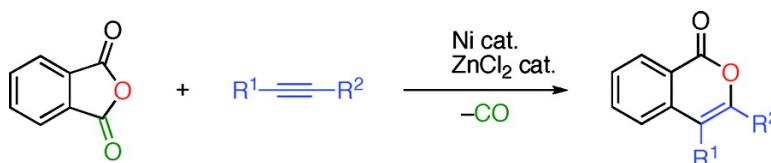Communication

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Nickel-Catalyzed Decarbonylative Addition of Anhydrides to Alkynes

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The transition metal-catalyzed insertion reaction of an unsaturated carbon−carbon bond into a carbon−oxygen bond of an oxacyclic compound is a useful transformation to prepare more complicated oxacyclic compounds in a single step (Scheme 1). However, there is no precedent for such a potentially valuable methodology. We postulated that oxidative addition of cyclic anhydrides to nickel(0) and subsequent decarbonylation are facile and might allow insertion of alkynes. Thus, we attempted the decarbonylative addition of phthalic anhydride to alkyne using nickel(0) catalyst to form isocoumarin,[1,2] which displays a wide range of biological activities.[3]

Our investigation began with an attempted addition of phthalic anhydride (1a) to 4-octyne (2a) with 10 mol % of Ni(cod)₂ and 40 mol % of PMe₃ in refluxing acetonitrile (80 °C) for 12 h.[4] However, this resulted in low conversion of 1a and led to isocoumarin 3aa in 12% yield (Table 1, entry 1).[5] A detailed examination of the reaction conditions revealed that, on addition of 20 mol % of ZnCl₂, the reaction proceeded smoothly to furnish 3aa in 96% isolated yield (entry 2).[6] Among the Lewis acids examined, ZnCl₂ gave the best yield of the product (entries 3−7). An addition of quaternary ammonium salts was also found to be effective for the reaction (entries 8−12). An electrostatic interaction between the carbonyl moiety of 1a and the quaternary ammonium might behave as a general Lewis acid.[7]

With the optimized conditions in hand,[8−10] we next investigated the scope of the reaction using various anhydrides (Table 2). The decarbonylative addition of maleic anhydride 1b to 4-octyne provides α-pyrone 3ba in 87% yield (Table 2, entry1). The reaction of 2,3-naphthalenedicarboxylic anhydride (1c) with 2a gave the product 3ca in 82% yield (entry 2). Unsymmetrical anhydrides 1d and 1e provide the corresponding products 3da and 3ea in 61% and 53% yields, along with formation of the respective regioisomers (entries 3 and 4). The addition of 1f to 2a proceeded smoothly to provide 3fa in 94% yield (entry 5). The addition of diphenyl-substituted maleic anhydride 1g to 4-octyne resulted in lower yield (23%) even with prolonged reaction time (entry 6).

The addition reaction is also compatible with aryl-substituted alkyne (Table 3, entry 1) and afforded the corresponding isocoumarin 3ab in 87% yield. The reaction of 1a with unsymmetrical alkynes such as 2c and 2d gave the products consisting of regioisomers in a 1/1 ratio (entries 2 and 3). The addition of 1a to 2e, containing sterically hindered groups, gave adduct 3ae as a major product with a regioselectivity ratio of 2/1 (entry 4). Bulky and electron-rich trimethylsilyl-substituted alkynes such as 2f and 2g reacted with 1a to provide adducts with complete regiocontrol in excellent yields (entries 5 and 6). Terminal alkynes, such as 1-octyne and phenylacetylene, failed to participate in the reaction, presumably due to rapid oligomerization of alkynes.

A plausible reaction pathway to account for the formation of isocoumarins 3 based on the observed results is outlined in Scheme 2. In view of the mechanism of the previously reported nickel-catalyzed cross-coupling reaction of anhydrides with organometalic reagents,[11] it is reasonable to consider that the catalytic cycle of

Table 1. Nickel-Catalyzed Decarbonylative Addition of Phthalic Anhydride to 4-Octyne[a]

| entry	additive	yield (%)[b]	entry	additive	yield (%)[b]
1	—	12	7	LiCl	76
2	ZnCl₂	96	8	Bu₄NPF₆	54
3	Zn(OTf)₂	92	9	Bu₄NCl	72
4	ZnBr₂	91	10	Bu₄NOTf	67
5	ZnI₂	90	11	Bu₄NBr	65
6	BPh₃	92	12	Bu₄NI	52

[a] All reactions were carried out using Ni(cod)₂ (10 mol %), PMe₃ (40 mol %), additive (20 mol %), phthalic anhydride (0.5 mmol), and 4-octyne (0.6 mmol) in 2 mL of refluxing acetonitrile (80 °C). [b] Isolated yields.

Table 2. Nickel-Catalyzed Decarbonylative Addition of Anhydrides to 4-Octyne[a]

entry	1	time (h)	3 (yield[b])
1	1b	15	3ba (87%)
2	1c	18	3ca (82%)
3	1d	18	3da (61%) 3da' (29%)
4	1e	18	3ea (53%) 3ea' (8%)
5	1f	15	3fa (94%)
6	1g	18	3ga (23%)

[a] All reactions were carried out using Ni(cod)₂ (10 mol %), PMe₃ (40 mol %), ZnCl₂ (20 mol %), 1 (0.5 mmol), and 2a in 2 mL of refluxing acetonitrile (80 °C). [b] Isolated yields.

the present reaction should consist of oxidative addition of an anhydride O−CO bond to nickel.[12] Subsequent decarbonylation and coordination of alkyne take place, in which the steric repulsive interaction is minimal between the bulkier R¹ and the PMe₃ ligand on the nickel, to give nickel(II) intermediate 4a. The alkyne would then insert into the aryl-nickel bond to give nickelacycle 5, which undergoes reductive elimination to give 3 and regenerates the

Table 3. Nickel-Catalyzed Decarbonylative Addition of Phthalic Anhydride to Alkynes[a]

entry	2 (eq)	time (h)	3	yield (%)[b]
1	2b (1.5)	12	3ab	87
2	2c (1.5)	15	3ac	91 (1/1)[c]
3	2d (1.5)	15	3ad	75 (1/1)[c]
4	2e (1.5)	15	3ae	89 (2/1)[c]
5	2f (6.0)	18	3af	93[d]
6	2g (1.5)	24	3ag	86[d]

[a] All reactions were carried out using Ni(cod)$_2$ (10 mol %), PMe$_3$ (40 mol %), 1a (0.5 mmol), and alkyne in 2 mL of refluxing acetonitrile (80 °C). [b] Isolated yields. [c] Ratio of regioisomers. [d] Only a single regioisomer was formed.

Scheme 1. Transition-Metal-Catalyzed Decarbonylative Addition of Cyclic Anhydrides to Alkynes
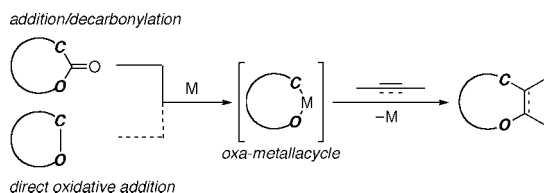
Scheme 2. Plausible Mechanism for the Nickel-Catalyzed Decarbonylative Addition of Phthalic Anhydrides to Alkynes
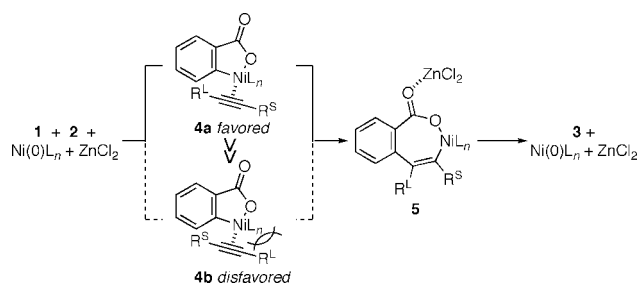
starting nickel(0). In-situ IR spectra analysis demonstrated that the stoichiometric reaction of Ni(cod)$_2$/PMe$_3$ with 1a and 2a without ZnCl$_2$ resulted in gradual consumption of 1a without formation of 3aa. Importantly, constant generation of 3aa was observed simultaneously on addition of ZnCl$_2$ (Figure S1, Supporting Information). These results imply that reductive elimination is specifically promoted by the addition of ZnCl$_2$. The origin of the effect of ZnCl$_2$ is likely to result from the coordination of a Lewis acid to a carbonyl

group, which may generate electron-poor alkenylnickel through a conjugated system.[5i]

In conclusion, the decarbonylative addition reaction of phthalic anhydrides to alkynes is successfully demonstrated using a nickel catalyst in association with a Lewis acid as a cocatalyst. Further efforts to expand the scope of the chemistry and studies of the detailed mechanism are currently underway in our laboratories.

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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(8) For detailed examination of the reaction conditions, see Supporting Information Table S1.

(9) The reaction of 1a and 2a using air-stable trimethylphosphonium tetrafluoroborate (40 mol %) and N,N-diisopropylethylamine (100 mol %) in place of trimethylphosphine under an existence of ZnCl$_2$ (20 mol %) as an additive also affords 3aa in 86% isolated yield. For detailed examination of the reaction conditions, see Supporting Information Table S2. Netherton, M. R.; Fu, G. C. *Org. Lett.* **2001**, *3*, 4295.

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JA806569H