

Communication

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Nickel-Catalyzed Decarbonylative Addition of Phthalimides to Alkynes

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A direct oxidative addition of a low-valent transition-metal catalyst into a C–N bond generates the active species (C–M–N), which may perform a carboamination with alkyne (Scheme 1).^{1–6} The reaction will form C–C and C–N bonds simultaneously. It should be a useful transformation to prepare a nitrogen atom containing compound, however, it has not been studied well because of the difficulty of such oxidative addition. We postulated that a nickel(0) with electron-donating phosphine ligands will attack an amide nucleophilically; the addition may afford the C–M–N species via decarbonylation and might allow an insertion reaction to alkynes.⁷ Thus, we attempted the addition of phthalimide **1** to alkyne **2** using a nickel(0) catalyst to form isoquinolone **3**.^{8,9}

Initially, *N*-phenylphthalimide (**1a**) was treated with 4-octyne (**2a**), 10 mol % of Ni(cod)₂, and 40 mol % of PMe₃ in toluene at 110 °C for 3 h. This led to isoquinolone **3aa** in 18% isolated yield (Table 1, entry 1). Trace or lower amounts of **3aa** were obtained in the case using PBu₃, PCy₃, and PPh₃ in place of PMe₃ (17, 11, and 8% yields, respectively). Under these conditions, the reaction of **2a** with *N*-phenylphthalimides possessing an electron-donating or -withdrawing group afford the correspondingly substituted isoquinolones in 13 and 34% yield (entries 2 and 3). Since an electron-withdrawing substituent gave the higher yield, we presumed that electron-deficient *N*-arylphthalimides react with alkynes efficiently. Indeed, the reaction of **2a** with *N*-perfluorophenylphthalimide (**1d**) successfully provided isoquinolone in 84% yield (entry 4). *N*-Pyridinylphthalimides (**1e–1g**) also reacted with **2a** smoothly to give the corresponding isoquinolones in good yields (entries 5–7).¹⁰ The reactions of **2a** with *N*-diazinephthalimides **1h** and **1i** afforded the products in 90 and 85% yields, respectively (entries 8 and 9). Imides such as **1j** also reacted with **2a** to provide the corresponding addition products in excellent yields (entry 10).

It is noteworthy that *N*-phenylquinolimine **1k** reacted with **2a** to give **3ka** as a single isomer along with a trace amount of *N*-phenylpicolinamide (Scheme 2). The starting material **1k** was recovered in 25% yield. This regioselectivity can be rationalized by nucleophilic attack of Ni(0) to more electrophilic carbonyl. The reaction with a regioisomer **1l**, which would not induce the directing effect for the formation of an intermediate, also showed regioselectivity. Actually, *N*-phenylquinolimine (**1l**) also reacted with **2a** to give **3la** as a major product in 65% yield.

Scheme 1. Pathways to C–M–N Species

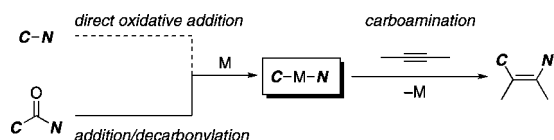
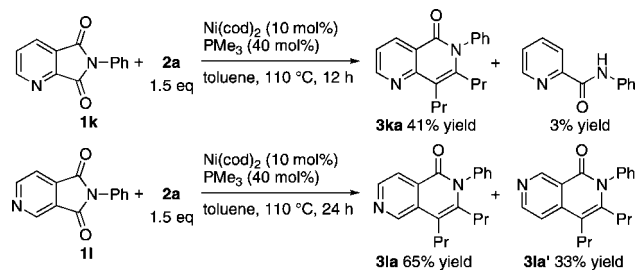


Table 1. Nickel-Catalyzed Decarbonylative Addition of *N*-Arylphthalimides to 4-Octyne^a

entry	1	3	yield (%) ^b
1			18
2			13
3			34
4			84
5			84
6			81
7			72
8			90
9			85
10			92

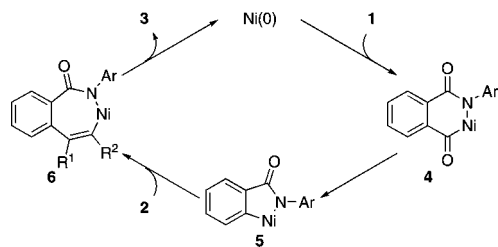
^a Reactions were carried out using Ni(cod)₂ (10 mol %), PMe₃ (40 mol %), *N*-arylphthalimide (0.5 mmol), and **2a** (0.75 mmol) in 2 mL of refluxing toluene (110 °C) for 7 h. ^b Isolated yields.

The additions of **1e** to various alkynes were examined (Table 2). The reaction of unsymmetrical dialkyl alkyne **2b** with **1e** gave the products consisting of regioisomers in a 1/1 ratio (entry 1), whereas reaction of 4-methyl-2-pentyne (**2c**) gave adduct **3ec** as a major product (entry 2). 1,4-Dimethoxy-2-butyne (**2d**)

Scheme 2. Nickel-Catalyzed Decarbonylative Addition of *N*-phenylquinolimidates to **2a**

Table 2. Decarbonylative Addition of **1e** to Alkynes^a

entry	2	3	time (h)	yield (%) ^b
1			12	86 (1/1) ^c
2			12	93 (2/1) ^c
3			7	90
4			15	56

^a All reaction were carried out using Ni(cod)₂ (10 mol %), PMe₃ (40 mol %), **1e** (0.5 mmol), and alkyne (0.75 mmol) in 2 mL of refluxing toluene (110 °C). ^b Isolated yields. ^c Ratio of regioisomers.

Scheme 3. Plausible Pathway for Decarbonylative Addition of *N*-Arylphthalimides to Alkynes


reacted similarly to give **3ed** in excellent yield (entry 3). The reaction of toluene (**2e**) was relatively slow to give corresponding isoquinolone **3ee** in moderate yield (entry 4). Terminal alkynes, such as 1-octyne and phenylacetylene, failed to participate in the reaction, presumably due to rapid oligomerization of alkynes.

We propose a plausible mechanism involving nucleophilic attack of Ni(0) having electron-rich phosphine ligands to an amide, giving the nickelacycle **4** (Scheme 3).^{11,12} Subsequent decarbonylation and insertion of **2** to the C–Ni bond leads to the seven-membered nickelacycle **6**, which undergoes reductive elimination to give **3** and regenerates the starting Ni(0) complex.

In summary, we have developed a new nickel-catalyzed reaction of alkynes with *N*-arylphthalimides to provide isoquinolones. It was demonstrated that amide C–N bonds are susceptible to nucleophilic attack of the Ni(0) complex, which allows intermolecular addition to alkynes via decarbonylation. Further studies for explanation of the detailed mechanism are currently under investigation in our laboratories.

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Supporting Information Available: Experimental procedures including spectroscopic and analytical data of new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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