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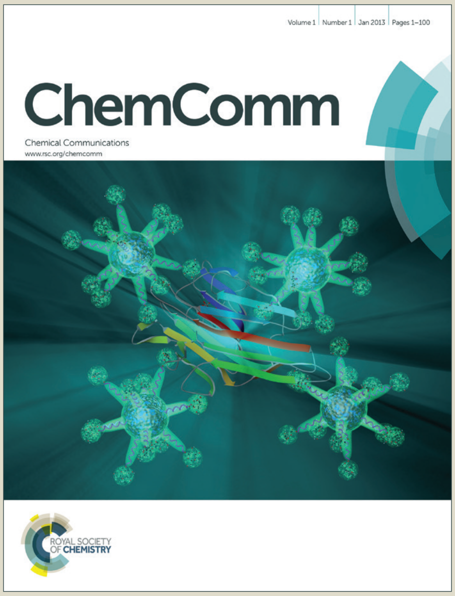

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Palladium-Catalyzed Addition Reaction of Aroyl/Heteroaroyl Acid Anhydrides to Norbornenes

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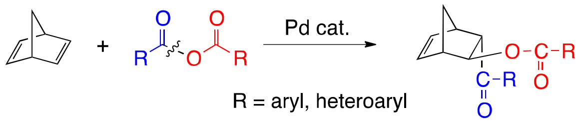
A palladium complex derived from $Pd_2(dba)_3$ and dppp catalyzes the addition reaction of aroyl/heteroaroyl acid anhydrides to norbornenes, giving 2-aroyl/heteroaroyl-3-aroyloxy/heteroaroyloxy-bicyclo[2,2,1]heptanes. The C-O bond of acid anhydride is cleaved, and the aroyl/heteroaroyl and aroyloxy/heteroaroyloxy groups are added to alkenes. *trans*-Adducts are selectively obtained with the *endo*-benzoyl group and *exo*-benzoyloxy group.

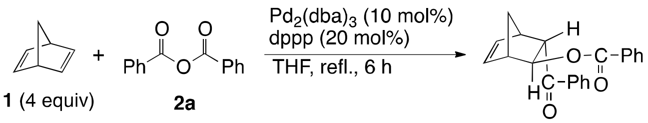
C-O Bond formation is one of the most fundamental processes in organic synthesis, and the addition reaction of alcohols and carboxylic acids to alkenes has been extensively utilized, where O-H bonds are cleaved.[1] Various catalysts and promoters have been developed including acids, bases, light, oxidants, major metal compounds, and transition-metal complexes. In contrast to the addition reaction using O-H bond cleavage, the addition reaction using C-O single bond cleavage has not been examined except for the recently reported intramolecular addition of cyanate.[2] This may be because the catalytic cleavage of the C-O bond is not facile, and thus a method of adding carbon and oxygen to alkene remains to be investigated. Such a reaction can be attractive for the construction of carbon frameworks of organic compounds with concomitant oxygen functionalization.

In terms of C-O bond cleavage using transition-metal catalysis, acid anhydride can be a candidate because of its relatively weak C-O bond. However, such a catalytic reaction is limited to the use of acid anhydride as an acylation reagent, where the acyloxy group, being a leaving group, does not participate in C-O bond formation.[3] Yamamoto developed a hydrogen reduction method for acid anhydrides to give aldehydes,[4] whereas Tanaka reported a rhodium-catalyzed *O*-acylation reaction.[5] Miura and Krische developed a hydroacylation reaction method for alkenes in hydrogen atmosphere.[6] However, no transition-metal-catalyzed addition reaction of acid anhydride to alkene has yet been reported. Described here is the palladium-catalyzed addition reaction of acid anhydrides to norbornene derivatives (Scheme 1). This reaction forms C-C and C-O bonds by the cleavage of the C-O bond in acid anhydrides.



Scheme 1.

When norbornadiene **1** (4 equiv) and benzoic acid anhydride **2a** were reacted in refluxing THF for 6 h in the presence of $Pd_2(dba)_3$ (10 mol%), dppp (20 mol%), (1*R**,2*S**,3*S**,4*S**)-2-benzoyl-3-benzoyloxy-bicyclo[2,2,1]hept-5-ene *trans*-**3a** was obtained in 79% yield (Scheme 2). X-ray analysis determined the *trans*-configuration of **3a** between the *endo*-benzoyl and *exo*-benzoyloxy groups (Figure 1).[7] The double bond in *trans*-**3a** seems to be less reactive than those in **1**, and the second addition to *trans*-**3a** was not observed under the same conditions. When the molar ratio of **1** to **2a** was changed from 4 to 1, the yield of *trans*-**3a** decreased to 41%. The palladium complex cleaved the C-O bond in **2a**, and added the benzoyl and benzoyloxy groups to **1**.



1 (4 equiv) **2a** *trans*-**3a** 79%

Scheme 2.

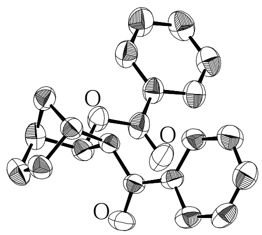
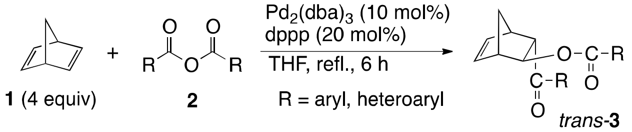


Figure 1. ORTEP view of *trans*-**3a**; thermal ellipsoid plot of *trans*-**3a** at 50% probability.

The palladium complex and dppp were both essential for the reaction, and no reaction occurred in the absence of either substance. Other metal complexes in the presence of dppp exhibiting similar activities include $Pd(PPh_3)_4$ (67%), $Pd(OAc)_2$ (57%), and $PdCp(C_3H_5)$ (69%); $RhH(PPh_3)_4$ and $RhH(CO)(PPh_3)_3$ were ineffective. The effect of a phosphine ligand was examined, and the following bidentate ligands were found to exhibit catalytic activity: 1,2-bis(diphenylphosphino)ethane (dppe: 41%), 1,2-bis(diphenylphosphino)benzene (dppBz: 29%), and 1,2-bis(diphenylphosphino)butane (dppb: 7%). Other bidentate ligands, i.e., 1,2-bis(diphenylphosphino)methane and 1,2-bis(diphenylphosphino)hexane, as well as monodentate ligands, i.e., $(p\text{-}MeOC_6H_4)_3P$ and $(p\text{-}ClC_6H_4)_3P$, were ineffective.

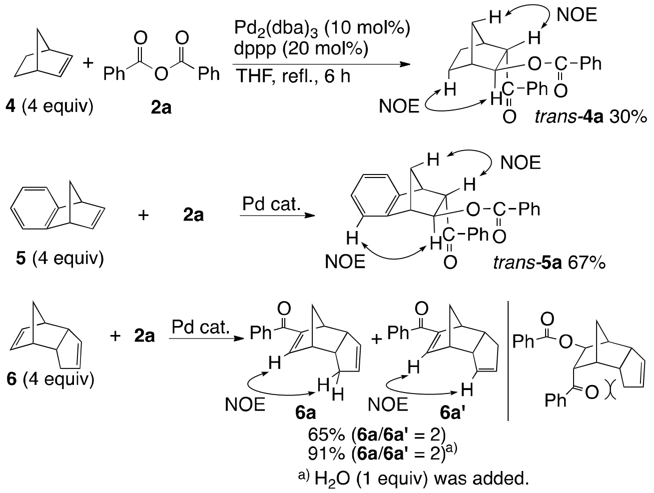
Norbornadiene **1** (4 equiv) reacted with various aromatic acid anhydrides giving the corresponding addition products in high yields (Table 1). Aromatic acid anhydrides can have either an electron-donating group or an electron-withdrawing group on their aryl moiety (entries 1-7). The addition of valeric anhydride, crotonic anhydride, and 4-fluorophthalic anhydride to **1**, however, did not occur. The addition reaction of the heteroaroyl acid anhydrides **2h**-**2k** containing 2-furyl, 2-thienyl, 2-pyridyl, and 3-pyridyl groups also gave the corresponding adducts (entries 8-11). The similar results of **2j** and **2k** showed a small effect of the position of the nitrogen atom.

Table 1. Palladium-catalyzed addition reactions of various aroyl/heteroaroyl acid anhydrides to **1**.



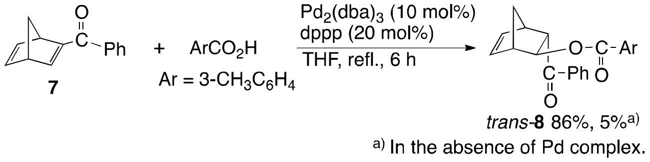
Entry	R (**2**)	Yield of *trans*-**3**/%
1	Ph (**a**)	79 (**a**)
2	4-MeC_6H_4 (**b**)	55 (**b**)
3	4-ClC_6H_4 (**c**)	58 (**c**)
4	2-MeC_6H_4 (**d**)	34 (**d**)
5	3-$MeOC_6H_4$ (**e**)	65 (**e**)
6	3-MeC_6H_4 (**f**)	78 (**f**)
7	3-$CF_3C_6H_4$ (**g**)	54 (**g**)
8	2-furyl (**h**)	45 (**h**)
9	2-thienyl (**i**)	56 (**i**)
10	2-pyridyl (**j**)	50 (**j**)
11	3-pyridyl (**k**)	50 (**k**)

Norbornene **4** and benzonorbornadiene **5** also reacted with **2a** to give the corresponding adducts *trans*-**4a** (30%) and *trans*-**5a** (67%), respectively (Scheme 3). The *trans*-stereochemistries of **4a** and **5a** between the benzoyl and benzoyloxy groups were determined by NMR study. The reaction of *exo*-dicyclopentadiene **6** gave a mixture of the acylated products **6a** and **6a'** in 65% combined yield. When water (1 equiv) was added, the combined yield of **6a** and **6a'** increased to 91%, and the proton source of this reaction was ascribed to the trace amount of contaminated water. The mixture of **6a** and **6a'** did not react with **2a** under the same palladium-catalyzed condition, which may be because of the steric hindrances between the cyclopentene and *endo*-benzoyl groups exerted in the product.



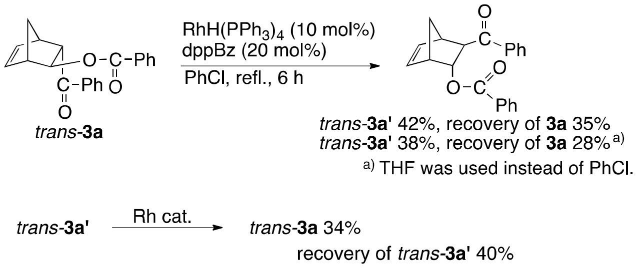
Scheme 3.

The following experiments were conducted to analyze the mechanism of C-C bond and C-O bond formation and the origin of *trans*-selectivity. When benzoyl norbornadiene **7**[8] was reacted with *m*-toluic acid in the presence of $Pd_2(dba)_3$ and dppp in refluxing THF for 6 h, (1*R**,2*S**,3*S**,4*S**)-2-benzoyl-3-(*m*-toluoyloxy)-bicyclo[2,2,1]hept-5-ene *trans*-**8** was obtained in 86% yield (Scheme 4). The yield of *trans*-**8** decreased to 26% using 3-methylbenzoic acid anhydride **2f**. *trans*-**8** was obtained only in 5% yield in the absence of the palladium complex. The results suggested that the mechanism involves the initial addition of the benzoyl group, which was followed by the addition of the benzoyloxy group.

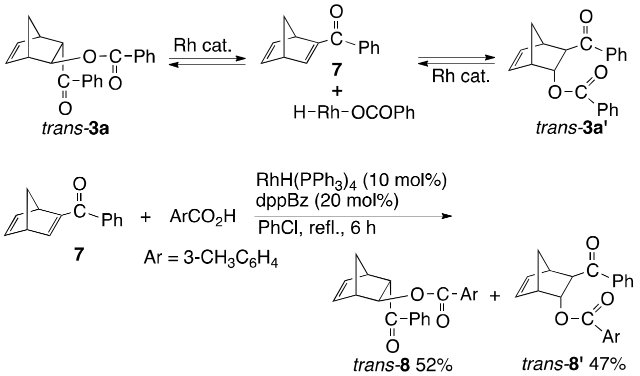


Scheme 4.

Note that this reaction exclusively gives *trans*-**3a**, and the other *trans*-isomer *trans*-**3a'** is not formed. It was found that the isomerization between *trans*-**3a** and isomer *trans*-**3a'** occurred under rhodium-catalyzed conditions. When *trans*-**3a** was reacted under $RhH(PPh_3)_4$ (10 mol%) and dppBz (20 mol%) in refluxing chlorobenzene for 6 h, *trans*-**3a'** was obtained in 42% yield, which was accompanied by the recovered *trans*-**3a** (35%) (Scheme 5). Pure isomer *trans*-**3a'** also isomerized to give a mixture of *trans*-**3a** and isomer *trans*-**3a'** under the same reaction conditions. *Trans*-**3a** isomerized to isomer *trans*-**3a'** in refluxing THF at a lower temperature. Thus, the thermodynamic stabilities of *trans*-**3a** and isomer *trans*-**3a'** were comparable, and rhodium catalysis gave an equilibrium mixture under thermodynamic control. The adducts *trans*-**3a** and isomer *trans*-**3a'** did not isomerize under the palladium condition, which showed that palladium catalysis gave the kinetic product *trans*-**3a**. The rhodium-catalyzed isomerization reaction of *trans*-**3a** might occur via the formation of the benzoyloxyrhodium hydride species, and the complex added to **7** giving a thermodynamic mixture of *trans*-**3a** and *trans*-**3a'** (Scheme 6). Accordingly, when **7** was reacted with *m*-toluic acid in the presence of $RhH(PPh_3)_4$ and dppBz in refluxing chlorobenzene for 6 h, (1*R**,2*S**,3*S**,4*S**)-2-benzoyl-3-(*m*-toluoyloxy)-bicyclo[2,2,1]hept-5-ene *trans*-**8** and isomer *trans*-**8'** were obtained in 52% and 47% yields, respectively (Scheme 6). The extremely high reactivities of benzoyloxyrhodium and benzoyloxypalladium in the addition to enone are notable.

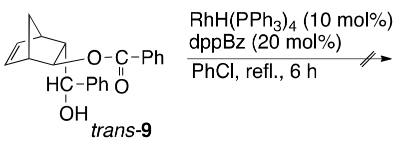


Scheme 5.



Scheme 6.

In order to determine the effect of ketone units, *trans*-**3a** was reduced by sodium tetrahydroborate giving *trans*-**9**, the treatment of which under rhodium-catalyzed condition gave no isomerized product (Scheme 7). The result is consistent with the conjugative addition mechanism in the addition of the benzoyloxyrhodium species to enone.



Scheme 7.

For a comparison of the catalytic activities of palladium and rhodium complex, 1) palladium complex can add an aroyl group of the acid anhydride to alkene, whereas, a rhodium complex does not exhibit the C-C bond formation ability and 2) the rhodium complex can isomerize the adduct by C-O bond cleavage, but not the palladium complex.

A possible mechanism of the present reaction is as follows (Figure 2). The C-O bond in benzoic acid anhydride **2a** undergoes oxidative addition to a Pd(0) complex to give the (benzoyl)(benzoyloxy)palladium(II) intermediate **A**. Benzoylnorbornadiene **7** is formed by the carbopalladation to alkene **1**, which is followed by the elimination of benzoyloxypalladium(II)hydride **B**. Then, *syn*-oxypalladation of **B** and **7** gives the alkylpalladium(II)hydride species **C**, and *trans*-**3a** is liberated by reductive elimination with the palladium catalyst regenerated. Although transition-metal-catalyzed *exo*-selective *cis*-addition reactions to norbornene are well known,[9] *trans*-addition has not yet been reported.[10]

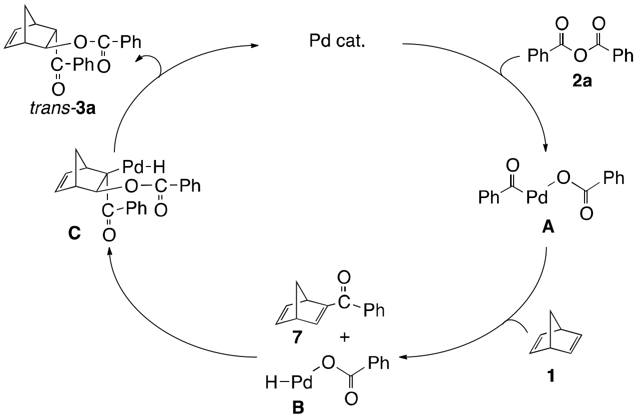
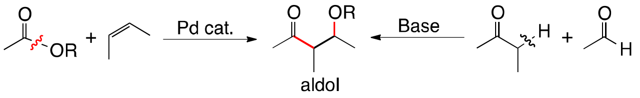


Figure 2. Possible mechanism.

Conclusions

In summary, in the presence of a palladium complex, the addition reaction of various aroyl/heteroaroyl acid anhydrides to norbornenes proceeded, and *trans*-adducts were selectively obtained with the *endo*-benzoyl and *exo*-benzoyloxy groups. The C-O bond of acid anhydride is cleaved and alkene is inserted, giving *β*-hydroxy carbonyl derivatives, i.e., aldols. Aldols are generally synthesized by the coupling of two carbonyl compounds in the presence of a base. The present transition-metal-catalyzed reaction produces aldols using the addition reaction of alkenes and acid anhydrides with simultaneous C-C and C-O bond formation (Scheme 8). The catalytic cleavage of the C-O single bond and the addition reaction to the unsaturated compounds can be a novel method of synthesizing organo-oxygen compounds.



Scheme 8.

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Notes and references

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† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/c000000x/

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