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Bidentate amidine ligands for nickel(0)-mediated coupling of carbon dioxide with unsaturated hydrocarbons†

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Novel bidentate amidines were designed and synthesized as easily available electron-donating *N*-ligands for Ni^0-mediated coupling of carbon dioxide with alkynes or allenes, and high regioselectivity was achieved even for the carboxylation of aryl substituted internal alkynes.

Design of a new type of easily available bidentate ligand having high flexibility in its steric and electronic character is of high importance in the development of transition-metal promoted reactions, as fine tuning of the nature of the ligand is frequently required for the efficient control of the reaction pathway. Concerning the electron-donating ligand for the transition metals, bidentate nitrogen ligands[1] such as bipyridines[2] and bis(oxazoline)s[3] are commonly employed. In this communication we describe the introduction of a new type of electron-rich bidentate nitrogen ligand, bis(amidine)s, for the Ni(0)-mediated oxidative coupling of unsaturated hydrocarbons with CO_2.[4]

The oxidative coupling of CO_2 with alkenes or alkynes using nickel(0) and electron-donating ligands was originally developed by Inoue's group[5] and Hoberg's group[6] in the 1970s ~ 1980s. Since then, various kinds of electron-donating ligand have been examined, and in particular, phosphines and N-donor ligands such as TMEDA,[6a,7] 2,2′-bipyridine,[8] and DBU[6c,9] have been shown to be good ligands for this reaction. We have focused our attention on the DBU's amidine-skeleton and have designed the following *exo*- and *endo*-type bis(amidine) ligands[10,11] with the expectation that steric and electronic factors could be controlled easily by appropriate ligand modifications (Fig. 1). Although bis(amidine)s have been known since the 1930s,[12a,b] use of bis(amidine) as ligand in transition-metal mediated C–C bond formation is quite limited,[12c] and the following two types of bis(amidine) have not been used for such a purpose before.

Exo-type bis(amidine)s **1a**,[10]**b** were prepared by the reaction of 1-methyl-5-(methylthio)-3,4-dihydro-2*H*-pyrrolinium iodide[11] and 1,2- or 1,3-diamine (Scheme 1). *Endo*-type bis(amidine)s **2a,b,c** were synthesized according to the method of Meyer's,[13] and their alkylation was carried out depending on the kind of substrate as follows. *N,N*′-Dimethylimidazoline derivative **2a** was dialkylated on the connecting carbon by repeated mono-alkylations using 1 equiv. of BuLi and 1 equiv. of methyl iodide to give **3a**. On the other hand, when the bis(imidazoline) derivative **2b** having no substituents was employed, addition of 2 equiv. of BuLi as base followed by 2 equiv. of alkyl iodide gave dialkylated *endo*-type bis(amidine)s **3b,c** directly (Scheme 1). By these protocols, a variety of bis(amidine)s can be synthesized easily in good yield. All of these bis(amidine)s could be handled in the air.

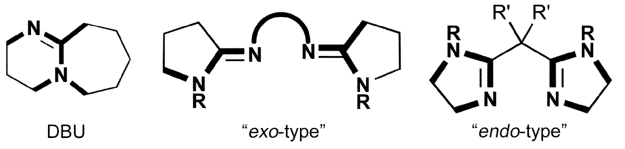
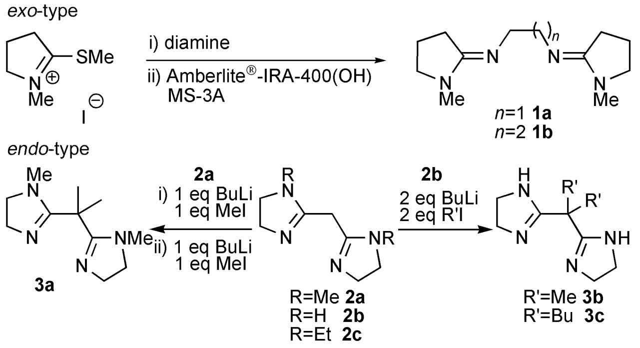


Fig. 1 Two-types of bidentate amidine.

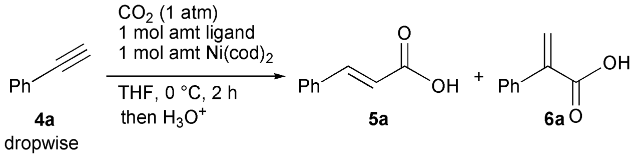


Scheme 1 Syntheses of bis(amidine) ligands.

As the methods for the preparation of bis(amidine)s had been established, we next examined the Ni(0)-mediated coupling reaction of CO_2 and alkynes in the presence of these bidentate ligands employing ethynylbenzene (**4a**) as substrate (Table 1).

In the absence of bis(amidine) no CO_2-coupling product was obtained but homo-oligomers of ethynylbenzene were produced, even when the alkyne was added very slowly (entry 1). When *exo*-type bis(amidine)s **1a** and **1b** were employed, CO_2-coupling product **5a** was obtained in low yield but with high regioselectivity (entries 2,3). On the contrary, *endo*-type bis(amidine)s generally gave better results. In particular, 2,2′-(dialkylated methylene) bis(imidazoline) derivatives **3b** and **3c** gave much better results than the *exo*-type bis(amidine)s and when dibutylated derivative **3c** was

Table 1 Effect of bis(amidine)s[a]



Entry	Ligand	Ligand type	Yield/%[b]	(**5a**:**6a**)[c]
1	none	—	0	—
2	**1a**	*exo*	6	(>98:<2)
3	**1b**	*exo*	5	(>98:<2)
4	**3a**	*endo*	<5	(25:75)
5	**3b**	*endo*	60	(>98:<2)
6	**3c**	*endo*	67	(>98:<2)
7	**2a**	*endo*	20	(10:90)
8	**2b**	*endo*	17	(12:88)
9	**2c**	*endo*	20	(7:93)

[a] Alkyne **4a** (0.18 mmol; added over 1 h), Ni(cod)$_2$ (0.18 mmol), bis(amidine) (0.18 mmol) were reacted in THF (4.5 mL) at 0 °C for 2 h under CO_2 (1 atm). [b] Products were extracted with 1M NaOH, and then the extracts were acidified with HCl for extraction with ether to give a mixture of **5a** and **6a**. Yields refer to these products. [c] Determined by ^{1}H NMR.

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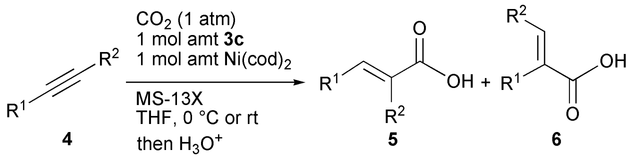
† Electronic supplementary information (ESI) available: preparative methods and experimental procedures and spectral and analytical data. See http://www.rsc.org/suppdata/cc/b4/b411802b/

Table 2 Coupling of CO_2 with various alkynes[a]



Entry	R^1	R^2		Yield/%[b]	(**5**:**6**)[c]
1	Ph	H	(**4a**)	63	(>98:<2)
2	cyclohexen-1-yl	H	(**4b**)	67	(92:8)
3	$PhCH_2CH_2$	H	(**4c**)	38	(47:53)
4	Ph	Me	(**4d**)	80	(95:5)
5	*p*-$MeOC_6H_4$	Me	(**4e**)	84	(>98:<2)
6	*p*-$F_3CC_6H_4$	Me	(**4f**)	56	(81:19)
7	$PhCH_2CH_2$	Me	(**4g**)	80	(40:60)
8	Ph	Ph	(**4h**)	52	—

[a] Terminal alkynes (0.55 mmol; added over 1 h), $Ni(cod)_2$ (0.50 mmol), **3c** (0.55 mmol), MS-13X (250 mg) were reacted in THF (10 mL) at 0 °C for 2 h under CO_2 (1 atm.); Internal alkynes (0.45 mmol), $Ni(cod)_2$ (0.55 mmol), **3c** (0.55 mmol), MS-13X (250 mg) were reacted in THF (10 mL) at RT for 8 h under CO_2 (1 atm.). [b] Products were purified by silica gel chromatography to give a mixture of **5** and **6**. [c] Determined by ^1H NMR.

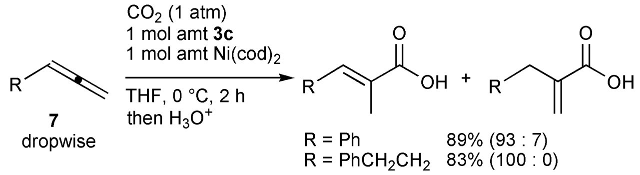
employed, cinnamic acid (**5a**) was obtained in 67% yield with high regioselectivity (>98:<2). Interestingly, when *endo*-type bis(amidine)s **2a–c** having no substituent on the connecting methylene carbon were employed, the regioselectivity was reversed and 2-phenylpropenoic acid (**6a**) was obtained as the major isomer although the yield was not very good (entries 7–9).

Regioselective couplings of CO_2 with terminal alkynes were already reported in several cases. For example, Duñach[14] reported electrode reaction using nickel(II) and 2,2′-bipyridine to give branched-type product **6**, while Yamamoto[9a] showed excellent opposite selectivity to give linear-type products **5** using DBU as ligand. However, it is still difficult to obtain both regioisomers selectively by a slight modification of the reaction conditions. The results obtained by using **3c** and **2c** indicate the possibility of controlling the regioselectivity of CO_2 coupling with alkyne by slight modification of the ligand.

Generality of the Ni(0)-mediated coupling of CO_2 was examined with several alkynes or allenes using dibutylated derivative **3c** as ligand. As summarized in Table 2, all alkynes were converted to the corresponding carboxylic acids in reasonable yield. Conjugated terminal alkynes **4a,b** showed good regioselectivity (**5**:**6** = >98:<2 and 92:8 (entries 1,2)), while *n*-alkyl-substituted terminal alkyne **4c** gave a nearly equal amount of regioisomers (entry 3). In the case of internal alkynes **4d–4h**, slow addition of alkynes was not necessary and good yields of the carboxylated products were obtained in these cases (entries 4–8). Importantly, a good level of regioselectivity (up to >98:<2) is achieved in the case of internal alkynes directly substituted with an aryl group, and furthermore, a notable effect of a *para*-substituent on the phenyl group was observed with an electron-donating group improving both the yield and the regioselectivity (entries 4–6). To our knowledge, Ni(0)-mediated regioselective CO_2 coupling with internal alkynes substituted with aryl and alkyl groups has not been previously reported.[15]

Reaction with terminal allenes **7** also proceeded smoothly in the presence of bis(amidine) **3c** to give the carboxylated products in good yields with high regioselectivities (Scheme 2).[16]

Although the detail of the reaction mechanism has yet to be clarified, an interesting phenomenon concerning the role of the ligand was observed. Thus, when the ligand **3c** was added to THF-d_8 solution of $Ni(cod)_2$, no change was observed in the ^1H NMR spectra, suggesting that this ligand does not coordinate to the zero valent state of Ni. Probably this ligand rapidly captures the Ni(II) species generated by CO_2 coupling with alkynes.



Scheme 2 Coupling of CO_2 with allenes.

In summary, a new type of bidentate nitrogen ligand, bis(amidine), is introduced into transition metal mediated C–C bond forming reactions. Application of these bis(amidine)s for Ni(0)-mediated coupling of CO_2 with unsaturated hydrocarbons resulted in good yield and regioselectivity when 2,2′-(dibutylated methylene) bis(imidazoline) derivative **3c** was employed. In particular, high regioselectivity was noted for the carboxylation of aryl substituted internal alkynes. It was also shown that regioselectivity of this coupling would be controllable by the appropriate choice of the bis(amidine).

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Notes and references

1 (*a*) A. Togni and L. M. Venanzi, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 497; (*b*) C. J. Elsevier, *Coord. Chem. Rev.*, 1999, **185–186**, 809.
2 G. Chelucci and R. P. Thummel, *Chem. Rev.*, 2002, **102**, 3129.
3 A. K. Ghosh, P. Mathivanan and J. Cappiello, *Tetrahedron: Asymmetry*, 1998, **9**, 1.
4 Reviews: (*a*) D. Walther, *Coord. Chem. Rev.*, 1987, **79**, 135; (*b*) A. Behr, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 661; (*c*) P. Braunstein, D. Matt and D. Nobel, *Chem. Rev.*, 1988, **88**, 747; (*d*) X. Yin and J. R. Moss, *Coord. Chem. Rev.*, 1999, **181**, 27; (*e*) M. Shi and Y. M. Shen, *Curr. Org. Chem.*, 2003, **7**, 737.
5 (*a*) Y. Sasaki, Y. Inoue and H. Hashimoto, *J. Chem. Soc., Chem. Commun.*, 1976, 605; (*b*) Y. Inoue, Y. Itoh and H. Hashimoto, *Chem. Lett.*, 1977, 855; (*c*) Y. Inoue, Y. Itoh, H. Kazama and H. Hashimoto, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 3329.
6 (*a*) G. Burkhart and H. Hoberg, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 76; (*b*) H. Hoberg and D. Schaefer, *J. Organomet. Chem.*, 1982, **236**, C28; (*c*) H. Hoberg, Y. Peres and A. Milchereit, *J. Organomet. Chem.*, 1986, **307**, C38.
7 D. Walther and G. Bräunlich, *J. Organomet. Chem.*, 1992, **436**, 109.
8 D. Walther, H. Schönberg, E. Dinjus and J. Sieler, *J. Organomet. Chem.*, 1987, **334**, 377.
9 (*a*) S. Saito, S. Nakagawa, T. Koizumi, K. Hirayama and Y. Yamamoto, *J. Org. Chem.*, 1999, **64**, 3975; (*b*) M. Takimoto and M. Mori, *J. Am. Chem. Soc.*, 2002, **124**, 10008; (*c*) K. Shimizu, M. Takimoto and M. Mori, *Org. Lett.*, 2003, **5**, 2323.
10 *Exo*-type bis(amidine) **1a** was prepared to examine its biological activity. P. Ahuja, J. Singh, M. B. Nigam, V. Sardana, K. Kar and N. Anand, *Indian J. Chem.*, 1982, **21B**, 849.
11 (*a*) D. Brillon, *Synth. Commun.*, 1990, **20**, 3085; (*b*) W. Walter, W. Ruback and C. O. Meese, *Chem. Ber.*, 1980, **113**, 171.
12 (*a*) H. K. S. Rao and T. S. Wheeler, *J. Chem. Soc.*, 1937, 1643; (*b*) *The Chemistry of Amidines and Imidates, Vol. 2*, Ed. S. Patai, Wiley, New York, 1991; (*c*) J. Dupont, G. Ebeling, M. R. Delgado, C. S. Consorti, R. Burrow, D. H. Farrar and A. J. Lough, *Inorg. Chem. Commun.*, 2001, **4**, 471.
13 To our knowledge, the following three papers dealt with these *endo*-type bis(amidine)s as intermediates for the synthesis of heterocyclic compounds. (*a*) H. Meyer and J. Kurz, *Liebigs Ann. Chem.*, 1978, 1491; (*b*) H. Meyer, *Liebigs Ann. Chem.*, 1981, 1523; (*c*) H. Meyer, *Liebigs Ann. Chem.*, 1981, 1545.
14 E. Duñach and J. Périchon, *J. Organomet. Chem.*, 1988, **352**, 239.
15 Duñach reported electrode reaction using Ni(II) and 2,2′-bipyridine (regioselectivity; up to 62:38). S. Dérien, E. Duñach and J. Périchon, *J. Am. Chem. Soc.*, 1991, **113**, 8447.
16 M. Takimoto, M. Kawamura and M. Mori, *Org. Lett.*, 2003, **5**, 2599 and references cited therein.