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Highly Regioselective Isomerization–Hydroaminomethylation of Internal Olefins Catalyzed by Rh Complex with Tetrabi-Type Phosphorus Ligands

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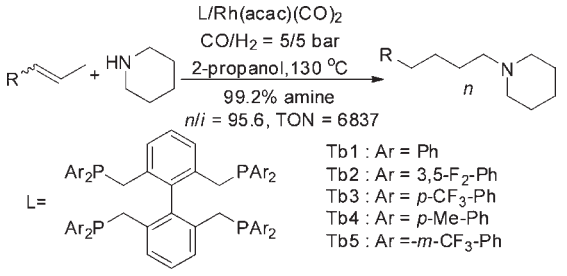
ABSTRACT



A highly regioselective isomerization–hydroaminomethylation of internal olefins has been developed. A 95.3% amine selectivity and 36.2 *n*/*i* ratio were obtained for 2-octene with a Tetrabi ligand and Rh(acac)$(CO)_2$, and a TON of linear amine was achieved of 6837 with a 39.1 *n*/*i* ratio of amine. The *m*-CF_3-Ph substituted ligand was the best of the applied Tetrabi-type phosphorus ligands for different internal olefins, as up to a 99.2% amine selectivity and 95.6 *n*/*i* ratio were obtained for 2-pentene.

Linear aliphatic amines are important intermediates and building blocks for various pharmaceuticals, agrochemicals, commodities, and fine chemicals in the bulk chemical and pharmaceutical industries.[1] Catalytic syntheses of these amines from readily available olefins are of particular interest in organic chemistry as they offer potential advantages over conventional methods of amine synthesis.[2] One of the most promising catalytic syntheses of amines in terms of atom-efficiency, selectivity, and applicability is the hydroaminomethylation[3] of olefins. This effective tandem reaction consists of an initial hydroformylation to aldehydes and subsequent reductive amination.[4] Since its discovery by Reppe in 1949,[5] great progress has been achieved for regioselective hydroaminomethylation of terminal olefins by Eilbracht[6] and Beller.[7] However, the more challenging

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isomerization–hydroaminomethylation of internal olefins, which are substantially cheaper and more easily available feedstock than the pure terminal olefins in the chemical industry, still needs to be improved. Some elegant ligands for isomerization–hydroaminomethylation of internal olefins include Iphos,[8] Naphos, and Xantphos-type ligands,[9] and the best one is Xantphenoxaphos,[9] reported by Beller's group with a 24 *n*/*i* ratio[10] of amine for 2-pentene and piperidine and a 15.7 *n*/*i* ratio of amine for 2-octene and morpholine. Generally, the reactivity of long chain olefins is lower than the low molecular weight one; thus it is still a challenging task to achieve amines with high regioselectivity from long chain internal olefins.

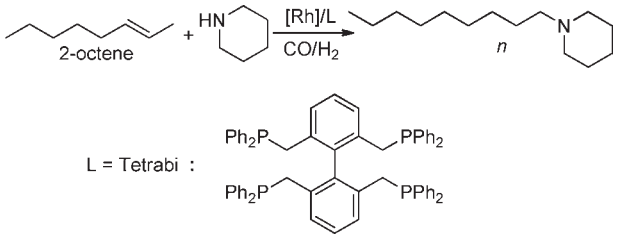
Recently, we have reported the synthesis and application of Tetrabi[11]-type phosphorus ligands, which show excellent regioselectivity for the hydroformylation of terminal olefins[11] and internal olefins[12] at high temperature. The Tetrabi ligand has already been applied successfully in the hydroaminomethylation of terminal olefins with very excellent regioselectivity and activity.[13] This prompted us to assess these Tetrabi-type ligands further in the isomerization–hydroaminomethylation of internal olefins, especially long chain one. Herein, we wish to disclose our recent studies on the isomerization–hydroaminomethylation of internal olefins with unprecedented high linear amine selectivity.

Table 1. Hydroaminomethylation of 2-Octene and Piperidine under Different Reaction Conditions with Tetrabi Ligand and $Rh(acac)(CO)_2$[a]

entry	solvent	temp (°C)	*t* (h)	L/Rh	con. (%)	amine sel.[b]	linear sel.[b]		TON[d]
							n/*i*	*n*-amine (%)[c]	
1	Pr/Et=2:1	125	28	4	99	91.1	16.5	94.3	850
2	Et/To=2:1	125	28	4	90	84.1	16.6	94.3	714
3	Me/To=1:1	125	28	4	99	81.6	28.8	96.6	780
4	Pr/Me=2:1	125	28	4	99	94.6	12.1	92.4	865
5	Pr/Me=1:1	125	28	4	99	92.2	13.4	93.1	850
6	Pr/Me=1:2	125	28	4	99	89.3	12.6	92.6	819
7	EtOH	125	28	4	99	90.2	11.7	92.1	822
8	2-PrOH	125	28	4	99	91.4	27.2	96.5	873
9	2-PrOH	125	28	2	99	90.7	25.9	96.3	856
10	2-PrOH	125	28	6	99	91.8	27.8	96.5	877
11	2-PrOH	130	28	4	99	93.6	29.2	96.7	896
12	2-PrOH	130	36	4	99	95.3	36.2	97.3	918
13	2-PrOH	135	36	4	99	95.1	28.2	96.6	909

[a] Reaction conditions: 1 μmol of $Rh(acac)(CO)_2$, ligand = Tetrabi, 1 mmol of 2-octene, 1 mmol of piperidine, 3 mL of solvent, CO/H_2 = 5/5 bar. Me = methanol, Et = ethanol, Pr = 2-propanol, To = toluene. [b] Selectivity and *n*/*i* ratio were determined by GC analysis using 2-methoxyethyl ether (0.1 mL) as an internal standard, the average value of three repeated runs, and two injections per run. [c] Percentage of linear amine in all amines. [d] Turnover number was determined on the basis of GC; error was estimated at < 20.

Scheme 1. Isomerization–Hydroaminomethylation of 2-Octene with Piperidine



Long chain internal olefin 2-octene was chosen as the standard substrate for this reaction, and the reaction conditions of terminal olefin 1-octene have been partially applied for the isomerization–hydroaminomethylation of 2-octene and piperidine (Scheme 1).[13] First, we identified the optimal pressure for our catalyst system of Tetrabi ligand and $Rh(acac)(CO)_2$, and the pressure dependency of this catalytic system was pronounced. It was found that the pressure was critical for this reaction; only a 5/5 bar H_2/CO pressure provided high conversion and linear amine selectivity as higher H_2 or CO pressure led to lower regioselectivity or amine selectivity. This was probably resulted from the pressure dependency of the catalytic system to the reaction step of isomerization–hydroformylation. As shown in Table 1, representative solvents were introduced to achieve better amine selectivity and an *n*/*i* ratio. Mixtures of 2-propanol and ethanol, ethanol and toluene, methanol and toluene, which supported an excellent *n*/*i* ratio of amine for terminal olefins,[14] were applied. Although full conversion was obtained, the amine selectivity and *n*/*i* ratio were not very high with these solvents (Table 1, entries 1–3). Methanol was used to replace ethanol for the mixture of 2-propanol and ethanol to obtain higher amine selectivity; unfortunately, the *n*/*i* ratio of amine could not be improved at all (Table 1, entries 4–6). In this way, single polar solvents ethanol and 2-propanol were employed, and the results showed that 2-propanol gave a 91.4% amine selectivity and 27.2 *n*/*i* ratio at the same time (Table 1, entry 8), which was the best solvent observed. Different Rh complex loadings were also investigated. Although there was minimal effect on the catalytic activity, the regioselectivity was improved to some extent (a 27.8 *n*/*i* ratio) while the L/Rh ratio[14] was changed from 2 to 6 (Table 1, entries 8–10). Then, the reaction temperature and time were increased. An increase of the temperature to 130 °C led to better activity and regioselectivity, and a 93.6% amine

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(14) L/Rh ratio = ligand to rhodium precursor ratio.

selectivity with a 29.2 *n*/*i* ratio was achieved (Table 1, entry 11). Increasing the reaction time to 36 h at 130 °C gave an apparent improvement in amine selectivity (95.3%) and *n*/*i* ratio (36.2) (Table 1, entry 12). Further increase of the temperature to 135 °C decreased the amine selectivity and *n*/*i* ratio slightly while other byproducts were produced (Table 1, entry 13). Hence, the optimized reaction conditions were as follows: H_2/CO = 5/5 bar, 2-propanol, S/L/Rh[15] = 1000/4/1, 130 °C, and 36 h; the highest turnover number of linear amine was achieved at 918 with a 95.3% amine selectivity and 36.2 *n*/*i* ratio at these conditions (see details in the Supporting Information).

Table 2. Turnover Number and Ligand Loading Test of Tetrabi[a]

entry	S/Rh	L/Rh	*t* (h)	con. (%)	amine sel.[b]	linear sel.[b]		TON[d]
						n/*i*	*n*-amine (%)[c]	
1	1000	4	60	99	95.2	32.3	97.0	914
2	2000	4	60	99	92.1	52.8	98.1	1789
3	5000	4	60	70	83.6	56.4	98.3	2876
4	8000	4	60	60	73.3	48.7	98.0	3448
5	10000	4	60	55	67.2	39.8	97.5	3604
6	5000	8	60	85	85.5	56.8	98.3	3572
7	5000	12	60	95	89.4	60.1	98.4	4179
8	8000	8	60	80	80.3	40.6	97.6	5016
9	8000	12	60	90	86.7	43.7	97.8	6105
10	10000	8	60	75	74.8	38.4	97.5	5470
11	10000	12	60	85	82.5	39.1	97.5	6837

[a] Reaction conditions: 1 mmol of 2-octene, 1 mmol of piperidine, 3 mL of 2-propanol, CO/H_2 = 5/5 bar, 130 °C. [b] Selectivity and *n*/*i* ratio were determined by GC analysis using 2-methoxyethyl ether (0.1 mL) as an internal standard, the average value of three repeated runs, and two injections per run. [c] Percentage of linear amine in all amines. [d] Turnover number was determined on the basis of GC; error was estimated at < 200.

Based on the optimized reaction conditions, we studied the turnover number and ligand loading of the Tetrabi ligand for 2-octene. The S/Rh ratio[16] was increased from 1000 to 10 000 while the L/Rh ratio was kept as 4, and a longer time was needed for the complete conversion of 2-octene. Although the *n*/*i* ratio of amine was increased, the conversion was decreased subsequently to 55% and the enamines could not be hydrogenated smoothly at a 10 000 S/Rh ratio (Table 2, entry 5). At a 2000 S/Rh ratio, the *n*/*i* ratio of amine was increased to 52.8 with a 92.1% amine selectivity (Table 2, entry 2). At ratios of 5000, 8000, and 10 000, the *n*/*i* ratio of amine was kept at a high level while the branched and linear enamines remained as main byproducts (Table 2, entries 3–5). The reason for the existence of the enamines might be the lower hydrogenation activity of the Tetrabi catalyst system for enamines at such a low ligand loading. To obtain excellent conversion and hydrogenation of enamines, the L/Rh ratio was increased to 8 and 12 at S/Rh ratio of 5000, 8000, and 10 000. As expected, the conversion of 2-octene was improved significantly while the amine selectivity was enhanced comparatively with a higher *n*/*i* ratio (Table 2, entries 7, 9, 11; see details in the Supporting Information). Therefore, the best TON[17] of linear amine was achieved with the S/L/Rh ratio of 10000/12/1, and it was 6837 according to $Rh(acac)(CO)_2$ with an 82.5% amine selectivity and a 39.1 *n*/*i* ratio (Table 2, entry 11). To the best of our knowledge, such a high TON of linear amine has never been achieved for long chain internal olefin 2-octene.

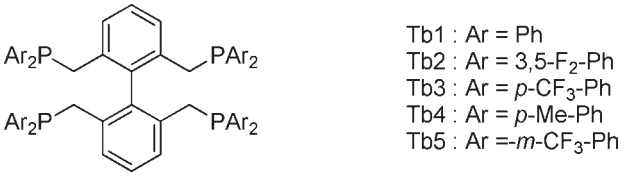

Figure 1. Structures of Applied Tetrabi-Type Ligands.

Table 3. Hydroaminomethylation of Different Internal Olefins with Tetrabi-Type Phosphorus Ligands[a]

entry	internal olefin	ligand	con. (%)	amine sel.[b]	linear sel.[b]		TON[d]
					n/*i*	*n*-amine (%)[c]	
1	2-pentene	Tb1	99	97.5	48.5	98.0	946
2	2-pentene	Tb2	99	50.3	197.8	99.5	495
3	2-pentene	Tb3	99	26.6	123.9	99.2	259
4	2-pentene	Tb4	99	>99	28.5	96.6	950
5	2-pentene	Tb5	99	99.2	95.6	99.0	972
6	2-hexene	Tb1	99	96.1	42,3	97.7	930
7	2-hexene	Tb2	99	61.8	168.4	99.4	608
8	2-hexene	Tb3	99	46.7	110.6	99.1	458
9	2-hexene	Tb4	99	>99	19.8	95.2	933
10	2-hexene	Tb5	99	98.8	89.7	98.9	967
11	2-octene	Tb1	99	94.9	33.8	97.1	912
12	2-octene	Tb2	99	66.6	146.8	99.3	655
13	2-octene	Tb3	99	52.9	92.4	99.0	518
14	2-octene	Tb4	99	>99	14.8	93.7	918
15	2-octene	Tb5	99	98.2	86.8	98.9	961

[a] Reaction conditions: 1 μmol of $Rh(acac)(CO)_2$, 4 μmol of ligand, 1 mmol of internal olefin, 1 mmol of piperidine, 3 mL of 2-propanol, CO/H_2 = 5/5 bar, 130 °C, 36 h. [b] Selectivity and *n*/*i* ratio were determined by GC analysis using 2-methoxyethyl ether (0.1 mL) as an internal standard, the average value of three repeated runs, and two injections per run. [c] Percentage of linear amine in all amines. [d] Turnover number was determined on the basis of GC; error is estimated at < 20.

Then, with the ligands Tb1–Tb5 at hand (Figure 1), isomerization–hydroaminomethylation of different internal olefins (2-pentene, 2-hexene and 2-octene) was conducted under the following reaction conditions: 130 °C, CO/H_2 = 5/5 bar, S/L/Rh ratio = 1000/4/1 (Table 3). It was found that the introduction of substituents at the diphenylphosphane moiety of Tb1 affected both the

(15) S = substrate, L = ligand, Rh = $Rh(acac)(CO)_2$.
(16) S/Rh ratio = substrate to rhodium precursor ratio.
(17) TON = turnover number, which refers to the number of moles of linear amine that a mole of catalyst can convert from the olefins before becoming inactivated.

regioselectivity of the amines and the activity of the catalytic system. In all cases, the catalytic system with ligands Tb2, Tb3, and Tb5, which contained electron-withdrawing substituents, showed higher regioselectivity than with ligand Tb4, which contained an electron-donating group. Nevertheless, the conversion and amine selectivity with these electron-withdrawing substituted ligands (Tb2, Tb3, and Tb5) were lower than with the electron-donating one (Tb4). Ligand Tb2 afforded the best *n*/*i* ratio (197.8) for 2-pentene although the conversion and amine selectivity were lower (Table 3, entry 2). The best conversion (>99%) and amine selectivity (>99%) were obtained with ligand Tb4 although the *n*/*i* ratio of amine was only 28.5 for 2-pentene (Table 3, entry 4). The position of the substituent also exerted some influence on the chemoselectivity of amine. Ligand Tb5, containing a CF_3 substituent at the *meta*-position of the diphenylphosphane moiety, gave a higher amine selectivity for 2-pentene than the corresponding ligand Tb3 with the same substituent at the *para*-position (Table 3, entries 3, 5). In consideration of conversion, amine selectivity, and linear selectivity, ligand Tb5 was found to be the best of the applied Tetrabi-type phosphorus ligands with a 99.2% amine selectivity and 95.6 *n*/*i* ratio for 2-pentene (Table 3, entry 5), a 98.8% amine selectivity and 89.7 *n*/*i* ratio for 2-hexene (Table 3, entry 10), and a 98.2% amine selectivity and 86.8 *n*/*i* ratio for 2-octene (Table 3, entry 15). Promisingly, this ligand could be applied in the further study of the isomerization–hydroaminomethylation of other functional olefins.

In conclusion, our Tetrabi-type phosphorus ligands were successfully applied in the one-pot synthesis of amines by isomerization–hydroaminomethylation of internal olefins. Key to the success was the use of Tetrabi-type phosphorus ligands together with $Rh(acac)(CO)_2$. Remarkably, 95.3% amine and a 36.2 *n*/*i* ratio were obtained for 2-octene and piperidine with the Tetrabi ligand at an S/L/Rh ratio of 1000/4/1, and the TON could reach 6837 with an 82.5% amine selectivity and a 39.1 *n*/*i* ratio at an S/L/Rh ratio of 10 000/12/1. The *meta*-CF_3-Ph substituted ligand was found to be the best ligand at hand with up to a 99.2% amine selectivity and 95.6 *n*/*i* ratio for 2-pentene. These ligands afforded much better regioselectivity than the other ligands applied in the isomerization–hydroaminomethylation of internal olefins, and our results were among the best reported results in the literature. Thus, this ligand system would probably show a great expectation for the regioselective isomerization–hydroaminomethylation of more challenging functional olefins.

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Supporting Information Available. General procedure for hydroaminomethylation. Determination of the *n*/*i* ratio of amine products, representative GC, NMR data and spectrum. This material is available free of charge via the Internet at http://pubs.acs.org.