utilizing these ligand types in the hydroformylation of 1,3-butadiene. The hydroformylation of 1,3-butadiene was initially conducted in toluene under 40 bar of syngas (1/1 H_2/CO) and at 90 °C with a ligand/metal (L/M) ratio of 1. The reaction was monitored over the course of 5 h. During this time, a number of products formed when the bisphosphite **13** displayed in eq 2 was used.

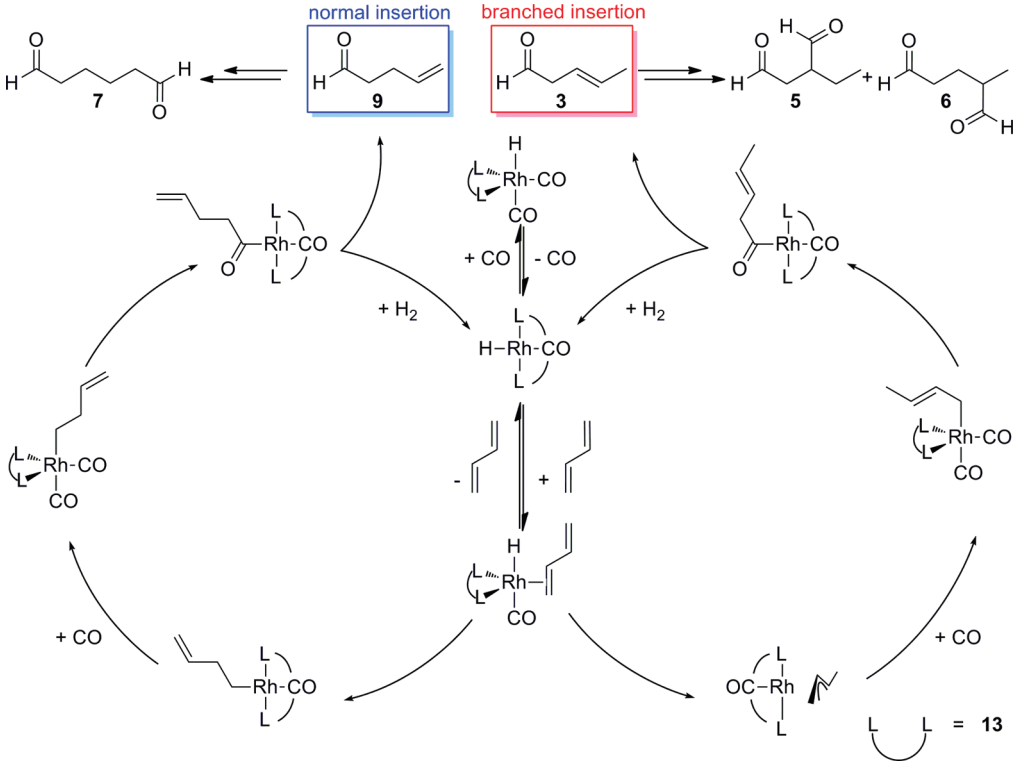


The compounds *trans*-3-pentenal (**3**), *cis*-3-pentenal (**4**), *trans*-2-pentenal (**10**), 4-pentenal (**9**), and 2-methylbut-3-enal (**8**) are transient and are eventually converted to the final products 2-methylbutyraldehyde (**1**), pentanal (**2**), 2-ethylbutanedial (**5**), 2-methylpentanedial (**6**), and adipic aldehyde (**7**). The products **3**, **4**, **8**, and **10** likely result from the branched (iso) addition of a rhodium hydride to the terminal position of 1,3-butadiene,[6,8,12,16] producing a π-methallyl complex (Scheme 1). The hydroformylation of this η^3-methallyl complex then produces **3** and **4**, which can either undergo an additional hydroformylation to produce **5** and **6** or isomerize to *trans*-2-pentenal (**10**). *trans*-2-Pentenal is then hydrogenated to form **2**; the rhodium-catalyzed hydrogenation of α,β-unsaturated aldehydes is known to be very fast.[18,27,28] Products **7** and **9** result from the normal addition of the rhodium hydride to the carbon–carbon double bond forming the rhodium alkyl complex (Scheme 1). This intermediate is eventually converted to 4-pentenal (**9**), which can undergo a further normal hydroformylation to yield **7**. The efficiency of the latter catalytic step from **9** toward adipic aldehyde (**7**) was tested independently: Rh hydroformylation of commercially available 4-pentenal (**9**) under standard conditions (viz. Table 5) using the bisphosphite displayed in Figure 1 (upper right) yields 94% adipic aldehyde (**7**).[24] Compound **12** results from the self-condensation of the desired dialdehyde **7**. These competing reaction pathways follow previously proposed mechanisms.[6,29−37] Due to these numerous reaction products, we sought to systematically study the effects of the ligand/metal ratio, temperature, and pressure on the selectivity for these products.

Hydroformylation of 1,3-Butadiene at 90 °C Under 40 bar Syngas with Variable L/M Ratios. Selectivity has previously been shown to be highly dependent on the L/M ratio.[38−42] We examined the possibility for this dependence by varying the L/M ratio from 1 to 8. As depicted in Table 1, the selectivity for adipic aldehyde is not dependent on the L/M ratio. However, the presence of excess ligand does decrease the rate of conversion of **3** and **4** to **2**, **5**, and **6**. The *i*:*n* ratio is defined here as the sum of aldehyde products **1**–**6**, **8**, and **10** divided by the sum of aldehyde products **7**, **9**, and **12**. While the aldehydes **2**–**4** and **10** are linear aldehydes, they do not arise from a normal addition of the rhodium hydride to the carbon–carbon double bond but from a branched 1,4-addition as depicted in Scheme 1.

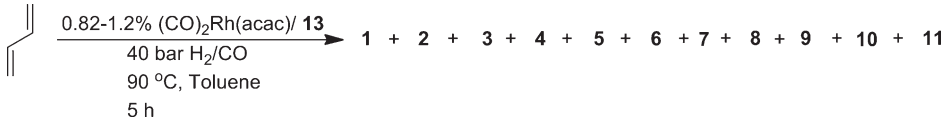
The use of 1.0 equiv of the ligand produces an *i*:*n* ratio of 4.40, higher than for all other reactions. This could result from partial ligand decomposition, a known phenomenon for phosphite ligands,[43−46] producing a second catalyst which could be less selective for dialdehyde **7** and be responsible for the slightly

Scheme 1. Proposed Mechanism for the Hydroformylation of 1,3-Butadiene[a]



[a] For trigonal-bipyramidal intermediates only the bis-equatorial chelate coordination modes are displayed.

Table 1. L/M Dependence on the Hydroformylation of 1,3-Butadiene



L/M	*i*:*n*	1[a]	2[a]	3[a]	4[a]	5[a]	6[a]	7[a]	8[a]	9[a]	10[a]	11[a]
1.0	4.40	7.0	41.4	0.0	0.0	6.3	24.3	18.5	1.8	0.0	0.3	0.2
2.0	3.44	2.5	42.8	0.0	0.0	8.7	23.5	22.2	0.1	0.0	0.0	0.2
3.7	3.69	1.3	14.5	33.2	9.2	4.0	13.6	21.1	0.0	0.0	1.8	1.2
8.1	3.80	0.7	5.3	44.4	17.1	1.9	8.4	20.5	0.0	0.3	1.3	0.0

[a] Relative percentages of the products. [1,3-butadiene] = 0.18−0.25 M.

higher *i*:*n* ratio. Consequently, all subsequent reactions were performed with a slight excess of ligand relative to rhodium.

Hydroformylation of 1,3-Butadiene at 40 bar of Syngas with Variable Temperatures. The selectivity dependence on temperature was investigated from 70 to 130 °C. The reactions were conducted with a L/M ratio ranging from 1.0 to 1.4 under 40 bar of syngas in toluene. The selectivity for adipic aldehyde (**7**) did not vary appreciably with temperature. However, there is a consistent trend toward decreasing amounts of **5** and increasing amounts of **2** with increasing temperature. This suggests that **5** and **2** are produced from a common intermediate. It seems likely that the rhodium hydride intermediate adds to the carbon−carbon double bond of **3**/**4**, producing an unsaturated rhodium alkyl complex (Scheme 2). This unsaturated complex can then undergo β-hydride elimination to generate *trans*-2-pentenal, or insert CO to form a rhodium-acyl complex, yielding **5**. As the temperature increases, the rate of β-hydride elimination to *trans*-2-pentenal (followed by rapid hydrogenation) increases relative to the rate of CO insertion (Table 2). At or above 110 °C, it is important to closely monitor the reaction, as adipic aldehyde undergoes self-condensation to cyclopent-1-enecarbaldehyde (**12**). This decomposition product can then be hydrogenated to yield cyclopentanecarbaldehyde. If the reaction is not closely monitored and decomposition ensues, then the observed selectivity could be lower than it otherwise actually is.

Hydroformylation of 1,3-Butadiene at 90 °C with Variable Syngas Pressures. The pressures of syngas (1/1 H_2/CO) were

Scheme 2. Putative Mechanism for the Formation of 2 and 5 from 3 and/or 4

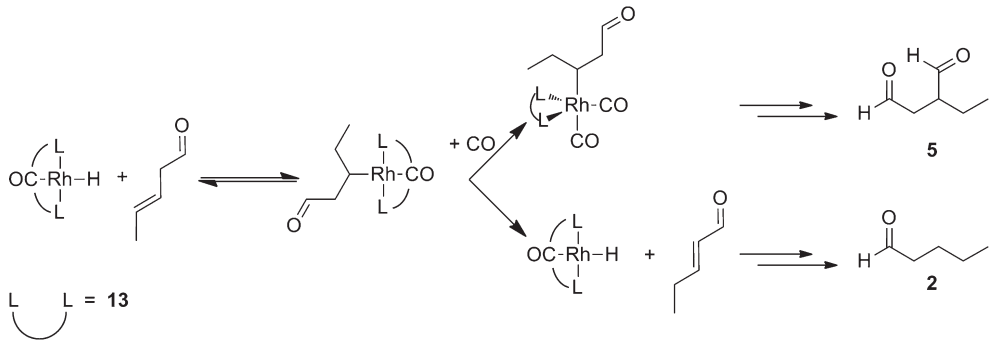
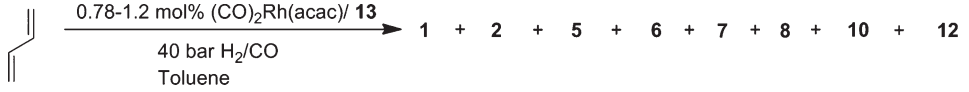


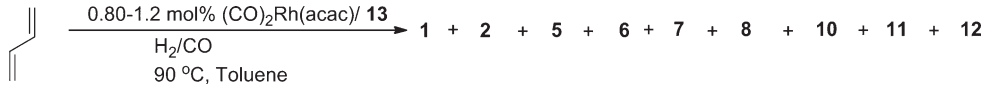
Table 2. Temperature Dependence on the Hydroformylation of 1,3-Butadiene



T (°C)	time (h)	*i*:*n*	1[a]	2[a]	5[a]	6[a]	7[a]	8[a]	10[a]	12[a]	L/M
70	22	3.93	2.9	38.8	13.1	24.8	20.1	0.0	0.0	0.1	1.1
90	5	4.40	7.0	41.4	6.3	24.3	18.5	1.8	0.3	0.0	1.0
110	1	3.50	4.6	45.2	4.4	20.6	22.2	0.0	2.9	0.0	1.2
130	1	3.69	13.6	45.6	2.4	17.0	21.1	0.0	0.1	0.2	1.4

[a] Relative percentages of the products. [1,3-butadiene] = 0.18−0.25 M.

Table 3. Pressure Dependence on the Hydroformylation of 1,3-Butadiene



P (bar)	time (h)	*i*:*n*	conversn (%)[a]	1[b]	2[b]	5[b]	6[b]	7[b]	8[b]	10[b]	11[b]	12[b]	L/M
10	23	3.72	94	5.1	56.8	0.6	11.8	19.8	0.0	2.7	3.0	0.2	1.4
20	5	3.81	88	2.9	53.4	2.7	16.6	20.4	0.0	2.6	1.2	0.2	1.4
40	5	4.40	ND	7.0	41.4	6.3	24.3	18.5	1.8	0.3	0.2	0.0	1.0
80	5	3.70	84	1.9	36.7	14.8	24.6	21.2	0.0	0.8	0.0	0.1	1.4

[a] Percent conversion to the products. ND = not determined. [b] Relative percentages of the products. [1,3-butadiene] = 0.18−0.25 M.

varied from 10 to 80 bar (Table 3). The concentrations of **5** and **2** appear to be the species most dependent on pressure. The concentration of **5** consistently increases with increasing pressure, while the concentration of **2** consistently decreases with increasing pressure. This observation is also consistent with the supposition that **5** and **2** are made from a common intermediate, *trans*-/*cis*-3-pentenal (**3**/**4**). At increasing pressures, the rate of CO insertion to yield **5** increases relative to the rate of β-hydride elimination and is consistent with the competing reactions described in Scheme 2.

Hydroformylation of 1,3-Butadiene at 110 °C with Variable Partial Pressures of H_2 and CO. The partial pressures of H_2 and CO have previously been shown to influence the *i*:*n* ratio for hydroformylation reactions.[30,47] The partial pressure of H_2 was varied from 20 to 43 bar while the CO partial pressure was fixed at 20 bar (Table 4). Similarly, the partial pressure of CO was varied from 20 to 48 bar while the H_2 partial pressure was fixed at 20 bar. These experiments demonstrate that the rates and selectivities to adipic aldehyde are not greatly affected by the partial pressure of either H_2 or CO; however, we note that these experiments are not rigorous kinetic studies, and no claims regarding the quantitative order of substrates are made. Frequently, the reaction rate is inverse order in CO,[47] as a result of the need to dissociate CO from the 18-electron resting state (Scheme 1). A possible reason for the qualitative independence of the reaction rate on the partial pressures in our system could result from the rate-determining step being the insertion of CO to form the rhodium acyl intermediate. The dissociation of CO would still be

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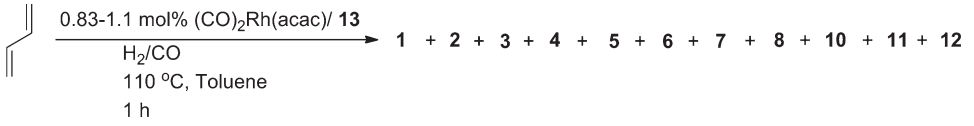
Table 4. Partial Pressure Dependence of H_2 and CO on the the Hydroformylation of 1,3-Butadiene



P_{H_2}[a]	P_{co}[a]	*i*:*n*	conversn (%)[b]	1[c]	2[c]	3[c]	4[c]	5[c]	6[c]	7[c]	8[c]	10[c]	11[c]	12[c]	L/M
43	20	3.47	86	5.1	44.7	0.0	0.0	5.7	20.6	22.1	0.0	1.5	0.0	0.3	1.4
34	20	4.22	79	6.0	42.9	0.0	0.0	4.8	17.7	18.9	8.4	0.8	0.2	0.2	1.1
20	20	3.50	85	5.0	45.4	0.0	0.0	4.0	20.2	21.8	0.0	2.5	0.9	0.3	1.2
20	31	3.54	82	6.8	41.2	0.0	0.0	5.7	23.5	21.9	0.0	0.8	0.0	0.1	1.3
20	48	3.54	80	2.4	34.1	6.0	2.8	7.6	21.4	21.8	0.0	3.6	0.0	0.2	1.4

[a] *P* = partial pressure in bar. [b] Percent conversion to the products. [c] Relative percentages of the products. [1,3-butadiene] = 0.19−0.25 M.

required to form an active intermediate, but CO recoordination to form the rhodium dicarbonyl alkyl complex would precede the rate-determining step, resulting in a negligible dependence on the partial pressure of CO. Since the reaction with H_2 would occur after the rate-determining step, the rate would be zero order in H_2.[48] If the concentrations of H_2 and CO are involved in the rate law for the formation of linear and branched products, the order is the same for each competing reaction and has no effect on the *i*:*n* ratio. Thus, it appears that the two competing transition states are of the same composition.

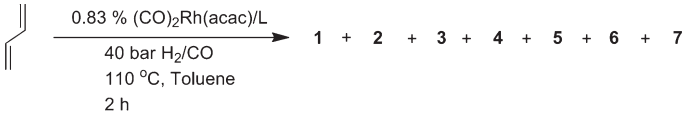
Hydroformylation of 1,3-Butadiene at 110 °C with New Ligand Systems. Since the selectivity for adipic aldehyde is not altered significantly by changing the temperature, pressure, or partial pressure, we decided to screen a number of different ligands. All of them (except PPh_3, which functioned as a standard) are members of our new ligand family derived from Triptyphos (Figure 1) and its congeners (bisphosphines, bisphosphites, entries 2−12 in Table 5), which had shown exceptional *n* selectivities for 1-alkene hydroformylation. We wanted to determine ligand structure effects on the selectivity for the Rh-catalyzed 1,4-bis-hydroformylation of 1,3-butadiene. The reactions were conducted at 110 °C under 40 bar of syngas (1/1 H_2/CO) in toluene by means of a Chemspeed high-throughput robot system (for details see the Experimental Section). Table 5 demonstrates that the bis-phosphines tested gave by far the least active catalysts and produced little, if any, adipic aldehyde. This decrease in reactivity is consistent with the notion that a more electron-donating ligand stabilizes the putative resting state, $L_2Rh(H)(CO)_2$.[45,49] The increased stability makes it more difficult for CO to dissociate to form the coordinatively unsaturated rhodium complex responsible for catalysis. Not unexpectedly, the bulky and electron-rich ligands used for entries 2−4 of Table 5 neither lead to active catalysts for butadiene hydroformylation nor are they active in the *n*-selective hydroformylation of 1-alkenes. Most remarkably, small changes in the ligand structure of the phosphites can have a profound impact on the selectivity. For instance, ligand **13** yields a selectivity for adipic aldehyde of 22.8% (entry 8), but when four methyl groups are added to the bisphenol backbone, the selectivity increases by 15% to 37.8% (entry 10). Notably, entry 12 with a 9,10-ethano bridge gave close to 50% selectivity to adipic aldehyde. To the best of our knowledge, this is the highest selectivity for adipic aldehyde reported to date. Oftentimes, the selectivity for adipic aldehyde has been found to be <10%,[6,11−13,16,18,19] except for the singular 31% claimed by Ohgomori et al.[8]

We suspect that the dependence of selectivity on ligand architecture within the ligand family of our bisphosphites is predominantly a result of variable steric interactions. The two putative intermediates produced from branched vs normal addition require substantially different coordination environments. Normal addition to the coordinated diene results in a linear alkenyl intermediate, occupying only one coordination site in the square-planar complex (Scheme 1). However, branched addition produces an η^3-coordinated π-methallyl ligand, occupying two coordination sites, and can thus be highly sensitive to the steric environment around rhodium. By creating and fine-tuning a sterically bulky environment at the rhodium center, it should be possible to relatively destabilize the π-methallyl complex, hindering the formation of the branched products. However, if the ligand is too sterically encumbering, then it is also possible that it prevents coordination of the alkene, inhibiting catalysis. We believe these factors determine the different selectivities and rates for this ligand class. Our observation that rather subtle structural changes, which are easily and broadly accessible from our modular synthetic strategy, can strongly influence the selectivity for adipic aldehyde, in our eyes makes ligand design based on a combination of appropriate experimental and theoretical strategies very attractive.

CONCLUSION

In conclusion, we have examined the influence of syngas pressure, H_2 and CO partial pressures, temperature, and ligand architecture on the selectivity for adipic aldehyde. The temperature and pressures have no significant effect on the selectivity, but substantial changes were observed upon alteration of the ligand backbone and the chelating P subgroups. Given the rather complicated structures of our chelate ligands and thus of the "reaction pocket" in which the transformation to either the *n*-insertion-based *n*-alkenyl complex or the *i*-insertion-based η^3-π-methallyl product is occurring at the Rh center, the energetic differentiation between these two stereoisomeric processes can only amount to a few kJ/mol, as adipic aldehyde is produced with some of the bisphosphites. In fact, extensive DFT calculations[34] for both complete catalytic cycles of Scheme 1, which will be reported separately, using the ethano-bridged ligand of Figure 1 without the 4-methyl substituents as a model ligand, predict an insertion barrier difference $\Delta\Delta G^{\ddagger}$ of only 5 kJ/mol in favor of *i* insertion. Given the large number of attractive and repulsive long-range intraligand and intracomplex interactions in these systems, it seems impossible to even qualitatively identify dominant selectivity

Table 5. Ligand Influences on the Hydroformylation of 1,3-Butadiene[50]



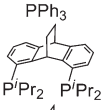
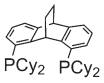
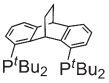
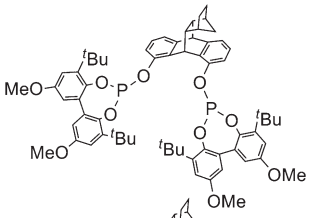
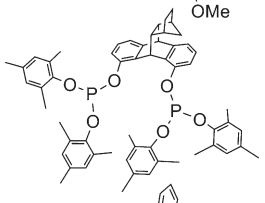
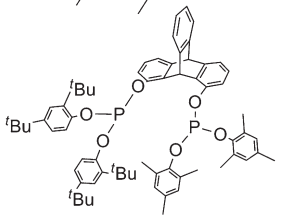
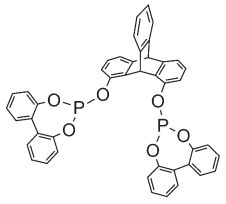
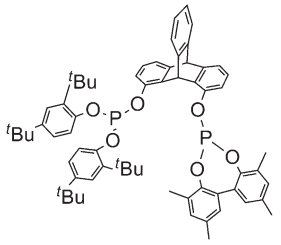
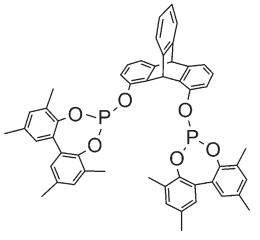
Entry	Ligand	L/M	*i*:*n*	Selec. 7[a]	% Conv.[b]	1[c]	2[c]	3[c]	4[c]	5[c]	6[c]	7[c]
1	PPh_3	5.1	6.3	11.8	67.0	4.8	4.6	31.1	10.8	0.3	4.6	7.9
2		1.6	3.2	0.0	1.1	0.2	0.0	0.1	0.2	0.0	0.0	0.0
3		1.5	3.1	0.0	1.6	0.2	0.0	0.5	0.2	0.0	0.0	0.0
4		1.5	NA	0.0	0.3	0.3	0.0	0.0	0.0	0.0	0.0	0.0
5		1.5	2.7	0.0	5.0	1.2	0.3	1.4	0.6	0.0	0.0	0.0
6		1.5	4.1	1.9	8.7	1.3	0.2	3.6	1.7	0.0	0.0	0.2
7		1.5	5.4	7.5	35.1	2.2	1.6	16.7	7.7	0.0	0.4	2.6
8		1.5	3.4	22.8	95.7	3.7	38.6	0.0	0.0	6.8	23.0	21.8
9		1.5	1.9	34.0	84.0	0.8	1.6	30.0	12.2	0.6	3.2	25.5
10		1.5	1.6	37.8	86.0	0.4	1.0	27.5	15.2	0.4	2.4	28.9

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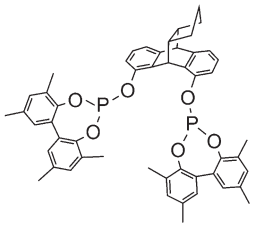
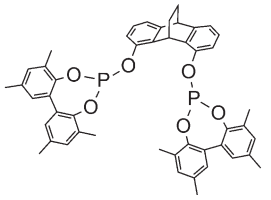
Table 5. Continued

Entry	Ligand	L/M	*i*:*n*	Selec. 7[a]	% Conv.[b]	1[c]	2[c]	3[c]	4[c]	5[c]	6[c]	7[c]
11		1.5	1.1	47.8	93.0	0.3	1.1	26.2	15.7	0.6	3.7	44.4
12		1.5	1.0	49.8	98.0	0.3	1.6	25.1	14.0	1.0	4.8	47.6

[a] Selectivity for 7. [b] Percentage conversions to the shown products. [c] Percentages of the respective product relative to the amount of added 1,3-butadiene. NA = not applicable. [1,3-butadiene] = 0.23 M. All values given are an average from two identical runs.

and rate-determining features for various, partially quite small structural modifications of electronically identical motifs: e.g., of our bisphosphites. We believe, however, that the small $\Delta\Delta G^{\ddagger}$ values computed by DFT and reflected by the formation of adipic aldehyde in our actual experiments is indicative of a good chance for ligand design toward improved 1,4-bishydroformylation selectivity.

Importantly, the selectivity for adipic aldehyde has been reproducibly improved to around 50%. Work in our laboratories is now directed toward rationally modifying our TTP-type ligands on the basis of systematic synthetic ligand structure variations, guided by experimental ligand and Rh complex structure determinations, in situ spectroscopy, mechanistic studies, Ir model chemistry, and DFT calculations. This combined approach will be applied for the development of structural ligand modifications, which will hopefully increase the selectivity for a catalytic 1,3-butadiene to adipic aldehyde conversion to a range where a practical application becomes feasible.

EXPERIMENTAL SECTION

General Experimental Details. Unless otherwise noted, all reactions and manipulations were carried out under an Ar atmosphere using standard Schlenk and high-vacuum-line techniques or in a Braun inert-atmosphere glovebox (Ar) at ambient temperature. Glassware was dried for a minimum of 8 h at 150 °C. Unless otherwise noted, all NMR spectra were obtained at ambient temperature using a Bruker DPX-200 MHz spectrometer. All NMR chemical shifts are reported as δ in parts per million (ppm). ^{1}H NMR spectra were referenced to residual protiated solvent, and chemical shifts are reported in parts per million downfield from tetramethylsilane. ^{31}P{^{1}H} NMR spectra are reported relative to trimethyl phosphate as the external standard. ^{13}C{^{1}H} NMR spectra were referenced to the solvent. Gas chromatographic analysis was performed on an Agilent Technologies 6890N Network GC System equipped with a 30 m BGB-5 column (5% diphenylpolysiloxane, 95% dimethylpolysiloxane). The He flow rate was kept at 2.0 mL/min. The column temperature was initially held at 40 °C for 1 min, then ramped at 4 °C/min to 90 °C, followed by an immediate temperature ramp of 30 °C/min to 200 °C, and held at this temperature for 5 min. Typical retention times (min) are as follows: 1.99 (1,3-butadiene), 2.02 ((*E*/*Z*)-2-butene), 2.82 (2-methylbut-3-enal), 3.06 (2-methylbutyraldehyde), 3.28 (4-pentenal), 3.42 (pentanal), 3.49 (*trans*-3-pentenal), 3.58 (*cis*-3-pentenal), 4.30 (*trans*-2-pentenal), 6.05 (4-vinylcyclohexene), 6.27 (cyclopentanecarbaldehyde), 7.58 (cyclopent-1-enecarbaldehyde), 7.96 (nonane), 9.01 (2-ethylbutanedial), 9.49 (2-methylpentanedial), 11.44 (adipic aldehyde). Peak assignments were confirmed with samples of commercially available or independently synthesized compounds. GC calibration curves were constructed for all of the compounds except for 1,3-butadiene and (*E*/*Z*)-2-butene. The amounts reported are estimates made using the effective carbon numbers (ECN) of 3.8 for 1,3-butadiene and 3.9 for (*E*/*Z*)-2-butene, as described in the literature.[51] Hydroformylation reactions were conducted using a Premex Reactor or a ChemSpeed Accelerator SLT 106 high-throughput robot system.

Materials. Unless otherwise noted, reagents were purchased from commercial suppliers and used without further purification. Toluene, hexane, THF, and methylene chloride were dried using an MBraun SPS-800 drying machine and degassed by either three freeze−pump−thaw cycles or by sparging with Ar for a minimum of 15 min. Deuterated solvents were purchased from Deutero GmbH or Aldrich. CD_2Cl_2 was vacuum-transferred from CaH_2 after stirring for at least 8 h at room temperature and was degassed by three freeze−pump−thaw cycles. The bisphosphine ligands from Table 5 were a generous gift from Dr. Thomas Schnetz[52] (entries 2−4), and the bisphosphite ligands (entries 5−7 and 9−12) were synthesized and characterized according to the thesis[24] of Dr. Tobias Rosendahl (see the Supporting Information), as was ligand **13**, used in Tables 1−4 and as entry 8 in Table 5.

Representative Procedure for the Catalytic Hydroformylation of 1,3-Butadiene Using Ligand 13. $(CO)_2Rh(acac)$ (10.1 mg, 0.0391 mmol) and **13** (32.9 mg, 0.0460 mmol) were added to an autoclave followed by 15 mL of toluene in the glovebox. The autoclave was sealed, removed from the glovebox, and charged to 30 bar of syngas (1/1 H_2/CO). The solution was stirred at 1000 rpm while being heated to 90 °C. Once the solution reached 90 °C, the autoclave was pressurized to 40 bar of syngas and the mixture stirred at this temperature and pressure for 1 h prior to the addition of 1,3-butadiene. After catalyst preformation, the temperature and pressure were adjusted to the desired values. In this experiment, the temperature was increased to 110 °C and the pressure vented to 40 bar of syngas. 1,3-Butadiene (1.00 M in toluene, 5.0 mL, 5.0 mmol) was added to a Swagelok 304 L SS/DOT-3E 1800 (ordering number 304 L-HDF2-40) double-ended cylinder in the glovebox, and the cylinder was sealed under Ar. The cylinder was charged to 69 bar of Ar,

attached to the autoclave, and added with this overpressure. An overpressure of 20−30 bar of Ar is typically used to add 1,3-butadiene to the reaction mixture. After the mixture was stirred for 1 h, an aliquot was removed for immediate GC analysis using the method described below. For reactions run at 90 °C, the reaction mixtures were typically stirred for 5 h.

Representative Procedure for the Catalytic Hydroformylation of 1,3-Butadiene under Variable Partial Pressures of H_2 and CO. $(CO)_2Rh(acac)$ (10.7 mg, 0.0415 mmol) and **13** (38.8 mg, 0.0543 mmol) were added to an autoclave followed by 15 mL of toluene in the glovebox. The autoclave was sealed, removed from the glovebox, and charged to 9 bar of CO. The solution was stirred at 1000 rpm while being heated to 110 °C. Once the solution reached 110 °C, the CO pressure was 11 bar and stirring was stopped. Syngas (40 bar, 1/1 H_2/CO) was charged to the autoclave, resulting in a total pressure of 51 bar. Stirring was commenced, and the catalyst was allowed to preform for 1 h. 1,3-Butadiene (0.94 M in toluene, 5.0 mL, 4.7 mmol) was added to a Swagelok 304 L SS/DOT-3E 1800 double-ended cylinder in the glovebox, and the cylinder was sealed under Ar. The cylinder was charged to 68 bar of Ar, attached to the autoclave, and added with this overpressure. After the mixture was stirred for 1 h, an aliquot was removed for immediate GC analysis using the method described below.

Procedure for Quantifying the Reaction Products from the Hydroformylation of 1,3-Butadiene. An aliquot (0.900 mL) from the reaction mixture was removed and added to a 1.00 mL volumetric flask followed by nonane (5.00 μL, 0.0280 mmol) and diluted to 1.00 mL with toluene. The sample was then analyzed by GC and the concentration determined from the calibration curve.

General Method for the High-Throughput Screening Using the Chemspeed Accelerator SLT 106. Toluene stock solutions of $(CO)_2Rh(acac)$ (5.8 mM), ligand (8.8−30 mM), and a mixture of 1,3-butadiene (0.71 M) and nonane (89 mM, internal standard) were prepared. The Chemspeed Accelerator programmable robot system then combined 2.0 mL of the rhodium stock solution and 2.0 mL of the ligand stock solution together. Catalyst preformation was achieved by heating at 90 °C under 40 bar of syngas for 1 h. After catalyst preformation, the solution was cooled to −10 °C and 2.0 mL of the 1,3-butadiene/nonane stock solution was added. The reaction mixture was heated to 110 °C under 40 bar of syngas while being vortexed at 800 rpm for 2 h. Afterward, the reaction mixtures were cooled to −10 °C, vented, and kept at −10 °C overnight. The following morning the samples were analyzed by GC using the GC method described above with calibrated GC response factors for each of the products (relative to nonane). The reactions were run in duplicate, and the yields reported are the average from these two runs.

Procedure for Preparing the 1,3-Butadiene Stock Solution. Dry toluene (172.31 g, 199 mL) was added to a premassed, oven-dried 250 mL Schlenk flask. 1,3-Butadiene was then bubbled through the toluene solution for 20 min. The Schlenk flask was remassed, and it was determined that ca. 11 g of 1,3-butadiene was added. The absolute concentration of 1,3-butadiene was determined by syringing 0.600 mL of the 1,3-butadiene stock solution into an NMR tube and adding dichloromethane (32.8 mg, 0.386 mmol), followed by ∼0.3 mL of C_6D_6. A ^1H NMR spectrum was acquired three times (number of scans 1, dummy scans 0, delay 60 s), and the average of these values was used as the concentration for the 1,3-butadiene solution (0.94 ± 0.03 M). The concentration of the 1,3-butadiene stock solution was periodically monitored in the same manner, and the stock solution was stored in the freezer at −30 °C.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Text giving details of the synthesis and characterization data of compounds **3**−**6**, **8**, and **12** and bisphosphite **13** (entry 8 in Table 5), Table S1, giving a more detailed version of Table 5, Figure S1, showing the possible aldehyde products resulting from the hydroformylation of 1,3-butadiene, figures giving calibration curves for compounds **1**−**10** and **12**, and text giving synthetic procedures for the bisphosphite ligands (entries 5−7 and 9−12 in Table 5). This material is available free of charge via the Internet at http://pubs.acs.org.

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