Synthesis of New Bulky Isocyanide Ligands and Their Use for Rh-catalyzed Hydrosilylation

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Bulky isocyanide ligands having *meta*-terphenyl backbone were developed. Their usefulness as a supporting ligand in catalysis was illustrated by the application to the rhodium-catalyzed hydrosilylation of cyclohexanone. The combined effect of the high ligand affinity to the rhodium atom and the ligand bulkiness to facilitate the formation of a catalytically active, monoligated isocyanide–rhodium species was proposed.

Isocyanides are isoelectronic with carbon monoxide and coordinate to various transition metals at the terminal isocyano carbon atom.[1] In general, both isocyanides and carbon monoxide are the ligands of extreme compactness. Unlike CO, however, the electronic and steric properties of the isocyanides are tunable by the substituent at the nitrogen atom. In fact, many different isocyanides exist and have been used as a ligand of transition-metal complexes with interesting properties in various aspects. One can also enjoy diverse reactivities of the isocyanides for the applications to organic and organometallic chemistries.[2,3] While cases are rare, some isocyanides having a bulky N-substituent were used as a supporting ligand of a transition-metal catalyst.[4–7] For example, Nile et al. and Yamazaki et al. used 2,6-disubstituted phenyl isocyanides in the rhodium- and platinum-catalyzed hydrosilylations.[4] Ito and co-workers developed the bis-silylations of carbon–carbon unsaturated bonds and related reactions by the use of *tert*-alkyl isocyanide–palladium complexes as a catalyst precursor.[5] Recently, Nagashima et al. reported that a nickel complex of 2-biphenyl isocyanide is highly active for the ethylene polymerization.[6]

We report here the synthesis of new bulky isocyanides (**1a**–**1d**, Chart 1) having a *meta*-terphenyl backbone and their use in the Rh-catalyzed hydrosilylation of cyclohexanone. The bulky isocyanide ligands markedly accelerated the reaction as compared with the effect of the conventional isocyanide and phosphine ligands, demonstrating the usefulness of the designed isocyanides as a supporting ligand in transition-metal catalysis.

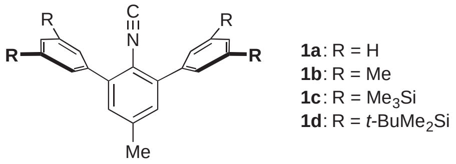
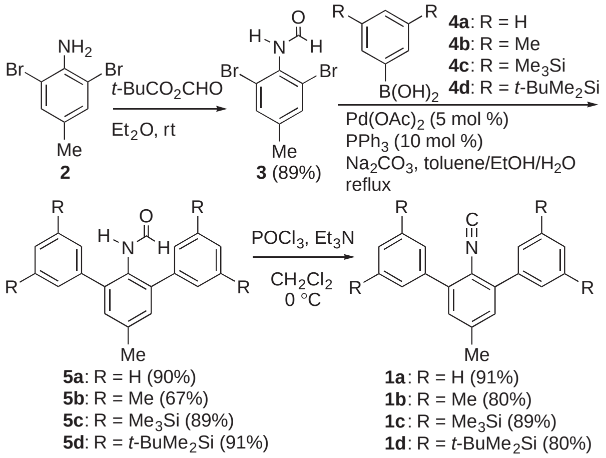


Chart 1.

Synthesis of the terphenyl isocyanides (**1a**–**1d**) is straightforward and easy (Scheme 1). It starts with N-formylation of 2,6-dibromotoluidine (**2**) to give *N*-formyl-2,6-dibromotoluidine (**3**) (89%). Suzuki–Miyaura coupling of dibromoarene **3** with 3,5-disubstituted phenylboronic acid (**4a**–**4d**) in the presence of 5 mol % of $Pd(OAc)_2$ and 10 mol % of PPh_3 gave *N*-terphenyl formamides **5a**–**5d** in 67–91% yields. Treatment of **5a**–**5d** with $POCl_3/Et_3N$ resulted in clear conversion to the desired isocyanides (**1a**–**1d**) in high yields (80–91%).[8] The new isocyanides are odorless and colorless crystals, and stable against oxidation and hydrolytic decomposition in the air. Therefore, they are easy to handle. The space-filling representation of the optimized structures (MMFF94, MacSpartan Pro 1.0.4.) of **1a** and **1c** (Figure 1) visualizes that the *meta*-terphenyl backbone is an ideal platform to create a concave steric environment around the isocyano carbon atom.



Scheme 1. Synthesis of substituted *m*-terphenyl isocyanides.

The Rh–isocyanide complexes were examined for catalytic activity in the hydrosilylation of cyclohexanone with dimethylphenylsilane.[8] Results of the hydrosilylation experiments carried out in benzene at rt in the presence of 1 mol % each of $[Rh(cod)_2]BF_4$ and the isocyanide ligand (**1a**–**1h**) are summarized in Table 1. Results with conventional phosphine ligands (PPh_3 and dppp) are also shown for comparison. The acceleration effect with each ligand was evaluated by the GC yield of the corresponding silyl ether after 1 h. The acceleration with isocyanides varied considerably depending on the ligand bulkiness. In particular, the Me_3Si-substituted terphenyl isocyanide (**1c**) exhibited the most significant effect, giving the silyl ether product in 97% yield (Table 1, Entry 4). The *t*-$BuMe_2Si$-substituted isocyanide (**1d**) showed slightly decreased acceleration effect (79% yield, Entry 5), suggesting that the bulkiness is too much. The terphenyl isocyanides (**1a** and **1b**) with smaller steric demand

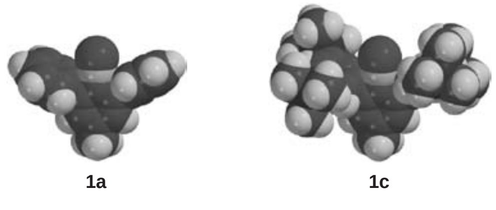
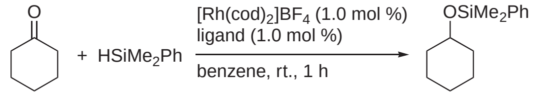


Figure 1. Space-filling models of isocyanides **1a** and **1c**.

Table 1. Rh-catalyzed hydrosilylation with various isocyanide and phosphine ligands[a]



Entry	Ligand	Yield/%[b]
1	—	13
2	**1a**	36 (85, 4 h)
3	**1b**	22 (89, 4 h)
4	**1c**	97
5	**1d**	79
6	**1e**	7
7	**1f**	14 (32, 4 *h*)
8	**1g**	39 (61, 4 h)
9	**1h**	36
10	PPh_3	34–71 (46–81, 3 h)
11	dppp	trace

[a]Conditions: ligand (0.015 mmol), $[Rh(cod)_2]BF_4$ (0.015 mmol), cyclohexanone (1.5 mmol), and Me_2PhSiH (1.8 mmol) in benzene (1.5 mL) at rt (21–24 °C). [b]GC yield of the silyl ether.

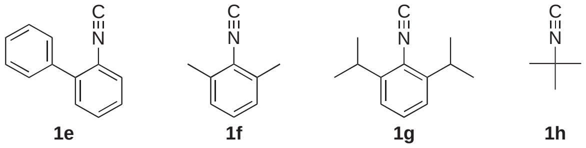


Chart 2.

than **1c** were much less effective (Entries 2 and 3). 2-Biphenyl isocyanide (**1e**)[6] and 2,6-xylyl isocyanide (**1f**) (Chart 2)[4] showed no acceleration effect, compared with the rate without added ligand (Entries 6 and 7). 2,6-Diisopropylphenyl isocyanide (**1g**) is comparable with the non-substituted terphenyl isocyanide (**1a**) in the acceleration effect (Entry 8),[4] suggesting that the steric effect of the *i*-Pr substituents at the positions ortho to the isocyano group is only comparable with the Ph substituents in simple terphenyl isocyanide **1a**. *tert*-Butyl isocyanide (**1h**)[5,7] gave a similar result (Entry 9). The yields with the small isocyanides (**1a**, **1b**, **1f**, and **1g**) increased reasonably by prolonging reaction time to 4 h (Entries 2, 3, 7, and 8), indicating that the low yields is responsible for low catalytic activity rather than catalyst deactivation. These results strongly suggest that the accelerating effect with **1c** and **1d** is due to their concave steric feature.[9]

Although the reaction with PPh_3 gave a good yield at 1 h, it suffered from poor reproducibility and substantial catalyst deactivation over time (Entry 10). Bidentate phosphine ligand dppp inhibited the reaction almost completely (Entry 11).

Next, correlations between the catalytic activities and the Rh:**1c** ratio were examined. The hydrosilylation with $[Rh(cod)_2]BF_4$ and **1c** in 1:1 ratio proceeded with the highest rate among the reactions carried out with five different Rh:**1c** ratios ranging from 1:0–1:3 (13% at 1 h (Rh:**1c** = 1:0), 71% (1:0.5), 97% (1:1), 80% (1:2), 55% (1:3)). According to these results, we postulate that the active species is a 1:1 Rh–isocyanide complex, and that the coordination of the second molecule of isocyanide inhibits the catalysis.[10,11]

In conclusion, we have developed the new bulky isocyanide ligands having a *meta*-terphenyl backbone. Their usefulness as a supporting ligand in the catalysis was illustrated by the application to the rhodium-catalyzed hydrosilylation. Efforts aimed at further developing efficient transition metal-catalyzed reactions influenced by the isocyanide ligands are ongoing in our laboratory.

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8 General procedure for the Rh(I)-catalyzed hydrosilylation: $[Rh(cod)_2]BF_4$ (6.1 mg, 0.015 mmol) and an isocyanide (0.015–0.045 mmol) were placed in a reaction tube. The tube was evacuated and backfilled with argon. After addition of anhydrous, degassed benzene (1.5 mL), the mixture was stirred at room temperature for 1 h. Cyclohexanone (147 mg, 1.5 mmol), 1,4-diisopropylbenzene (66.9 mg, 0.412 mmol, as an internal standard for GC analysis), and dimethylphenylsilane (245 mg, 1.8 mmol) were then added. The yield of product was determined by GC.

9 Similar rate acceleration effect was observed when $[RhCl(C_2H_4)_2]_2$ was used as a catalyst precursor (yields at 3h, **1a**: 48%, **1c**: 97%, **1g**: 15%, PPh_3: 24%).

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