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PALLADIUM CATALYZED DOUBLE SUBSTITUTION REACTIONS OF IODOPHENOL AND IODOANILINE DERIVATIVES WITH HOMO-CONJUGATED COMPOUNDS TO FORM CYCLIC ETHER AND CYCLIC AMINES THROUGH HOMO-CONJUGATED INTERACTION

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Abstract-------Palladium(II) acetate catalyzed double substitution reaction of a bicyclo[2.2.2]octadiene derivative (**1**) with *o*-substituted iodobenzenes afforded six membered cyclic compounds (**3b** and **3c**) *via* a homo-conjugation type interaction accompanied by a five-membered cyclic compound (**4a**). On the other hand, a similar type of reaction but using a bicyclo[2.2.1]heptadiene derivative (**5**) formed only the corresponding five-membered cyclic compound (**6a**).

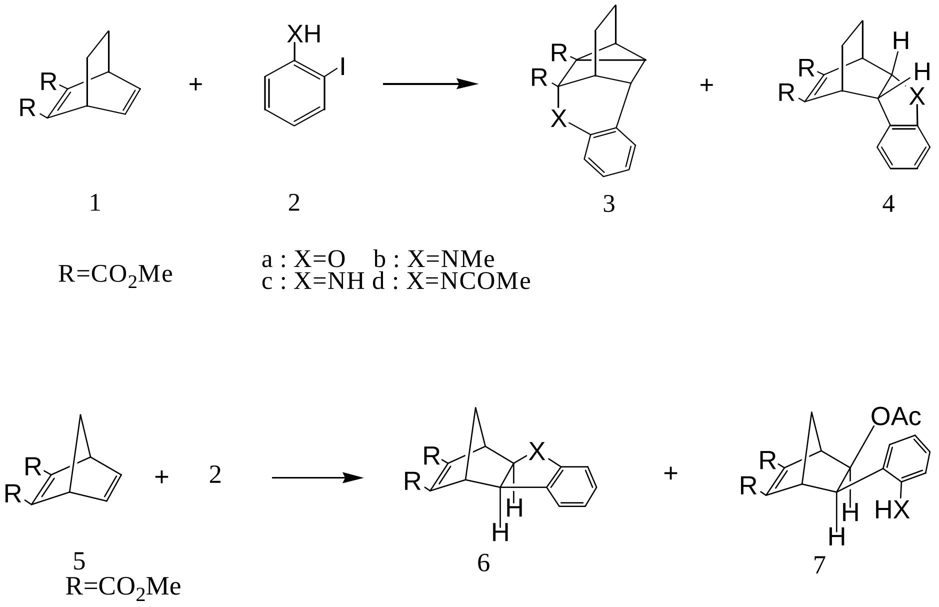
Chemistry of palladium complexes has attracted attention of chemists not only from synthetic utility but also from theoretical stand point.[1] Palladium complexes are well known to catalyze aromatic or vinylic substitution reactions on several kinds of olefinic compounds.[1] Previously, reactions of alcohol derivatives with allenic compounds to form ether derivatives were documented.[2]

As a particular type of conjugation, homo-conjugation has been a target of theoretical investigations of many chemists.[3] A 1,4-cyclohexadiene moiety has a good possibility to construct a bishomo-conjugation system, which is contained in bicyclo[2.2.1]heptadiene and bicyclo[2.2.2]octadiene systems.[4]

Researches on the reactivities of homo-conjugated compounds have been progressed intensively. Homo-Diels-Alder reaction is one of these reactions, which is investigated in detail.[5] While thermal or photochemical behaviors have been investigated extensively, the documents concerning their reactions under the presence of any transition metal complexes are scarce in number.[6]

The authors have researched on reactivities of palladium(II) acetate,[7] and documented on the reactions of homo-conjugated compounds, tricyclo[3.2.2.$0^{2,4}$]nonadiene derivatives with benzene[8] or *o*-iodophenol[9] under the presence of palladium(II) acetate.

As a series of our studies on palladium complexes and strained homo-conjugated compounds,[10] reactions of bicyclo[2.2.1]heptadiene and bicyclo[2.2.2]octadiene systems with phenol and aniline derivatives in the presence of palladium(II) acetate were investigated. Herein the results are discussed.



Scheme 1

A mixture of a bicyclo[2.2.2]octadiene derivative (1), three molar equivalents of *o*-iodophenol (2a), an equimolar amount of palladium(II) acetate, five molar amount of sodium acetate, and an equimolar amount of tetra-*n*-butylammonium chloride in acetonitrile was refluxed for 3 days. After filtration and evaporation of the solvent, the resulted residue was thin-layer chromatographed on silica gel to give a five-membered cyclic ether compound (4a) in 42 % yield. The same type of reaction but using a bicyclo[2.2.1]heptadiene derivative (5) afforded the corresponding five-membered cyclic ether (6a) in 83 % yield.

The analogous reactions with *o*-iodoaniline derivatives showed an obvious substitution effect. Thus a reaction of **1** with *o*-iodo-*N*-methylaniline (**2b**) resulted in a formation of an another type of compound, *i.e.*, a homo-conjugated type six-membered cyclic amine compound (**3b**) in 25 % yield. On the other hand, a reaction of **2b** with **5** failed to form any isolable product except the recovery of the starting materials. However, the reaction with *o*-iodoacetanilide (**2d**) afforded a product (**7d**) through an attack of an acetate ion.

The results of these reactions of **1** and **5** with phenol and aniline derivatives are summarized in the following table.

Table. Yields of Pd-catalyzed reactions of 1 or 5 with 2a-d

Homo-conjugated compounds	Benzene derivatives	Yields of products (%)
1	a : X = O	4a : 42
	b : X = NMe	3b : 25
	c : X = NH	3c : 7
	d : X = NCOMe	0
5	a : X = O	6a : 83
	b : X = NMe	0
	c : X = NH	0
	d : X = NCOMe	7d : 16

The structures of the products were deduced on the basis of their spectral properties[11] and confirmed by good resemblance of these properties with those of the analogous compounds.[12] The structure of **7d** was finally decided by a single crystal X-Ray analysis.

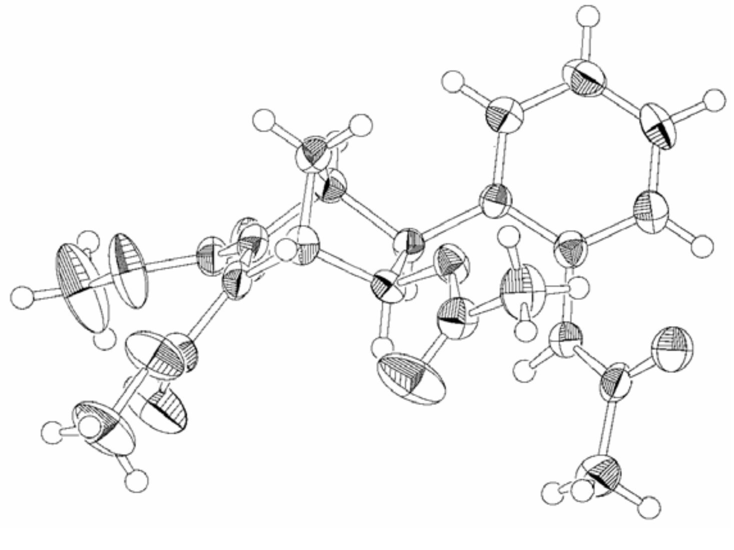
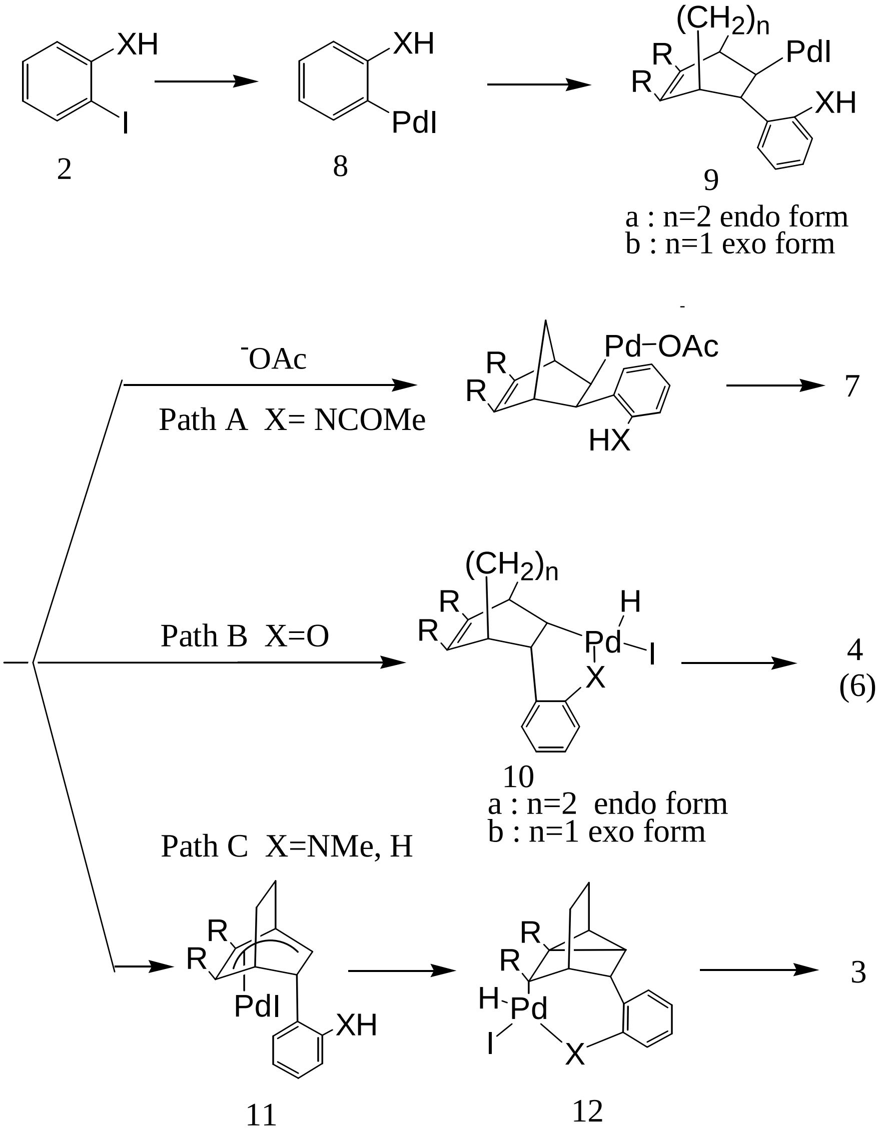


Figure. 1

The reactions are considered to proceed as follows. Reactions of palladium(II) acetate with the aryl iodides (2) generate an aryl palladium complex (8). An addition of 8 to the homo-conjugated compounds (1 or 5) forms a palladium σ-complex (9).[13] An attack of an acetate ion to 9 affords 7 (Path A). On the other hand, the five-membered cyclic ether compounds (4 or 6) are formed *via* a six-membered cyclic σ-complex (10) (Path B).

A σ-π transformation in 9 generates a palladium π-complex (11)[14] (Path C). The subsequent insertion of palladium to the XH bond forms a seven-membered cyclic σ-complex (12), which then affords the final product (3).



Scheme 2

An obvious difference can be seen in the type of product between the reactions of 1 and 5. Thus, the reaction of 1 generated both six- (3) and five- membered cyclic compounds (4).

Contrary to this, only the five-membered cyclic compound (**6**) was afforded in the reaction of **5**. This discrepancy is thought to be explained by the differences in the steric hindrance in the exo-space of **1** and **5**. An extensive exo-space of **5** leads the addition of **8** from the exo-side to form the palladium σ-complex (**9b**), which can generate only the cyclic complex (**10b**). Thus, the product of the reaction of **5** becomes only exo-products.

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11. The spectral properties of the typical compounds are as follows.

    3b.: Brown oil. HRMS m/z 327.1452 Calcd for $C_{19}H_{21}O_4N$: 327.1471. IR (neat): 2951, 1730 cm^{-1}. ^{1}H NMR (CDCl$_3$) δ 1.44〜1.96 (m, 5 H), 2.29 (s, 1 H), 2.33 (d, J = 8.0 Hz, 1 H), 2.80 (s, 1 H), 2.98 (s, 3 H), 3.77 (s, 3 H), 3.84 (s, 3 H), 6.56 (m, 2 H), 6.90 (dd, J = 7.2, 1.6 Hz, 1 H), 7.10 (m, 1 H).

    4a.: Yellow oil. HRMS m/z 314.1126 Calcd for $C_{18}H_{18}O_5$: 314.1149. IR (neat): 2951, 1719 cm^{-1}. ^{1}H NMR (CDCl$_3$) δ : 1.50 (m, 2 H), 1.54 (m, 2 H), 3.41 (d, J = 3.9 Hz, 1 H), 3.57 (s, 3 H), 3.57 (dd, J = 3.9, 2.8 Hz, 1 H), 3.65 (dd, J = 3.9, 9.1 Hz, 1 H), 3.73 (s, 3 H), 5.00 (dd, J =9.1, 3.9 Hz, 1 H), 6.65 (d, J = 7.4 Hz 1 H), 6.78 (t, J = 7.4 Hz, 1 H), 7.05 (t, J = 7.4 Hz, 1 H), 7.13 (d, J = 7.4 Hz, 1 H)

    6a.: Colarless crystals. HRMS m/z 300.0982 Calcd for $C_{17}H_{18}O_5$: 300.0993. IR (KBr): 2988, 1711 cm^{-1}. ^{1}HNMR (CDCl$_3$) δ : 1.68 (m, 1 H), 1.79 (m, 1 H), 3.30 (s, 1 H), 3.59 (s, 1 H), 3.75 (dd, J = 5.4, 2.0 Hz, 1 H), 3.81 (s, 3H), 3.84 (s, 3H), 5.05 (dd, J = 5.4, 2.0 Hz, 1H), 6.76 (d, J = 7.3 Hz, 1H), 6.87 (t, J = 7.3 Hz, 1H), 7.14 (t, J = 7.3 Hz, 1H), 7.21 (d, J = 7.3 Hz, 1H)

    7d.: Colarless crystals. HRMS m/z 401.1457 Calcd for $C_{21}H_{23}O_7N$: 401.1474. IR (KBr): 3331, 1734, 1718 cm^{-1}. ^{1}HNMR (CDCl$_3$) δ : 1.60 (s, 3 H) 2.13 (d, 1 H, J = 9.7 Hz), 2.24 (s, 3 H) 2.40 (d, J = 9.7 Hz, 1 H), 3.33 (d, J = 6.6 Hz, 1 H), 3.36 (s, 1 H), 3.44 (s, 1 H), 3.79 (s, 3 H), 3.83 (s, 3 H), 5.37 (d, J = 6.6 Hz, 1 H), 7.21 (m, 2 H), 7.57 (m, 2 H).

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