

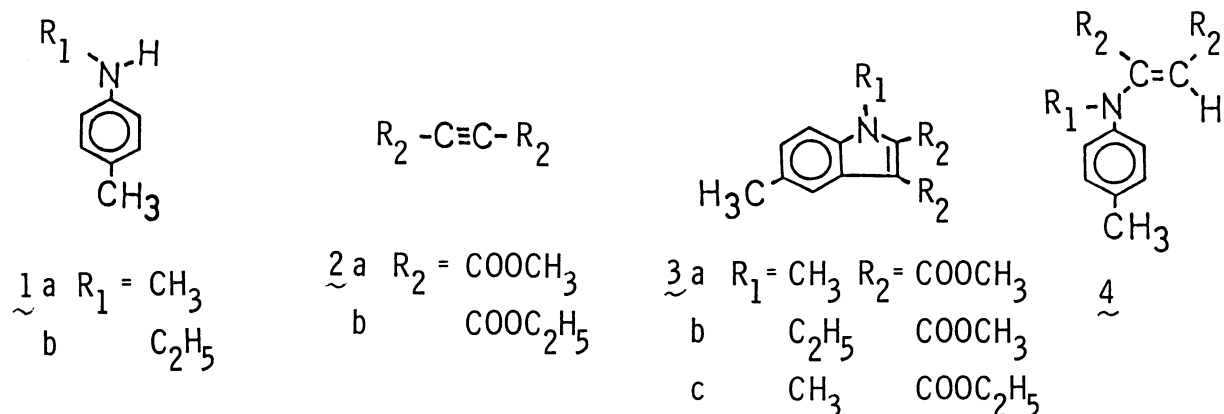
PALLADIUM-PROMOTED AROMATIC ANNELEMENT WITH  
ACETYLENE DICARBOXYLATES

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Benzene rings of N-alkyltoluidine and benzene (or iodobenzene) in acetic acid were annelated with acetylenedicarboxylates by palladium(II) acetate to give N-alkylindole-2,3-dicarboxylate and naphthalene-1,2,3,4-tetracarboxylate. The formation of the products are explained in terms of toluidine radical cation intermediates.

Recent work elucidates that N,N-dialkylanilines react with Pd(II) compounds to give the radical cation intermediates which may lead to interesting oxidation products.<sup>1)</sup> On the other hand, many palladium-catalyzed intramolecular cyclizations which are usually explained in terms of polar mechanisms in nature, have been reported to convert functionalized anilines into aromatic fused heterocyclic compounds.<sup>2)</sup> We now report novel palladium-promoted annelation of benzene (or iodobenzene) and N-alkylanilines with acetylenedicarboxylates to give naphthalene-1,2,3,4-tetracarboxylates and 1-alkylindole-2,3-dicarboxylates, respectively. Since one-pot formation of naphthalenes by annelation of acetylenes onto benzene rings has been hitherto unknown,<sup>3)</sup> some related reactions were also investigated from mechanistic view-points. The reactions are reasonably explained in terms of homolytic process of toluidine radical cation intermediates.



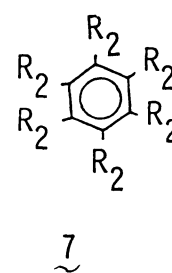
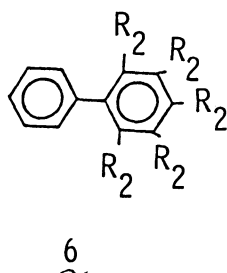
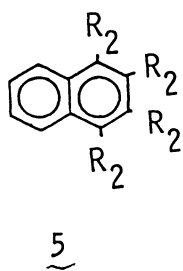


Table 1. Aromatic Annellation with Acetylene Dicarboxylate

Run	Aromatics (mmol )	Alkyne (mmol )	Metals (mmol )	Products
1.	<u>1a</u> , (10) Benzene (900)	<u>2a</u> (10)	Pd(II) <sup>a)</sup> (10)	<u>3a</u> , 24% <sup>b)</sup> ( 24% <sup>c)</sup> <u>4a</u> , 5.8% ( 5.8%) <u>5a</u> , 24% ( 12%)
2.	<u>1b</u> , (10) Benzene (900)	<u>2a</u> (10)	Pd(II) <sup>a)</sup> (10)	<u>3b</u> , 22% ( 22%) <u>4b</u> , 26% ( 26%) <u>5a</u> , 2.0% ( 1.0%)
3.	<u>1a</u> , (4.8) Benzene (450)	<u>2b</u> (4.8)	Pd(II) <sup>a)</sup> (4.8)	<u>3c</u> , 3.2% ( 3.2%) <u>4c</u> , 1.0% ( 1.0%) <u>5b</u> , 39% ( 20%)
4.	<u>1a</u> , Benzene, Iodobenzene (10) (450) (22.5)	<u>2a</u> (5.0)	Pd(II) <sup>a, d)</sup> (0.5)	<u>3a</u> , 7.3% ( 73%) <u>4a</u> , trace ( 1.0%) <u>5a</u> , 43% ( 220%)
5.	<u>1a</u> , Toluene, Iodobenzene (10) (380) (45)	<u>2a</u> (10)	Pd(II) <sup>a, d)</sup> (1.0)	<u>3a</u> , 3.0% ( 30%) <u>4a</u> , 9.5% ( 94%) <u>5a</u> , 17% ( 86%)
6.	Benzene (450)	<u>2a</u> (5.0)	Pd(II) <sup>a)</sup> (5.0)	<u>5a</u> trace (trace) <u>6a</u> , 31% ( 10%)
7.	Benzene, Iodobenzene (450) (10)	<u>2a</u> (5.0)	Pd(II) <sup>a)</sup> (0.5)	<u>5a</u> , 4.5% ( 23%) <u>6a</u> , 1.4% ( 4.5%) <u>7a</u> , 8.9% ( 30%)
8.	<u>1a</u> , Benzene (10) (1700)	<u>2a</u> (10)	Pd(II) <sup>a)</sup> /Cu(II) <sup>e)</sup> (2.0) (10)	<u>3a</u> , 5.3% ( 26%) <u>4a</u> , 0.8% ( 4.1%) <u>5a</u> , 4.2% ( 11%)

a) Pd(OAc)<sub>2</sub> and acetic acid (40 ml) as a solvent were used.

b) Yields are based on 2.

c) Yields are based on Pd(II).

d) Triphenylphosphine and triethylamine were added.

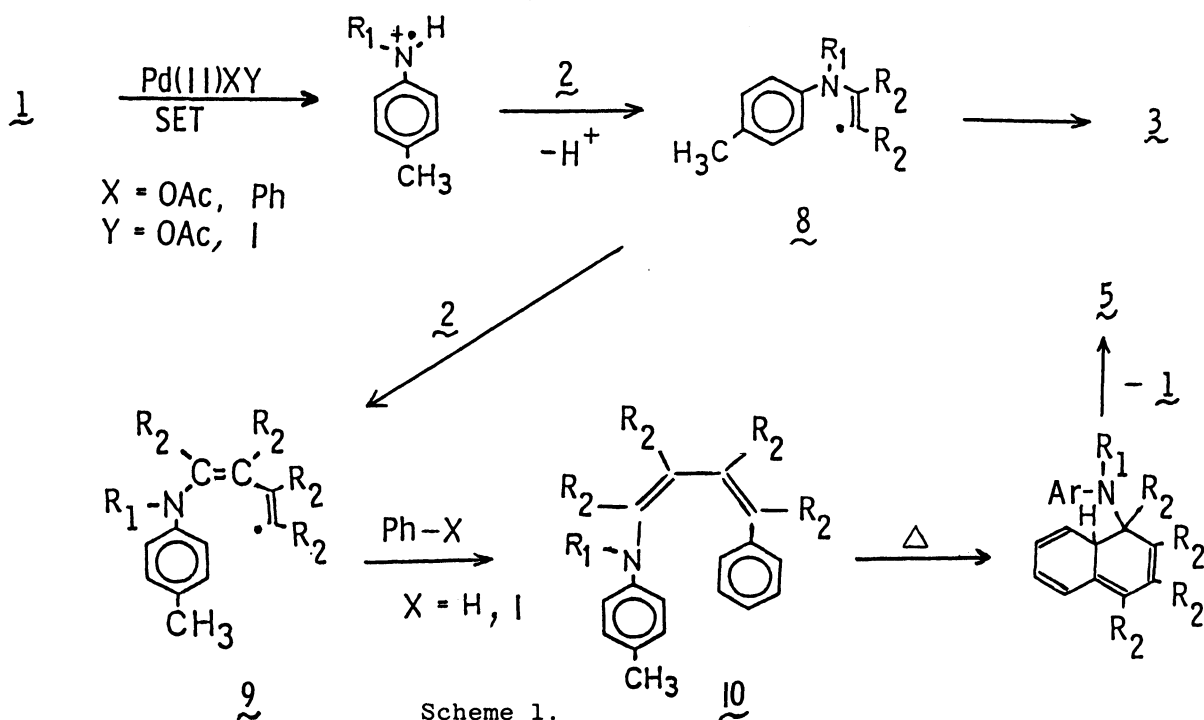
[Pd(II): P(Ph)<sub>3</sub>:NEt<sub>3</sub>=1:2:7]

e) Cu(OAc)<sub>2</sub> was used.

In a typical experiment, a mixture of N-methyl-p-toluidine (1a, 10 mmol), benzene (900 mmol), dimethyl acetylenedicarboxylate (2a, 10 mmol), and Pd(OAc)<sub>2</sub> (10 mmol) in acetic acid (40 ml) was stirred at 60 °C for 5 h under an atmosphere of nitrogen. After usual work-up, 2.35 mmol of dimethyl 1,5-dimethylindole-2,3-dicarboxylate (3a) and 1.20 mmol of tetramethyl naphthalene-1,2,3,4-tetracarboxylate (5a) were isolated by silica gel column-chromatography, together with 0.58 mmol of dimethyl N-methyl-N-(p-tolyl)aminomaleate (4a) and 1.84 mmol of recovered 1b. The use of N-ethyl-p-toluidine (1b) or diethyl acetylenedicarboxylate (2b) in place of 1a or 2a gave the corresponding products as were summarized in Table 1. The typical 3 and 5 were characterized as follows; 3a: IR (KBr) 1700, 1740 cm<sup>-1</sup> (-COOCH<sub>3</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 7.82 (s, 1H), 7.45-7.07(m, 2H), 3.90(s, 3H), 3.82(s, 3H), 3.67(s, 3H), 2.37(s, 3H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>, TMS) δ 164.7(s), 163.3(s), 135.4(s), 134.4(s), 132.3(s), 126.3(d), 125.5(s), 121.8(d), 109.8(d), 107.7(s), 52.9(q), 51.4(q), 31.4(q), 21.5(q). MS m/e 261(M<sup>+</sup>), 230, 171. Found: C, 64.20; H, 5.77; N, 5.27. Calcd for C<sub>14</sub>H<sub>15</sub>NO<sub>4</sub>: C, 64.37; H, 5.75; N, 5.36. 5a: IR (KBr) 1740 cm<sup>-1</sup> (-COOCH<sub>3</sub>). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 7.57-8.23 (m, 4H), 3.93 and 4.03(s, 6H, resp.). MS m/e 360(M<sup>+</sup>), 329. Found: 360.0825. Calcd for C<sub>18</sub>H<sub>16</sub>O<sub>8</sub>: 360.0845.

Iodobenzene is known to be an effective reoxidant of metallic palladium.<sup>4)</sup> The aromatic annelation catalytically proceeded in the presence of iodobenzene (runs 4 and 5). Therein, the improved yields of 5a may show that iodobenzene also should be one of reactants leading to 5a. Moreover, the reactions of 2a with benzene or iodobenzene in the absence of 1 resulted in formation of various cyclized oligomers of 2a, such as 6a<sup>5)</sup> or 7a,<sup>6)</sup> along with relatively poor yields of 5a. The results suggest that 5a might be derived from a common intermediate with that of 3. The metallocyclic intermediates shown in olefin annelation by 2<sup>7)</sup> may not be important concerning the formation of 5.

The possibility of intramolecular cyclization of 4 as an intermediate to give 3 was investigated. The reaction of 4a with an equimolar amount of Pd(OAc)<sub>2</sub> at 60 °C was relatively slow in a mixed solvent of acetic acid and benzene, and only after 24 h gave 48.6 % of 3a (based on consumed 4a; the conversion of 4a, 83%). Furthermore, a similar reaction of 4a with a catalytic amount of Pd(OAc)<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> complex [4a:Pd(II)=25:1] at 90 °C for 20 h<sup>8)</sup> formed 44.6% of 1a (conversion of 4a, 89%), together with some oligomers of 4a, but neither 3a nor 5a. Thus, the formation of 3a in the present aniline annelation by 2a may not be completely attributed to 4a. It has been already elucidated that the reaction of N,N-dialkylanilines with palladium(II) compounds may involve a single electron transfer process.<sup>1)</sup> A similar SET process between 1 and Pd(II) species might generate the radical cation intermediate of 1 which could react with 2 to form vinyl radicals (8) followed by intramolecular aromatic substitution to produce 3. A possible mechanism for the formation of 3 and 5 is tentatively shown in Scheme 1. Therein, the product 5 is explained in terms of homolytic addition and substitution by 8, and subsequent thermal electrocyclization of conjugated aromatic diene (10). Copper(II) salts are known to be an effective radical scavenger.<sup>9)</sup> The suppression of the aromatic annelation in the presence of Cu(II) (run 8), in spite of its ability to reoxidize metallic palladium, may support the homolytic process.



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- 5) **6a**: mp 152-154°C, IR(KBr) 760, 700  $\text{cm}^{-1}$  (-Ph),  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  3.48 and 3.90 (s, 6H,  $-\text{CH}_3$ , resp.), 3.87 (s, 3H,  $-\text{CH}_3$ ), 7.03-7.50 (m, 5H, Ar-H), MS m/e 444( $\text{M}^+$ ), 413, 381.
- 6) **7a**: IR(KBr) 1745  $\text{cm}^{-1}$  ( $-\text{CO}_2\text{CH}_3$ ),  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  3.83 (s, 18H,  $-\text{CH}_3$ ), MS m/e 427( $\text{M}^+$ ), 396, 395.
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- 8) Iodobenzene was added (Pd:PhI=1:100).
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