

Oxidative Addition of Anhydride to Nickel(0) Species: Reactivity and Regioselectivity

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[Introduction]

Ni-catalyzed intermolecular decarboxylative cycloaddition provides an efficient method for the synthesis of heterocyclic compounds, which plays a vital role in life processes due to their biological activities. Recently, Kurahashi and Matsubara et al. successfully developed a new nickel-catalyzed decarboxylative [4 + 2] cycloaddition of isatoic anhydrides with alkynes to provide quinolones (Scheme 1).¹ The catalytic cycle of the present reaction consists of four elementary processes: (1) oxidative addition, (2) decarboxylation, (3) alkyne insertion, and (4) reductive elimination. The first oxidative addition process is the rate-determining step of the catalytic cycle, which determines what product is obtained. Hence, one important task is to understand the reactivity and regioselectivity of the oxidative addition; the experimentally reported product is obtained only when the C2–O2 bond rather than the other C–O, C–C, and C–N bonds undergoes the oxidative addition (Scheme 2).

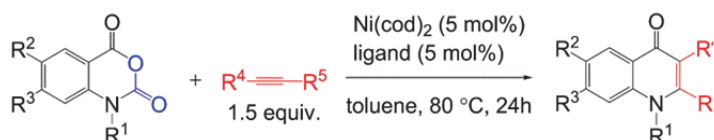
[Computational methods]

Geometries were optimized with the M06 hybrid functional, where solvent effect of toluene was taken into consideration by the CPCM method. Two kinds of basis set system were employed here. In basis set I (BS-I), the Los Alamos relativistic ECPs were employed for the core electrons of Ni and the (541/541/311/1) basis set was used for its valence electrons. The 6-31G(d) basis sets were employed for other main group elements. A better basis set system was employed for the evaluation of energy changes. In BS-II, (311111/22111/411/11) basis set was employed for Ni with the ECPs of the Stuttgart–Dresden–Bonn group. The 6-311+G(2d,p) basis sets were employed for other elements. All calculations were carried out by the Gaussian 09 program.

[Results and Discussion]

The oxidative addition step is the approach of a bis-ligated Ni(0) catalyst

Scheme 1. Nickel-Catalyzed Decarboxylative Carboamination of Alkynes with Isatoic Anhydrides



Scheme 2. Regioselectivity of the Oxidative Addition

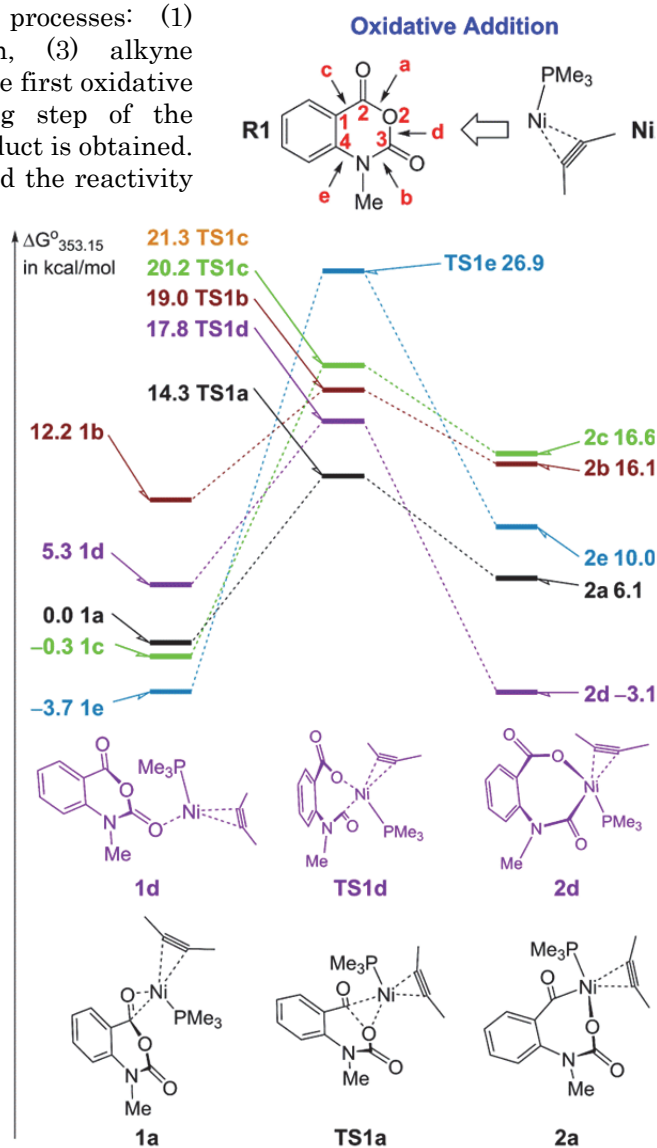


Figure 1. Energy Profiles ($\Delta G^{\ddagger}_{353.15}$) for the Oxidative Addition.

Ni(PMe₃)(alkyne) **Ni2** to isatoic anhydride **R1**, leading to the formation of five kinds of adduct, where the C=O bond, the C=C bond in the phenyl ring, the O atom, and the C–N bond in the heterocyclic ring participate in coordination. Among them, η^2 -complexes **1e** is the most stable; see Figure 1. From the above initial intermediates, five kinds of TS for bond activation are optimized here; **TS1a** for the C2–O2 bond activation, **TS1b** for the C3–N bond activation, **TS1c** for the C1–C2 bond activation, **TS1d** for the C3–O2 bond activation, and **TS1e** for the C4–N bond activation. All products of the oxidative addition are pseudo-square-planar four-coordinated Ni(II) complexes. **TS1a** is the most stable among all TSs, indicating the anhydride C2–O2 bond is preferentially activated. Although **2d** is much stable, the strong C–CO₂ bond obstructs the next decarboxylation.

For the most favorable pathway, **R1** approaches **Ni2** to form a η^2 -adduct **1a**, as shown in Figure 2, in which the carbonyl group coordinates with the Ni center. Transition state **TS1a** takes a three-membered-ring. In **TS1a**, the Ni–C2 and Ni–O2 distances become shorter from 1.97 and 2.81 to 1.87 and 2.14 Å, respectively, while the C2–O2 bond is elongated to 1.79 Å from 1.43 Å in **1a**, suggesting that the C2–O2 bond breaking is in progress. The immediate **2a** is a pseudo-square-planar four-coordinated Ni(II) complex. The ΔG^{\ddagger} and ΔG° values of this process are 14.3 and 6.1 kcal/mol, respectively.

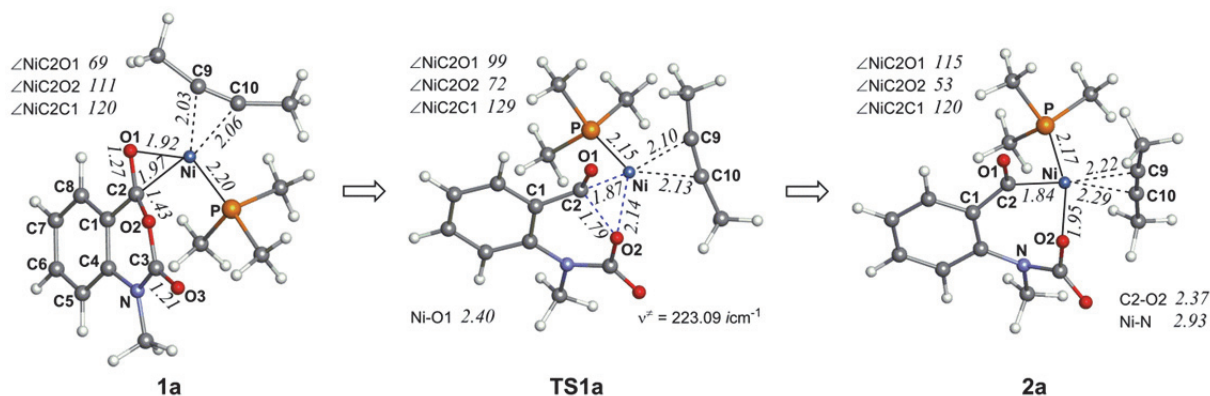
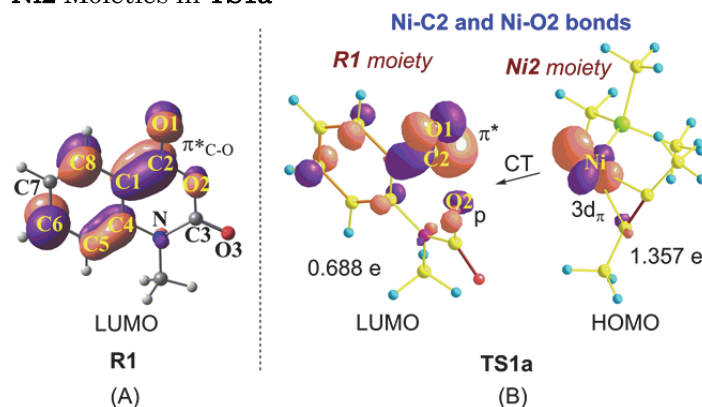


Figure 2. Optimized Structures and Selected Geometrical Parameters (Bond Length in Angstrom Unit and Bond Angle in Degree) of **1a**, **TS1a**, and **2a**.

In the oxidative addition process, **Ni2** considerably donates $3d_\pi$ electrons of Ni to the low-lying unoccupied π^* anti-bonding orbital of **R1**. As shown in Scheme 3(A), the LUMO of **R1** mainly consists of the $\pi^*_{\text{C-C}}$ anti-bonding orbitals in the phenyl moiety into which the $\pi^*_{\text{C-O}}$ anti-bonding orbital of the heterocyclic ring mixes in a bonding way. The HOMO of **Ni2** mainly consists of the $3d_\pi$ of Ni orbital, which overlaps with the p_π - p_π anti-bonding overlap between C2 and O2 atoms. Hence, this CT leads to the C2–O2 bond breaking and Ni–acyl and Ni–carboxylate bond formations. The p_π - p_π anti-bonding overlap is not found in the other C3–O2, C3–N, and C4–N pairs. Thus, the CT to the LUMO of **R1** explains the reason why the anhydride C2–O2 bond is preferentially activated by **Ni2**; in other words, this CT determines the regioselectivity. The use of strong electron-donating ligand such as PCy₃ enhances the CT accordingly to promote the anhydride C(=O)–O bond cleavage.

Scheme 3. LUMO of **R1** and Important Kohn-Sham MOs and Their Electron Populations of each MO of **R1** and **Ni2** Moieties in **TS1a**



[Reference]

1. Yoshino, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* 2009, *131*, 7494.