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PALLADIUM(II)-CATALYZED OXIDATIVE COUPLING OF ARENES BY THALLIUM(III)+

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Abstract - *Oxidation of benzenes with electron-donating and moderate electron-withdrawing substituents by thallium(III) trifluoroacetate in the presence of catalytic amounts of palladium(II) acetate affords biaryls in good yields. The GLC study of the isomer distribution has shown that 4,4'-biaryls are the major products. Thus, the pure 4,4'-biaryls can be easily isolated either by recrystallization or column chromatography. The competitive experiments and kinetic study using arenes and arylthallium derivatives as starting materials as well as quenching experiments have demonstrated the first step of the reaction to be fast thallation of arene to form arylthallium intermediate* $ArTl(OOCCF_3)_2$*. The latter undergoes the rate-determining transmetallation step reacting with monomeric complex* $Pd(OAc)_2$*, which is formed upon depolymerization of trimer* $Pd_3(OAc)_6$*. Subsequent fast decomposition of arylpalladium species gives the final reaction products. The thallation of arene and substitution of* Tl^{III} *for* Pd^{II} *in* $ArTl(OOCCF_3)_2$ *are characterized by the slopes of Hammett plots of -5.6 (*σ^+*) and -3.0 (*σ*), respectively.*

Palladium(II)-catalyzed oxidative coupling of arenes appears to be very promising among other modern methods of biaryl formation.[1,2] This method, however, has one substantional drawback. When a substituted benzene is utilized all possible isomeric biaryls are formed and the relative yield of any particular isomer never exceeds markedly the yields of the remaining isomers.[3-6] It has been accounted for in terms of a low selectivity of initial palladation of arene, which is believed to determine the isomer distribution.[6,7] Thus, an obvious approach to increase the selectivity is to replace palladation for other more selective metallation procedure as an initial step of the reaction. Unger and Fouty have shown[8] that the addition of Hg^{II} to the reaction mixture increases the selectivity of the toluene coupling with respect to 4,4'-isomer as a result of the substitution of initial palladation for more selective mercuration. Thallation is known[9-11] to be even more selective than mercuration. One might expect that coupling of thallium(III) with palladium(II) could be more useful. The first attempt to utilize Tl^{III} and Pd^{II} did not lead to substantional increase in the selectivity[12] (for reasons see

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+Abbreviations used: TFA - trifluoroacetic acid, TTFA - thallium(III) trifluoroacetate.

below). However, recent works have demonstrated that a combination of Tl^{III} and Pd^{II} compounds in a variety of catalytic reactions gives good results. In particular, arylthallium compounds can be easily transformed to aromatic esters,[13] arylolefins,[14,15] or biaryls[16] in the presence of catalytic amounts of Pd^{II}. Recently, it has been shown that toluene reacts with CO in the presence of TTFA to produce, after a work up, almost exclusively p-toluic acid.[17] The present paper shows that TTFA and Pd^{II} acetate constitute a highly efficient catalytic system of biaryl formation. The results of the study of isomer distribution and the reaction kinetics together with the proposed mechanism are also given. The preliminary communication has been published elsewhere.[18]

RESULTS and DISCUSSION

Synthetic Procedure and Isomer Distribution. A majority of runs have been performed in arene as a solvent, sometimes in the presence of TFA (5-10%), using TTFA as an oxidant and catalytic amounts of Pd^{II} acetate. Under these conditions arenes undergo oxidative coupling, eqn.1, to form biaryls without noticable amounts of by-products, as it is evident from GLC analysis. Yields of biaryls and

$$2\ ArH + Tl^{III}(OOCCF_3)_2 \xrightarrow{Pd^{II}} Ar\text{-}Ar + Tl^{I}(OOCCF_3) + 2\ HOOCCF_3 \qquad (1)$$

their isomer distribution under various conditions are shown in Tables 1 and 2.

The most important feature of reaction (1) is a high selectivity with respect to 4,4'-biaryls. Under certain conditions the yields of 4,4'-biaryls exceed 70%, providing a convenient method for the synthesis of pure symmetrical biaryls which can be easily isolated from a crude product either by recrystallization from EtOH or column chromatography

A series of mono-substituted benzenes with electron-donating (Me,Et, OMe) and moderate electron-withdrawing substituents (F, Cl, Br) can be converted to respective biaryls by reaction (1). The ability of disubstituted benzenes to react depends on their structure. Para-xylene does not react, but ortho-xylene gives smoothly only one isomer of bixylenyl, Table 1.

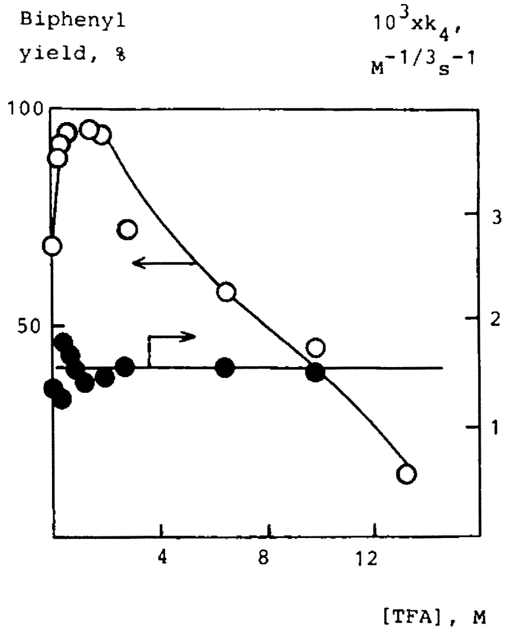

Fig.1. The dependence of the biphenyl yield (○) and k_4 (●) on TFA concentration. [TTFA]=0.05 M, [Pd(II)]= 0.001 M, 70°C, 40 h.

The stoichiometric oxidation of arenes by Pd^{II} acetate to biaryls proceeds under the same conditions as in the presence of TTFA, but much slower giving a wide distribution of all possible isomers, Table 2. run 1, typical for palladium(II)-promoted oxidative coupling.[3-6] It is of interest that TTFA without Pd^{II} is able to couple benzene or toluene, Table 2, runs 2,3. Previously this type of reaction has been reported to proceed only with electron-rich arenes.[19] The 'poorest' in the series anisole affords 4,4'-dianisyl only in a 16% yield in a TFA solvent. In our case, i.e. using arene as a solvent, electron-withdrawing substituents also lower the yield of biaryl. In particular, the yield of bitolyl was higher compared to that of biphenyl, and we did not

Table 1. Oxidation of arenes to biaryls by TTFA in the presence of Pd^{II} acetate in arene solvent. TTFA - 1.0 mmol, Pd(II) acetate - 0.02 mmol, solvent - 20 ml, 70°C. The yields were determined by GLC.

Arene	Time (h)	Total yield of biaryl, %, based on TTFA	Yield of 4,4'-biaryl, %, based on total Ar_2	m. p.[a] of 4,4'biaryl (°C)	lit. m. p.
Anisole	20	79	69.1	177	174[b]
ortho-Xylene	20	83	99.3[c]	75	76-77[d]
Toluene	40	95	74.2	122-123	123-124[e]
Ethylbenzene	20	61	71.9	83-84	76-78[f]
Benzene	40	98		70	69[g]
Fluorobenzene	40	81	52.0	81-85[h]	88.5[i]
Chlorobenzene	50	78	73.0	150	148-149[i]
Bromobenzene	60	71	53.5	165	166.5-167[i]

[a] Pure 4,4'-isomers were obtained by recrystallization from EtOH except 4,4'-dianisyl, which was separated by column chromatography (silica gel, chloroform-hexane); [b] G. W. K. Cavill, D. H. Solomon, *J. Chem.Soc.*, 1955, 1404; [c] 3,4,3',4'-tetramethylbiphenyl; [d] W. Crossley, C. H. Hampshire, *J. Chem.Soc.*, 99, 721, 1911; [e] Y. Fujiwara, I. Moritani, K. Ikeganai, S. Teranishi, *Bull.Chem.Soc. Jpn.*, 43, 863, 1970; [f] ref. 5; [g] ref. 3; [h] we failed to separate 2,4'- and 4,4'-isomers; [i] B. Williamson, W. H. Rodebush, *J.Amer.Chem.Soc.*, 63, 3018, 1941.

observe the formation of difluorobiphenyl. Probably, the change of the solvent results in an extention of the series of arenes able to form coupled products.

We have found that pure TFA is a very unfavorable medium for the coupling process in the Tl^{III}-Pd^{II} system.[20] The yield of biphenyl drops to 10-20% in TFA, Fig. 1. On the other hand the addition of low concentrations of TFA increases the yield of biphenyl, Fig. 1. Since it is known that TTFA contains substantional amounts of hydrolyzed Tl^{III},[21] a yield increase at a low TFA content may be a result of suppression of hydrolysis by TFA. Some other solvents (acetone, dioxane, and their mixtures with arenes) were also tested, but neither was as good as pure arenes. As it is seen from Table 2, run 3, oxidation without Pd^{II} is less selective with respect to 4,4'-isomer compared with catalytic process (1). The difference will be discussed later in the light of the reaction mechanism.

Table 2 points out some factors affecting the selectivity. An increas in $[Pd^{II}]$ at a fixed $[Tl^{III}]$ shifts the isomer distribution towards that typical of Pd^{II} oxidations, runs 5-7, 14-16, the effect being more pronounced for electron-poor arenes. A possible reason is some contribution of a direct oxidation of arenes by Pd^{II} at enhanced $[Pd^{II}]$ without involving TTFA. Temperature increase decreases the selectivity, runs 12,17. Finally, addition of small concentrations of TFA has no effect on the selectivity.

TTFA is not very useful synthetic reagent since it is unstable, highly susceptible to hydrolysis, and contains Tl^{I} admixture.[21] It has been shown recently[21] that TTFA can be replaced for a more available $Tl(OAc)_3 x 1.5H_2O$ in the presence of TFA in arene thallations. We have found that in our case $Tl(OAc)_3 x 1.5H_2O$ in the presence of 5-10% of TFA possesses the same reactivity as TTFA without any loss in the selectivity, Table 2, runs 8-9. Thus, the optimal reaction conditions to obtain the highest yields of 4,4'-substituted biaryls with electron-donating and moderate electron-withdrawing groups are TTFA or $Tl(OAc)_3 x 1.5H_2O$ as oxidants in the medium of oxidizing arene containing

Table 2. The dependence of the isomer distribution of biaryls on reaction conditions. [TTFA] = 0.05 M.

Run	Arene	Temp. (°C)	$10^3 \times [Pd^{II}]$ (M)	Yield (%)	Isomer distribution (%)					
					2,2'	2,3'	2,4'	3,3'	3,4'	4,4'
1	PhMe	70	44.3[a]	51	2.2	20.4	14.3	20.8	25.3	17.0
2	PhH	70	-	43						
3	PhMe	70	-	65	-	0.2	0.6	18.8	43.5	36.9
4	PhOMe	70	2.8	79	0.2	-	30.7	-	-	69.1
5	PhMe	70	0.1	72	0.02	0.05	0.18	2.1	25.32	72.33
6	-"-	70	1.1	75	0.1	0.1	0.3	1.8	23.5	74.2
7	-"-	70	10.2	88	2.7	4.5	5.2	4.4	25.6	57.6
8	-"-	70	0.1[b]	77	-	0.03	0.13	2.09	26.08	71.67
9	-"-	70	1.0[b]	83	-	0.15	0.41	1.96	24.47	73.01
10	PhEt	20	2.5	39	-	0.8	1.6	1.3	19.9	76.4
11	-"-	70	5.1	62	0.04	0.06	0.10	2.2	25.7	71.9
12	-"-	140	6.8	54	0.4	1.3	1.4	7.2	36.1	53.6
13	PhF	70	1.1	81	2	2	43	-	1	52
14	PhCl	70	0.6	78	0.2	1.8	7.3	0.6	17.1	73.0
15	-"-	70	1.3	76	0.3	1.4	8.9	0.6	17.3	71.5
16	-"-	70	10.8	86	4.5	8.0	18.2	2.4	18.2	48.7
17	-"-	135	7.1	48	11.4	16.3	21.7	2.8	19.2	28.6
18	PhBr	70	0.9	71[c]	0.5	4.5	24.0	1.2	16.3	53.5

[a] Without TTFA; [b] in the presence of $Tl(OAc)_3 \times 1.5H_2O$ and 5% of TFA; [c] monobromobiphenyls are also formed in a 8% yield.

5-10% v/v of TFA at low concentrations of Pd^{II} acetate at 70°C.

Competitive experiments. This type of the study gives information about the origin of a reaction selectivity.[22,23] The results of the competitive oxidations of arenes and benzene are summarized in Table 3. Runs 6-8 from the Table show that the isomer distribution is slightly dependent on a degree of convertion. However, since the effect is small we will neglect this variation in calculations presented below.

Assuming that both arene (ArH) and benzene (PhH) are attacked in the Tl^{III}-Pd^{II} system simultaneously with the rate constants k_A and k_B, respectively, the ration k_A/k_B may be calculated using eqn. 2.

$$\frac{k_A}{k_B} = \frac{[PhH]^n}{[ArH]^n} \; \frac{[Ar_2] + \frac{1}{2}[ArPh]}{[Ph_2] + \frac{1}{2}[ArPh]} \qquad (2)$$

where n is the reaction order in arene; $[Ar_2]$, $[ArPh]$, and $[Ph_2]$ are the

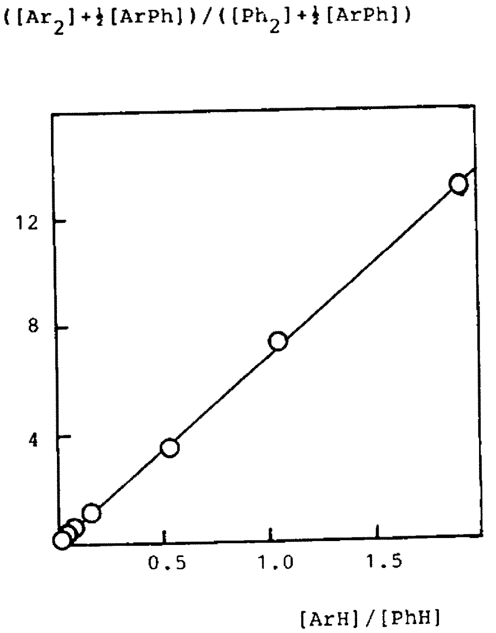

Fig. 2. The plot $([Ar_2]+\frac{1}{2}[ArPh])/([Ph_2]+\frac{1}{2}[ArPh])$ against the ratio [ArH]/[PhH], see eqn. 2. The data from Table 3. ArH = PhEt.

Table 3. A competitive oxidation of benzene and various arenes. [TTFA] = 0.05 M, [Pd(II)] = 0.002 M, 70°C.

Run	Arene	$\frac{[PhH]}{[ArH]}$	Time (h)	$[Ph_2]$ (%)	[ArPh] (%)	$[Ar_2]$ (%)
1	PhOMe	11.0	20	-	1.8	98.2
2	-"-	29.2	20	0.1	4.7	95.2
3	-"-	61.1	20	0.4	12.5	87.1
4	$o\text{-}Me_2C_6H_4$	30.9	4	8.9	51.0	40.1
5	-"-	30.9	10	11.3	52.2	36.5
6	PhMe	1.0	0.1	-	12.9	87.1
7	-"-	1.0	2	1.3	16.4	82.3
8	-"-	1.0	20	1.3	18.4	80.3
9	PhEt	0.59	20	0.5	13.5	86.0
10	-"-	1.00	20	1.2	20.1	78.7
11	-"-	2.06	20	4.7	36.2	59.1
12	-"-	5.52	20	17.3	52.9	29.8
13	-"-	12.4	20	39.0	48.8	12.2
14	-"-	32.7	20	66.7	30.8	2.5
15	-"-	68.9	20	84.4	15.1	0.5
16	PhCl	0.064	20	35.1	50.0	14.9
17	PhBr	0.050	20	32.0	53.3	14.7
18	-"-	0.050	50	26.9	53.8	19.3
19	PhEt[a]	12.4	20	8.2	47.0	44.8
20	-"-	32.7	20	20.9	53.7	25.4

[a] In the presence of C_6D_6.

concentrations of the respective biaryls formed. Data from Table 3, runs 9-15, are presented in coordinates of eqn. 2 in Fig. 2. The latter shows that the reaction is a first-order process in arene. The slope of a linear plot is equal to k_A/k_B. Thus obtained ratios k_A/k_B for other arenes are collected in Table 4. The value of kinetic isotope effect of 4.0±0.5 was calculated from the data of runs 19-20, Table 3.

The data from Tables 2 and 3 have been used to calculate the partial rate factors[23] f_o, f_m, and f_p, collected in Table 4, according to eqn. 3

$$f_i = \frac{6k_A}{k_B} \times \frac{\%[\text{isomer}]}{l \times 100} \qquad (3)$$

where l=2 for ortho and meta isomers, l=1 for para isomer; %[isomer]=[ii]+ +½[ij]+½[ik], here [ii], [ij], and [ik]

Table 4. The ratios k_A/k_B and the partial rate factors, calculated from the data of Tables 2 and 3.

Arene	k_A/k_B	f_o	f_m	f_p
PhOMe	1050	485	-	5330
$o\text{-}Me_2C_6H_4$	55.6	0.58[a]	166[b]	
PhMe	8.0	0.048	3.6	40.8
PhEt	7.7	0.024	3.5	39.2
PhCl	0.045	0.0065	0.014	0.23
PhBr	0.043	0.016	0.012	0.19

[a] f_{om}; [b] f_{mp}.

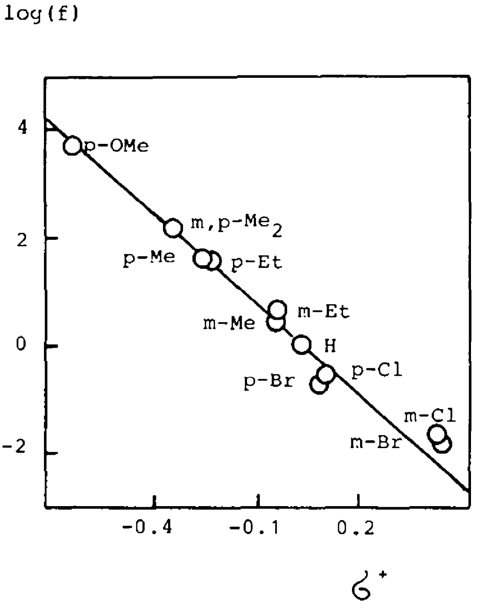

Fig. 3. The Hammett plot of $\log(f_p)$ and $\log(f_m)$ against σ_p^+ and σ_m^+, respectively. Data from Table 4.

are percent yields of symmetrical and two unsymmetrical biaryls, respectively. Fig. 3 depicts the plot of $\log(f_p)$ and $\log(f_m)$ against σ_p^+ and σ_m^+, respectively, with a slope $\rho = -5.6$. This value is very close to those reported for arene thallation of -6.9[9] and -5.3,[21] but much more negative than that for palladation, $\rho = -2.2$.[6] The partial rate factors as well as the relative rate constants k_A/k_B are also very close to those reported for thallation[9,24] and differ markedly from those reported for palladation.[6] Finally the deuterium kinetic isotope effect of

Table 5. The kinetic data for reaction (1) in the presence of 5-10% TFA.

Run	Arene	Temp. (°C)	10^3x[Pd^{II}] (M)	10^2x[TTFA] (M)	10^4xk_{obs} (s^{-1})	10^3xk_4 ($M^{-1/3}s^{-1}$)	Mean value 10^3xk_4
1	PhOMe	70	0.1	2.5	6.7	14.3	14.6±0.4
2	-"-	70	1.0	2.5	15.0	15.0	
3	o-$Me_2C_6H_4$	70	0.1	2.0	3.3	7.2	8±1
4	-"-	70	1.0	2.0	9.2	9.2	
5	PhMe	70	1.0	1.0	4.5	4.5	4.3±0.3
6	-"-	70	1.0	1.5	4.0	4.0	
7	PhH	50	0.1	5.0	0.14	0.32	0.33±0.02[a]
8	-"-	50	1.0	5.0	0.35	0.35	
9	-"-	60	0.1	5.0	0.28	0.62	0.7±0.1[a]
10	-"-	60	1.0	1.0	0.82	0.82	
11	-"-	60	1.0	2.4	0.82	0.82	
12	-"-	60	1.0	5.0	0.70	0.70	
13	-"-	60	1.46	0.24[b]	0.89	0.78	0.71±0.08
14	-"-	60	1.46	0.58[b]	0.78	0.69	
15	-"-	60	1.46	1.41[b]	0.82	0.72	
16	-"-	60	1.46	2.52[b]	0.76	0.67	
17	-"-	70	0.1	5.0	0.83	1.83	1.7±0.3[a]
18	-"-	70	0.3	5.0	1.28	1.83	
19	-"-	70	1.0	5.0	1.60	1.60	
20	-"-	70	12.4	5.0	3.07	1.33	
21	PhCl	70	1.34	5.0	0.30	0.27	0.29±0.02
22	-"-	70	10.8	5.0	0.67	0.30	

[a] $\Delta H^{\#}$ = 73.5 kJ/mol; $\Delta S^{\#}$ = -84.9 J/K mol; [b] without TFA.

4.0 found in this study is in good agreement with those reported for thallation, 3.7[9] and 4.3.[21] (For palladation it is higher, 5.0[7]). All these observations convincingly demonstrate that Tl^{III} rather than Pd^{II} attacks arene initially in our system. There is only one apparent discrepancy. Although usually the yields of ortho-thallated toluene and ethylbenzene are 10-25%,[9,25] the yields of 2-substituted coupled derivatives of these arenes are much lower, Table 2, runs 5-6, 11. The explanation of this finding is given below.

Kinetic study. Most of kinetic runs were performed in the presence of 5-10% of TFA, since the reproducibility was much better under these conditions than in pure arene. At the same time TFA does not alter the reaction rate, Fig. 1. Obviously, the suppression of TTFA

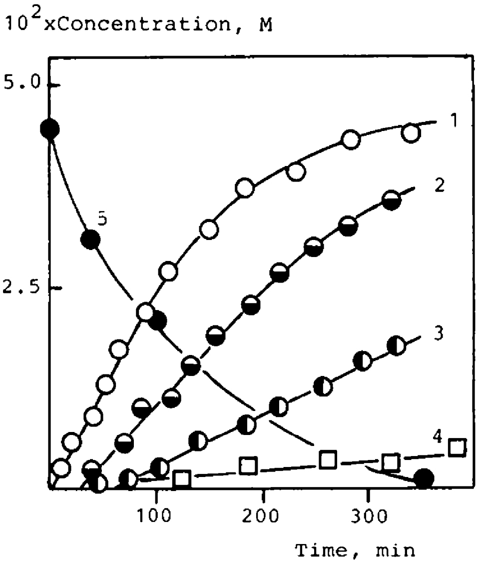

Fig.4. The kinetic curves of biaryl formation (1,2,3, and 4) and phenyl iodide 'consumption' (5), see text. [TTFA]=0.05 M, 1(○)[Pd(II)]=0.001 M, 70°; 2(◒)[Pd(II)]=0.001 M, 60°; 3(◑)[Pd(II)]=0.001 M, 50°; 4(□) without Pd(II), 70°; 5(●)[Pd(II)]=0.001 M, 70°.

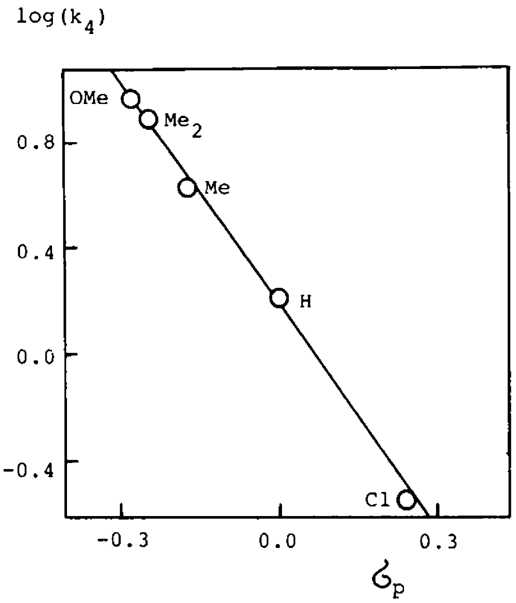

Fig. 5. The Hammett plot of $\log(k_4)$ against σ_p.

hydrolysis discussed above is manifested here.

Typical kinetic curves are shown in Fig. 4. A simple first-order kinetics is observed at 70°C, k_{obs} being independent of [TTFA], Table 5. At lower temperatures there are noticable induction periods. In these cases k_{obs} were calculated using the portions of the curves after induction periods. Pd^{II} concentration has little effect on the reaction rate, Table 5. The logarithmic treatment of the data gives the reaction order in Pd^{II} of 0.33±0.05. Thus the complete rate equation is

$$\frac{d[Ar_2]}{dt} = k_4[TTFA][Pd^{II}]^{1/3} \qquad (4)$$

Here k_4 includes a constant solvent arene concentration and $k_{obs} = k_4[Pd^{II}]^{1/3}$. The values of k_4 are summarized in Table 5. Fig. 5 shows the Hammett type correlation between $\log(k_4)$ and σ_p with a slope $\rho = -3.0$.

Since the competitive experiments have shown that Tl^{III} attacks arenes in the initial reaction step, it is of interest to investigate a reaction of arylthallium derivative as a starting material with Pd^{II} acetate under the same conditions. We have found that this reaction is a catalytic process with respect to Pd^{II} and follows equation (5).

$$2\,ArTl(OOCCF_3)_2 \xrightarrow{Pd^{II}} Ar\text{-}Ar + Tl(OOCCF_3)_3 + Tl(OOCCF_3) \qquad (5)$$

Some representative kinetic data of reaction (5) are included in Table 6. The reaction follows equation (6).

$$\frac{d[Ar_2]}{dt} = k_6[ArTl(OOCCF_3)_2] \times [Pd^{II}]^{1/3} \qquad (6)$$

Table 6 lists the rate constants k_6. It is evident that both the rate eqns. 4 and 6 and numerical values of the rate constants k_4 and k_6 are the same within experimental errors. This suggests that arene thallation to form arylthallium intermediate should be fast and subsequent palladium-catalyzed decomposition of the latter is the rate-determining.

Quenching experiments. Taylor and McKillop have shown[26] that arylthallium compounds are easily converted to respective aryl iodides in the presence of KJ thus providing a convenient diagnostic method of analysis of whether an aryl-thallium bond is formed

Table 6. The kinetic data for reaction (6).

Run	Solvent	$\underline{Ar}Tl(OOCCF_3)_2$	Temp. (°C)	$10^3 \times [Pd^{II}]$ (M)	$10^2 \times [ArTl^{2+}]$ (M)	$10^4 \times k_{obs}$ (s^{-1})	$10^3 \times k_6$ ($M^{-1/3}s^{-1}$)
1	PhCl	$p\text{-}ClC_6H_4$	70	1.4	5.0	0.25	0.22
2	-"-	-"-	70	10.3	5.0	0.72	0.33
3	PhH	C_6H_5	60	0.1	2.4	0.25	0.53
4	-"-	-"-	60	1.0	2.4	0.48	0.48
5	PhH	$p\text{-}MeC_6H_4$	70	1.0	1.0	4.5	4.5

or not. We applied the method to our system.

Intermediate arylthallium species were quenched with KJ and organic products of reaction (7) analyzed by GLC.

$$ArTl(OOCCF_3)_2 + 2\ KJ \longrightarrow ArJ + TlJ + 2\ KOOCCF_3 \qquad (7)$$

We have found that treatment of the reaction mixture thermostatted for 30 min at 70°C either in the presence or in the absence of Pd^{II} with KJ gives aryl iodide which concentration is close to [TTFA]. When Pd^{II} is present the concentration of PhJ decreases with a concomitant increase in biphenyl concentration, Fig. 4, curves 1 and 5, indicating that phenylthallium is converted to biphenyl.

The quenching technique has been also used to clarify almost complete absence of ortho-substituted biaryls in the case of toluene and ethylbenzene and the absence of coupled products in the case of para-xylene despite of a known ability of TTFA to form ortho-thallated compounds, see refs. 9, 25.

The mixture of PhEt, TTFA, and TFA was thermostatted at 70°C for 30 min, then a part of the solution was quenched with KJ to form three isomeric ethylbenzene iodides, Fig. 6. To the other part of the solution Pd^{II} acetate was added to start the coupling procedure. After 30 and 80 min aliquots of the solution were withdrawn and quenched with KJ. The products formed were analyzed by GLC. The results in Fig. 6 show that only para- and meta-thallated ethylbenzenes are consumed reacting with Pd^{II}, while ortho-thallated ethylbenzene does not react with Pd^{II} and remains intact.

The reaction mechanism. All the results are consistent with the mechanism shown on the Scheme, which involves

$$ArH + TlX_3 \xrightarrow{k_A} ArTlX_2 + HX \qquad (8)$$

$$Pd_3(OAc)_6 \overset{K_9}{\rightleftharpoons} 3\ Pd(OAc)_2 \qquad (9)$$

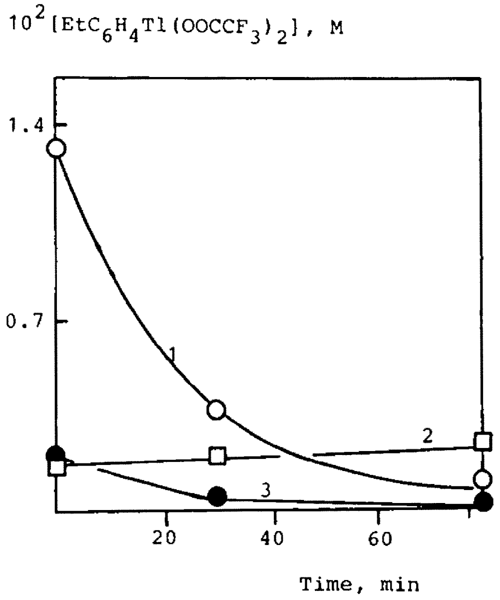

Fig. 6. The change of concentration of isomers of $EtC_6H_4Tl(OOCCF_3)_2$ (1(○)para, 2(☐)ortho, 3(●)meta) with time during the formation of diethylbiphenyls from ethylbenzene. [TTFA] = 0.02 M, [Pd(II)] = = 0.00022 M, 70°C.

$$ArTlX_2 + Pd(OAc)_2 \xrightarrow{k_{10}} ArPd(OAc) + TlX_2(OAc) \qquad (10)$$

$$2\ ArPd(OAc) \xrightarrow{fast} Ar\text{-}Ar + Pd(OAc)_2 + Pd^o \qquad (11)$$

$$Pd^o + Tl^{III} \xrightarrow{fast} Pd^{II} + Tl^I \qquad (12)$$

Scheme

fast thallation of arene to form arylthallium intermediate, step (8). Palladium(II)-catalyzed decomposition of the latter leads to biaryl, steps (10), (11). The fractional order in Pd^{II}, eqns. 4 and 6, has been observed previously in palladium-catalyzed arene[27] and alkene[28] reactions and can be accounted for depolymerization phenomena. The dominant form of Pd^{II} acetate in benzene is trimer $Pd_3(OAc)_6$ which undergoes reversible depolymerization to monomer $Pd(OAc)_2$.[29] Thus, the reaction order of 1/3 implies that monomer is a reactive species. According to this proposal we have found the reaction order in Pd^{II} to increase up to 0.75 upon addition of the excess of acetate ions (n-Bu_4N]OAc) or up to 0.5 performing the reaction in boiling benzene. Both factors are known to induce $Pd_3(OAc)_6$ depolymerization.[29,30] The route of $ArTlX_2$ to the final reaction products is a sequence of the rate-determining transmetallation (10) and fast reductive decomposition of arylpalladium species to afford biaryl, step (11). The mechanism put forward is in line with those accepted for related Pd^{II}-promoted processes.[2] Let us discuss some features of reaction (1) in terms of the proposed mechanism.

The reaction selectivity is governed by steps (8) and (10). Thallation is one of the most selective electrophilic substitution processes with respect to para-isomer among those involving metal ions.[10,11] However, the isomer distribution of thallated arenes is time-dependent due to actual isomerization of thallated product.[9] More stable meta-isomer is accumulated on standing of a reaction mixture.[9] This accounts for a higher content of 4,4'-biaryls in reaction (1) compared with that without Pd^{II}. It is seen from Fig. 4 that biaryl formation in the presence of Pd^{II} is faster than in the absence of the latter, although step (8) giving arylthalliums is fast. So the arylthallium intermediate may undergo isomerization providing an equilibrium isomer distribution of low selectivity. Transmetallation step (10) not only 'freezes' the most selective[9] initial isomer distribution, but introduces an additional second act of selection. Step (10) is rather sensitive to steric effects. When Tl^{III} is ortho to metyl or ethyl groups in $ArTlX_2$, no reaction of the latter with Pd^{II} is observed, while in the case of less bulky groups (Cl, F, OMe) a steric demand is lower and transmetallation proceeds. This observation makes clear why para-xylene does not couple and ortho-xylene gives the only isomer. In competitive experiments another type of selectivity is manifested, namely with respect to arene substituent. Since the attack of Pd^{II} in step (10) is characterized by negative ρ, $ArTlX_2$ with a more donor aryl group should react faster. This is a possible reason for the time dependence of a product distribution shown in Table 3, runs 6-8. Evidently tolylthallium will be converted first affording bitolyls and monomethylbiphenyls, but only later the convertion of phenylthallium giving biphenyl and additional amounts of monomethylbiphenyl will be observed.

The Hammett constant $\rho = -3.0$, Fig. 5, refers to the reaction of $ArTlX_2$ with Pd^{II}, step (10). The value is in agreement with $\rho = -2.2$ found for direct palladation of arene.[6] A more positive ρ for palladation compared with thallation accounts for a higher contribution of a direct reaction with Pd^{II} for arenes with electron-withdrawing groups, see above.

The relative reactivity of Tl^{III} and Pd^{II} towards arenes depends on reaction conditions. In particular, Tl^{III} reacts with benzene much slower than Pd^{II} acetate does in acetic acid solvent containing $HClO_4$.[7] Thus, under the latter conditions $Tl(OAc)_3$ may participate only as palladium reoxidant in reaction (1). That is why addition of Tl^{III} to the system Pd^{II} acetate - toluene - HOAc - methane sulfonic acid does not improve the isomer distribution.[12]

Less clear is the effect of high concentrations of TFA on the product yield in reaction (1), Fig. 1. Obviously, the change of the solvent has minor effect on step (8), since in pure TFA thallation is almost quantitative.[21,26] More likely that TFA inhibits somehow a transformation of arylthallium intermediate. It has been reported[31] that Pd^{II} trifluoroacetate reacts with arenes forming rather stable complexes of

Table 7. The conditions of chromatographic analysis and retention volumes of biaryls with respect to biphenyl.

R	Temp. (°C)	Flow rate (ml/min)	$R-C_6H_4-C_6H_4-R$						$R-C_6H_4-Ph$		
			2,2'	2,3'	2,4'	3,3'	3,4'	4,4'	2	3	4
Me	180	20-30	0.96	1.41	1.54	2.44	2.59	2.74	0.96	1.54	1.68
Et	210	30-40	1.55	2.05	2.36	3.91	4.43	4.96	1.15	2.00	2.22
OMe	220	30-40	2.14	3.58	4.10	5.93	6.69	7.15	1.54	2.40	2.66
F	160	15-20	0.62	0.68	0.71	-	0.78	0.82			
Cl	210	20-30	2.01	2.88	3.10	4.46	4.66	4.90	1.33	2.00	2.11
Br	230	30-40	3.43	5.15	5.65	8.50	8.93	9.50	1.83	2.86	3.00

Pd^I. So one of the possible reasons for a low yield under these conditions is the convertion of Pd^{II} to some unreactive arene complexes of Pd^I.

Conclusion. A combination of TTFA and Pd^{II} acetate affords a useful system for oxidative coupling of arenes to form biaryls. Only catalytic quantities of rather expensive palladium salt is required. The system appears to be rather regiospecific; a double selection provides a formation of predominantly 4,4'-biaryls. More available $Tl(OAc)_3x1.5H_2O$ can be used in the presence of small concentrations of TFA. Benzenes with electron-donating and moderate electron-withdrawing substituents undergo the reaction readily. This method is unapplicable to arenes with bulky substituents, initial thallation of which would lead mainly to ortho-thallated products.

EXPERIMENTAL

Materials. Published methods were used for preparation of metal salts: thallium(III) trifluoroacetate,[26] thallium(III) acetate sesquihydrate,[32] and palladium(II) acetate.[29] All the arenes and TFA were Reakhim reagents and purified by standard procedures.[33] Arylthalliums $PhTl(OOCCF_3)_2$, $p\text{-}MeC_6H_4Tl(OOCCF_3)_2$, and $p\text{-}ClC_6H_4Tl(OOCCF_3)_2$ were synthesized according to Taylor and McKillop method.[26]

Methods. GLC analyses were performed with a Chrom-5 gas chromatograph. Most of reaction mixtures were analyzed using a 3.6 m column packed with 15% Apiezon L on Chromaton N-AW (Chemapol). Carrier gas was nitrogen. Tetramethylbiphenyls were analyzed at 220°C, flow rate 30-40 ml/min, retention volumes 2.15 (2,3,2',3'), 3.27 (2,3,3',4'), and 5.84 (3,4,3',4') and unsymetrical dimethylbiphenyls 1.47 (2,3) and 2.34 (3,4) with respect to biphenyl; ethylbenzene iodides at 135°C, flow rate 15-20 ml/min, retention volumes 2.77 (2), 3.03 (3), and 3.21 (4) with respect to PhJ. The data for other biaryls are given in Table 7.

In kinetic measurements a 2.0 m column packed with 5% Silicone DC 550 on Chromaton N-AW (Chemapol) was used under conditions given above. Naphtalene and biphenyl were used as internal standards in the case of oxidation of benzene and all other arenes, respectively.

General procedure of biaryl synthesis from arenes. The solution of TTFA (0.543 g, 1.0 mmol) or thallium(III) acetate sesquihydrate either in the presence or in the absence of TFA (5-10% by volume) (TFA was always necessary in the case of acetato salt) and palladium(II) acetate (0.01 g, 0.045 mmol) in aromatic hydrocarbon (20 ml) was thermostatted at 50-70°C for an appropriate period of time. Then the solvent was evaporated in *vacuo* and the residue extracted three times with hot n-hexane. Hexane fractions were combined, concentrated, and passed through a short silica gel column to remove traces of metals (eluent chloroform -hexane mixtures). Evaporation of a solvent gave crystalls of biaryl, from which a pure 4,4'-isomer was obtained either by recrystallization from ethanol or by column chromatography using ca. 20 cm column (silica gel - hexane). Only 4,4'-difluorobiphenyl was not isolated in a pure form, since we failed to separate the mixture of 2,4'- and 4,4'-isomers.

Competitive experiments. For conditions see *General procedure*. The arene - benzene mixture was used in this case. The ratio [benzene]/[arene] employed was dependent on a reactivity of arene. After work up of the reaction mixture products were analyzed by GLC using naphtalene as internal standard.

Kinetic measurements. Reactions (1) and (5) were followed by GLC. Aliquots (0.2-0.5 ml) were withdrawn from the reaction mixture and diluted with hexane in which naphtalene or biphenyl was dissolved. The solution was washed with dilute nitric or acetic acid to remove the traces of metals. The concentration of biaryls was measured by GLC. The pseudo-first-order rate constants k_{obs} were calculated from a least-squares treatment of the linear $\ln(A_{\infty}-A)$ *versus* time plots. Accuracy of rate constants determination was 10-15%.

Quenching experiments. Aliquots (5-10 ml) were taken from reaction mixtures. The solvent was removed in *vacuo*. Aqueous KJ was added to the residue and a subsequent treatment was performed in full accord with the method of Taylor and McKillop.[26] Organic products were extracted with ether, dried over $MgSO_4$, concentrated up to 10 ml, and analyzed by GLC.

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