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IMIDAZOLE AND IMIDAZOLINE DERIVATIVES AS *N*-DONOR LIGANDS FOR NICKEL-CATALYZED KUMADA-TAMAO-CORRIU COUPLING

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Abstract – Imidazole and imidazoline (dihydroimidazole) derivatives can serve as simple and efficient ligands for the nickel-catalyzed Kumada-Tamao-Corriu coupling reaction. Among the imidazole and imidazoline derivatives in our investigations, the 2-phenyllimidazoline–nickel (II) chloride complex exhibited the highest catalytic activity.

In 1972, Kumada-Tamao and Corriu independly reported Ni-catalyzed cross coupling reaction between aryl halides and Grignard reagents. Kumada and Tamao used $NiCl_2$(dppe) (dppe = 1,2-bis(diphenylphosphino)ethane)[1] and Corriu used $Ni(acac)_2$[2] as a catalyst, respectively. After these two reports, several reactions using palladium catalysts combined with Grignard reagents or organolithium reagents were also explored.[3] In most of these reactions, phosphine ligands[4] have been employed, though recently, carbene type ligands have also been examined.[5] On the other hand, we have interest in cross-coupling reactions catalyzed by nitrogen-based ligand metal complexes, because nitrogen-based ligands are generally easier to handle. For examples, we reported 2-phenylimidazole–$PdCl_2$ and 2-phenylimidazoline–$PdCl_2$ complex catalyzed Mizoroki-Heck and Suzuki-Miyaura coupling reactions.[6] In these reactions, 2-phenylimidazoline–$PdCl_2$ complex was found to exhibit higher reactivity than 2-phenylimidazole–$PdCl_2$ complex. Furthermore, we also reported Ni and Cu-catalyzed Suzuki-Miyaura coupling reaction using 2-(4,5-dihydro-1*H*-imidazo-2-yl)phenol as a versatile phosphine-free ligand.[7] Here, we will report Kumada-Tamao-Corriu coupling between substituted haloarenes and phenylmagnesium chloride catalyzed by $NiCl_2$ and a nitrogeneous ligand system.[8]

We first examined the reaction of 4-bromotoluene (**1**) with phenylmagnesium chloride in the presence of

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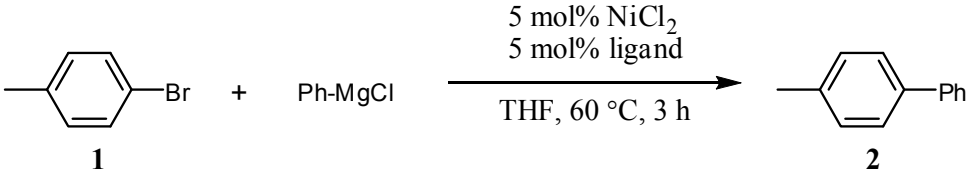
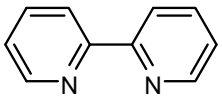
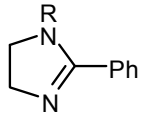
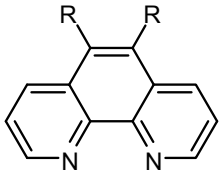
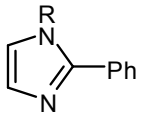
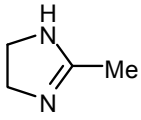
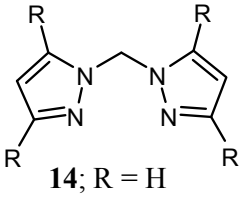
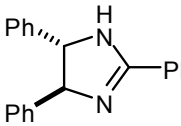
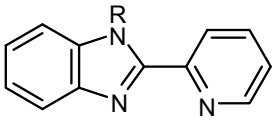
This paper is dedicated to Prof. Dr. Ei-ichi Negishi on the occasion of his 77th birthday.

5 mol% of nickel precursors such as $NiCl_2$ (51%), $NiBr_2$ (18%), $Ni(OAc)_2{\cdot}4H_2O$ (41%), $Ni(OH)_2$, (43%) and $Ni(acac)_2$ (35%). Among the nickel precursors we examined, $NiCl_2$ gave the best result (51% yield). After the choice of $NiCl_2$ as a Ni precursor, we then examined the effect of addition of imidazole and imidazoline derivatives on reactivity. Phenylmagnesium chloride (1.2 eq) was used for

Table 1. Kumada-Tamao-Corriu coupling catalyzed by $NiCl_2$ and a nitrogeneous ligand system.[a]



1 **2**

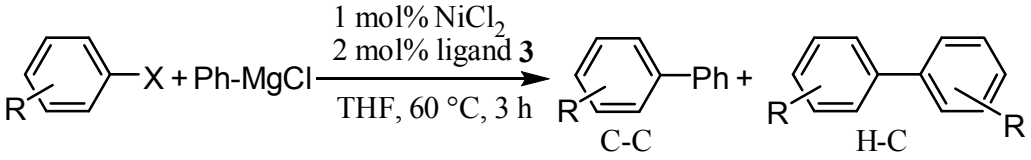
entry	ligand	yield[b]	entry	ligand	yield[b]
1	none	51% (22%)	8	 **9**	58% (5%)
					
2	**3**; R = H	81% (0%)			
3	**4**; R = Me	27% (65%)			
			9	**10**; R = H	43% (12%)
			10	**11**; R = Me	55% (1%)
			11	**12**; R = OMe	65% (3%)
				13; R = Ph	
4	**5**; R = H	51% (39%)	12		62% (0%)
5	**6**; R = Me	66% (12%)			
6	 **7**	59% (20%)			
			13	**14**; R = H	52% (0%)
			14	**15**; R = *i*-Pr	66% (8%)
			15	**16**; R = Ph	60% (6%)
7	 **8**	79% (0%)			
			16	**17**; R = H	52% (34%)
			17	**18**; Me	54% (27%)

[a] All reactions were carried out in THF at 60 °C for 3 h using 5 mol% of $NiCl_2$ and 10 mol% of the nitrogen-based ligand. For entries 8—17, 5 mol% of ligand was used. The values in the parentheses indicate the yield of recovery **1**. Phenylmagnesium chloride (1.2 eq) was used for 4-bromotoluene.[b] GC analysis using naphthalene as an internal standard.

4-bromotoluene. It was clear that addition of 2-phenylimidazoline (**3** and **8**) accelarated the reaction to give the cross coupling product **2** in 81% yield (entry 2). *N*-Methylated 2-phenyllimidazoline **4** remarkably retarded the reaction (entry 3). 2-Methylimidazoline (**7**) was not so effective compared with 2-phenylimidazoline (**3**). Remarkable rate enhancement was not observed in 2-phenylimidazole (**5**) and *N*-methylated one **6**. The bidentated ligands (**9**—**18**) also did not exhibited ligand accelaration.

After confirmation that the combination of $NiCl_2$ and 2-phenylimidazoline (**3**) was the best choice, we then examined the reaction of a variety of substituted haloarenes with phenylmagnesium chloride (1.2 eq). The results are shown in Table 2. The substituted haloarenes possessing both of electron withdrawing group and electron donating group worked as a substrate to give the desired coupling products in 60—88% yield, however, unfortunately, in all cases undesired homo-coupling products were obtained in 5—25% yield.

Table 2. Kumada-Tamao-Corriu coupling between substituted haloarenes and phenylmagnesium chloride.[a]



			yield[b,c]	
entry	R	X	C-C	H-C
1	*o*-Me	Br	78%	20%
2	*o*-Me_2	Br	50%	5%
3	*m*-Me	Br	71%	22%
4	*p*-Me	Br	81%	17%
5		I	88%	12%
6		OTf	73%	25%
7	*p*-CF_3	Br	72%	22%
8	*p*-MeO	Br	60%	20%

[a] All reactions were carried out in THF at 60 °C for 3 h using 1 mol% of $NiCl_2$ and 2 mol% of ligand **3**. Phenylmagnesium chloride (1.2 eq) was used for substituted haloarenes. [b] GC analysis using naphthalene as an internal standard. [c] C-C means cross coupling products and H-C means homo coupling products.

In summary, $NiCl_2$–2-phenylimidazoline (**3**) catalyst system worked efficiently in Kumada-Tamao-Corriu coupling to afford the cross-coupling products in good to high yield (60–88% yield), though homo-coupling products were also obtained in 5–25% yield.

EXPERIMENTAL

General: All reactions were performed under argon atmosphere using Schlenk tube techniques and freshly distilled solvents. ^{1}H and ^{13}C NMR spectra (400 and 100.6 MHz, respectively) were recorded on a JEOL JNM-LA 400 using Me_4Si as the internal standard (0 ppm). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Preparative column chromatography was carried out on Fuji Silysia BW-820MH or YMC*GEL Silica (6 nm I-40—63 um). Thin layer chromatography (TLC) was carried out on Merck 25 TLC aluminum sheets silica gel 60 F_{254}. Gass chromatographic analysis was done using Hitach G-5000 (FID ditector) and NEUTRABOND-5 column (30 m × 0.25 mm I.D., 0.25 μm film).

General procedure for coupling reaction

A mixture of $NiCl_2$ (2.6 mg, 0.02 mmol) and 2-phenylimidazoline (5.8 mg, 0.04 mmol) in THF (3.8 mL) was stirred at 50 °C for 1 h under an argon atmosphere. To this mixture was added haloarenes (2 mmol) and phenylmagnesium chloride (2 M in THF, 1.2 mL, 2.4 mmol), then it was stirred at 60 °C for 3 h. After allowing the reaction mixture to cool to room temperature, 1 M HCl was added, and products were extracted with diethyl ether. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and evaporated to afford the crude product. The distribution of the products was done by GC analysis. The condition was as follows; condition A: initial temp 100 °C, initial time 5 min, progress rate 10 °C /min, final temp 120 °C (t_R of naphthalene as internal standard, 9.27 min); condition B: initial temp 100 °C, initial time 5 min, progress rate 5 °C /min, final temp 120 °C (t_R of naphthalene as internal standard, 10.24 min).

4-Methylbiphenyl

GC (condition A): t_R, 14.61 min; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69–7.70 (d, 2H, J = 7.8 Hz), 7.60–7.62 (d, 2H, J = 8.4 Hz), 7.52–7.54 (t, J = 7.8 Hz, 2H, J = 7.8 Hz), 7.42–7.44 (t, 1H, J = 7.8 Hz), 7.35–7.36 (d, 2H, J = 7.8 Hz), 2.50 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 141.3, 138.5, 137.1, 130.9, 129.6, 128.8, 127.2, 127.1, 21.2.

3-Methylbiphenyl

GC (condition A): t_R, 14.44 min; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H), 7.17–7.30 (m, 9H). ^{13}C

NMR (100.6 MHz, $CDCl_3$): δ 21.5, 125.5, 128.0, 128.3, 128.8, 129.6, 129.7, 135.6, 138.9.

2-Methylbiphenyl

GC (condition A): t_R, 13.10 min; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (s, 3 H), 7.18–7.39 (m, 9 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.5, 125.3, 127.6, 128.2, 128.4, 128.5, 129.3, 129.7, 133.7, 136.5, 137.2;

4-(Trifluoromethyl)biphenyl

GC (condition B): t_R, 16.23 min; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.7 (bs, 4H), 7.61–7.62 (d, 2H, J = 7.8 Hz), 7.48–7.50 (t, 2H, J = 7.8 Hz), 7.4–7.44 (t, 1H, J = 7.8 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 144.9, 139.9, 135.8, 129.4, 128.3, 127.6, 127.4, 125.9, 125.8.

4-Methoxybiphenyl

GC (condition A): t_R, 17.15 min; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.58 (m, 4H), 7.42–7.46 (t, 2H, J = 7.8 Hz), 7.31–7.34 (t, 1H, J = 7.8 Hz), 6.99–7.01 (t, 2H, J = 9.0 Hz), 3.87 (s, 3H). ^{13}C NMR (100.6 MHz, CDCl3): δ 159.3, 140.9, 133.9, 128.8, 128.3, 126.9, 126.8, 114.3, 55.5.

2,6-Dimethylbipheyl

GC (condition A): t_R, 13.77 min; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.41 (m, 2H), 7.40–7.32 (m, 1H), 7.26–7.09 (m, 5H), 2.10 (s, 6H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 141.8, 141.0, 136.0, 128.9, 128.4, 127.2, 127.0, 126.6, 20.8.

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