portions) and dried under nitrogen.

Preparation of the Guest–Zeolite–Solvent Slurry. Known amounts of guest ketones or acenaphthylene and the activated zeolites were stirred together in 5 mL of hexane (pentane in the case of dibenzyl ketone) for about 2 h. In a typical preparation 200 mg of the zeolite and 5 mg of the guests were taken up in 5 mL of the solvent. The amounts taken in each case were the same as those listed above in the case of dry solid preparations. At the end of 2 h, the hexane layer was analyzed by GC (Hewlett-Packard Model 5890, supelcowax capillary column) for the presence of the guest. In no case did we find any guest in the hexane layer, indicating that all the guest molecules initially taken have been adsorbed into the zeolite.

Photolysis of Solid and Slurry Samples. Dry solid samples prepared as above were taken in Pyrex tubes (10 mm diameter and 5 cm length) fitted with Teflon stopcocks, degassed thoroughly (10^{-4} mm), and sealed. These were irradiated with 450-W mercury lamps with Pyrex filters. Irradiation cells were rotated periodically to provide uniform exposure. Generally about 15% conversion was obtained in about 2 h of irradiation. After photolyses, products were extracted by stirring the samples in ether (20 mL) for about 10 h. In some cases the zeolite was dissolved with concentrated HCl and extracted with ether. Control experiments established that the products are stable to the acid extraction conditions. A known amount of internal standard (dibenzyl ketone, 4-methylbenzophenone; α-alkylbenzyl benzyl ketones, pyrene; acenaphthylene, *trans*-stilbene; and valerophenone and octanophenone, dibenzyl) was added to the above extracted solutions and products analyzed by GC. The percentage cage effects in the experiments comprising DBK-d_5 were determined by quantitative single ion monitor GC–MS analysis. Analyses were carried out on a Hewlett-Packard (HP 5890) GC connected to a HP 5988 mass selective detector and a HP 9216 work station. The ion intensities (EI 70 EV) corresponding to DPE-d_0 (AA), DPE-d_5 (AB), and DPE-d_{10} (BB) were monitored simultaneously at M$^+$ 210, 215, and 220. The values obtained were corrected for detector response. Structures of all products have been established earlier, and the spectral data are consistent with the literature reports.[8-11,25]

The guest–zeolite–solvent slurry taken in a Pyrex test tube was bubbled with helium (making sure no evaporation of hexane occurred) for about 10 min and sealed. The above slurry while being magnetically stirred was irradiated with 450-W mercury lamps with Pyrex filters for about 15 min. Solvent hexane (or pentane) was decanted and analyzed by GC. Neither starting reactants nor products were found in the supernatent solvent. Products and reactants from zeolites were extracted by stirring them with diethyl ether (10 mL) for about 10 h. To the ether extract a known amount of internal standard was added, and the mixture was analyzed by GC as above. The mass balance in all cases was ~90%.

Irradiation of ketones and acenaphthylene in hexane in the absence of zeolite were also carried out for comparison.

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Palladium-Catalyzed Coupling Reactions of Aryl Triflates or Halides with Ketene Trimethylsilyl Acetals. A New Route to Alkyl 2-Arylalkanoates

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Palladium complexes with phosphines, in the presence of lithium acetate, catalyze the coupling reaction of aryl triflates and ketene trimethylsilyl acetals to yield alkyl 2-arylalkanoates, 1,1′-bis(diphenylphosphino)ferrocene gives the best results. Aryl halides may also be used, provided that a stoichiometric amount of thallium acetate is present. Added acetate anions act both as palladium-bonded groups in the ArPdL$_2$OAc reactive intermediates and as nucleophiles promoting the Si–O bond breaking of the silyl enolate moiety. The reaction represents a novel method for the preparation of alkyl 2-arylalkanoates which, after hydrolysis, afford the corresponding 2-arylalkanoic acids, well known as antiinflammatory and antipyretic drugs.

Introduction

Ketene silyl acetals are extensively used in organic synthesis as enolate equivalents for aldol condensations and Michael addition reactions.[1] The coupling reaction is catalyzed either by Lewis acids as TiCl$_4$[2-5] or by nucleophiles as fluoride anions.[6] Recently it has been found that Pd–phosphine or phosphine free complexes catalyze the coupling reactions of ketene silyl acetals and allylcarbonates to yield α-allylated carboxylic esters.[7,8] Since aryl triflates and aryl bromides are electrophiles widely used in carbon–carbon bond formation reactions catalyzed by Pd complexes,[9-15] we deemed it interesting to study

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Table I. Palladium-Catalyzed Coupling Reaction of $C_6H_5OSO_2CF_3$ (1a) and (*E*)-$CH_3CH{=}C(OCH_3)[OSi(CH_3)_3]$ (2b)[a]

run	ligand[b]	Pd/ligand (molar ratio)	Pd/1a (molar ratio)	3ab yield,[c] %
1	DPPF	1:2	1:50	73
2	DPPF	1:2	1:100	72
3	DPPF	1:2	1:200	70
4	DPPF	1:1	1:50	13
5	DPPB	1:2	1:50	24
6	DPPP[d]	1:2	1:50	10
7	DPPE	1:2	1:50	traces
8	PPh_3	1:3	1:50	15

[a] Catalyst: $(\eta^3\text{-}C_4H_7PdOAc)_2$ and the appropriate phosphorous ligand; **1a**:**2b** = 1:1 (molar ratio); lithium acetate *1a* = 2:1 (molar ratio); THF at reflux temperature; reaction time, 6 h. [b] DPPF = 1,1'-bis(diphenylphosphino)ferrocene; DPPB = 1,4-bis(diphenylphosphino)butane; DPPP = 1,3-bis(diphenylphosphino)propane; DPPE = 1,2-bis(diphenylphosphino)ethane. [c] Yields estimated by GLC with an appropriate internal standard. [d] Reaction time 12 h.

their reactivity with ketene trimethylsilyl acetals. The particular interest of aryl triflates stems from their stability and facile preparation from the corresponding phenols.

Results and Discussion

Aryl triflates and ketene trimethylsilyl acetals couple in the presence of Pd(0) tertiary phosphine complexes and lithium acetate to yield methyl 2-arylalkanoates according to eq 1. The presence of lithium acetate in the reaction medium is essential in order the reaction to occur.

$$\underset{\mathbf{1a{-}e}}{ArOTf} + \underset{\mathbf{2a{-}e}}{R_1R_2{=}C(OR_3)[OSi(CH_3)_3]} \xrightarrow[AcOLi]{PdLn} \underset{\mathbf{3}}{ArCR_1R_2COOCH_3} + (CH_3)_3SiOAc + TfOLi \qquad (1)$$

	Ar		R_1	R_2	R_3
1a:	Ph	**2a**:	H	H	Me
b:	4-NO_2Ph	**b**:	Me	H	Me
c:	4-MeOPh	**c**:	Et	H	Et
d:	2-naphthyl	**d**:	Me	Me	Me
e:	2-(6-MeO-naphthyl)	**e**:	Ph	H	Me

Phenyl triflate (**1a**) and (*E*)-1-methoxy-1-(trimethylsiloxy)propane (**2b**) were chosen as model substrates to investigate both the ligand influence in the conversion to methyl 2-phenylpropanoate (**3**) and to find the best reaction conditions. The results are reported in Table I. The reaction is catalyzed by Pd(0) complexes which are conveniently formed in the reaction medium according to eq 2.

$$\tfrac{1}{2}(\eta^3\text{-methallylPdOAc})_2 + \underset{\mathbf{2b}}{MeCH{=}C(OCH_3)[OSi(CH_3)_3]} + nL \rightarrow PdL_n + CH_2{=}C(Me)CH_2CH(Me)COOCH_3 + AcOSi(CH_3)_3 \qquad (2)$$

Preformed Pd(0) complexes as $Pd(PPh_3)_4$ or Pd_2(dibenzalacetone)$_3$·$CHCl_3$ and the appropriate ligand may also be used although they appear to be somewhat less efficient. The reaction is conveniently run in boiling THF. The yields of cross coupling products markedly depend on the ligands, whose efficiency follows the order: 1,1'-bis(diphenylphosphino)ferrocene (DPPF) ≫ 1,4-bis(diphenylphosphine)butane (DPPB) > 1,3-bis(diphenylphosphino)propane (DPPP) > 1,2-bis(diphenylphosphino)ethane (DPPE), (Table I, runs 1, 5–7).

Table II. Palladium-Catalyzed Coupling of $ArOSO_2CF_3$ 1a–e and 2a–e To Yield $ArCR_1R_2$ ($COOCH_3$) (3)[a]

run	1	2	Pd:1 (molar ratio)	product 3	yield,[b] %
1	**1d**	**2b**	1:50	**3db**	traces[c]
2	**1d**	**2b**	1:50	**3db**	70[d]
3	**1b**	**2b**	1:50	**3bb**	25[d]
4	**1c**	**2b**	1:20	**3cb**	30[c]
5	**1e**	**2b**	1:20	**3eb**	40[c]
6	**1a**	**2c**	1:50	**3ac**	80[c]
7	**1b**	**2c**	1:50	**3bc**	30[d]
8	**1a**	**2a**	1:20	**3aa**	53[c]
9	**1c**	**2a**	1:20	**3ca**	50[c]
10	**1e**	**2a**	1:20	**3ea**	40[c]
11	**1a**	**2e**[e]	1:20	**3ae**	60[c]
12	**1a**	**2d**	1:20	**3ad**	0[c]

[a] Catalyst: $(\eta^3\text{-}C_4H_7PdOAc)_2$/DPPF = 1:4 (mol/mol); **2**/**1** = 1:1 (mol/mol); lithium acetate/**1** = 2:1 (mol/mol); 6 h at reflux. [b] Yields estimated by GLC with an appropriate internal standard. [c] THF solvent. [d] DME solvent. [e] *E*/*Z* ratio = 1:2.

Table III. Palladium-Catalyzed Coupling of Aryl Bromides 4a–e and 2a–e To Yield $ArCR_1R_2(COOCH_3)$ (3)[a]

run	2	4	ligand	3	yield,[b] %
1	**2b**	**4a**	DPPF	**3ab**	70
2	**2a**	**4a**	DPPF	**3aa**	56
3	**2e**[c]	**4a**	DPPF	**3ae**	20
4	**2b**	**4d**	DPPF	**3db**	80
5	**2b**	**4e**	DPPF	**3eb**	80
6	**2b**	**4c**	DPPF	**3cb**	70
7	**2b**	**4b**	DPPF	**3bb**	40
8	**2c**	**4a**	DPPF	**3ac**	80
9	**2c**	**4a**	PPh_3[d]	**3ac**	10
10	**2c**	**4a**	DPPB	**3ac**	8
11	**2c**	**4a**	DPPE	**3ac**	traces

[a] Catalyst: $(\eta^3\text{-}C_4H_7PdOAc)_2$/ligand = 1:4 (mol/mol); 5 mol % palladium catayst; **2**:**4**:TlOAc = 1:1:1 (mol/mol/mol). [b] Yield estimated by GLC with an appropriate internal standard. [c] *E*/*Z* = 1:2. [d] Pd/PPh_3 = 1:3 (mol/mol).

PPh_3 gives intermediate results between those of DPPB and DPPP. In order to widen the scope of the reaction we investigated the cross coupling of a number of ketene trimethylsilyl acetals (**2**) and aryl triflates (**1**). The results are reported in Table II. In some cases the use of a higher boiling solvent as dimethoxyethane (DME) was necessary (Table II, runs 2, 3, 7). Among the ketene silyl acetals investigated, the methyl disubstituted derivative (**2d**) appears to be unreactive, likely due to steric crowding at the vinyl carbon (run 12). Aryl bromides and iodides may also be used as partners in the coupling reaction with (**2**). Appreciable conversion to coupling products was observed provided that a stoichiometric amount of thallium(I) acetate was present (eq 3).

$$\underset{\mathbf{4}}{ArBr} + \underset{\mathbf{2}}{R_1R_2C{=}C(OR_3)[OSi(CH_3)_3]} + TlOAc \xrightarrow{PdLn} \underset{\mathbf{3}}{ArCR_1R_2(COOR_3)} + AcOSi(CH_3)_3 + TlBr$$

Ar: **4a** = phenyl; **4b** = 4-NO_2-phenyl; **4c** = 4-MeO-phenyl; **4d** = 2-naphthyl; **4e** = 2-(6-MeO-naphthyl) (3)

Table III reports the pertinent results. The presence of the methoxy group on the aryl bromide appears to affect the yields of the reaction to a much lower extent than in the triflate case.

We propose the mechanism shown in Scheme I for the coupling reaction. The aryl triflate oxidatively adds to the

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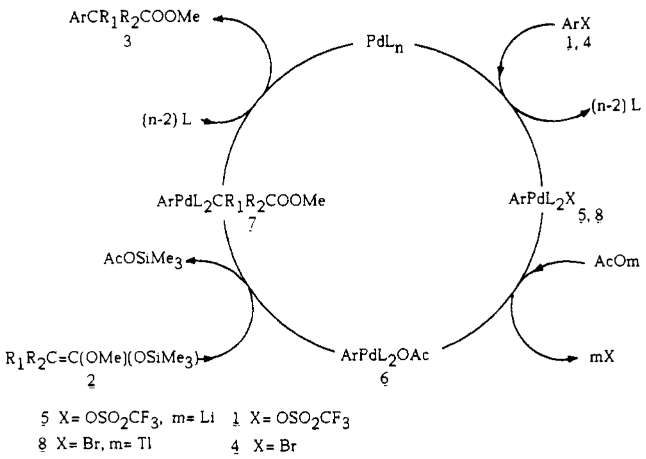
Scheme I



Pd(0) complex to yield the intermediate (**5**). The addition product does not react with ketene silyl acetals as no reaction occurs in absence of acetate anions. The role played by lithium acetate is dual: metathetical displacement of the triflate anion to yield (**6**) and nucleophilic activation of the O–Si bond.[6,16]

The Si–Pd transmetalation yields the Pd complex (**7**) which provides (**3**) through reductive elimination. The acetate complex (**6**) can also be found through oxidative addition of aryl bromides to the Pd(0) phosphine complex followed by metathetical displacement of the halogen in (**8**) with thallous acetate. Complexes (**6**) have been isolated and fully characterized.[17] Recently the coupling reaction of 2-naphthyl triflate with the Reformatsky reagent, BrZnCH(CH$_3$)COOtBu to yield the coupling product analogous to (**3db**) has been reported.[18] The reaction is catalyzed by PdCl$_2$(dppf) reduced with diisobutylaluminum hydride. In spite of the similarity of this catalytic system with ours, conversions to cross-coupling products are rather limited.

Although phosphine-free nickel complexes have been used in the coupling reaction of aryl and vinyl halides with lithium enolates coordination of DPPF to palladium seems to prevent the β-hydrogen elimination from the intermediate.[19] The efficiency of DPPF as ligand in the coupling reaction remains intriguing although not unprecedented.[20,21]

Conclusions

We have found that DPPF-based palladium complexes effectively promote the cross coupling of aryl triflates or halides with ketene silyl acetals. Our reaction represents a simple route to the preparation of α-arylalkanoic acids derivatives which are known to be pharmacologically active as antiinflammatory agents.[22] We are now actively pursuing the synthesis of enantiomeric pure α-arylalkanoic acids through a Pd-catalyzed asymmetric reaction.

Experimental Section

^{1}H NMR spectra were recorded in deuteriochloroform on a Brücker 200 AC instrument; all data are reported in ppm relative to TMS. Mass spectra were recorded either on a Varian MAT 112 F mass spectrometer or on a Finningan MAT INCOS 50 quadrupole mass spectrometer. GC analyses were performed on a DANI 3800 gas chromatograph using (1) a glass column (10 m × 0.22 mm i.d.) coated with SP 2100 (CB), film thickness 1 μm; (2) a silica fused capillary column (30 m × 0.22 mm i.d.) coated with SE-30 (CB), film thickness 1 μm. Peak areas were obtained by using a Spectra Physics SP 4200 computing integrator. Silica gel 60 (230–400 mesh) (Merck) was used for flash chromatography.

Materials. 1,4-Bis(diphenylphosphino)ferrocene was prepared according to ref 23. The other ligands were Fluka products and used as received. (η^3-C$_4$H$_7$PdOAC)$_2$ was prepared reacting (η^3-C$_4$H$_7$PdCl)$_2$ and AcOTl (1:1 molar ratio) in CH$_2$Cl$_2$. Lithium acetate was dried under vacuum at 100 °C for 2 h. Aryl triflates[17] and ketene silyl acetals[24,25] were prepared according to published procedures. Tetrahydrofuran (THF) was distilled prior to use from sodium/benzophenone. Dimethoxyethane was freshly distilled from CaH$_2$; 2-(phenyl)propanoic acid, 2-(4-nitrophenyl)propanoic acid, 2-[2′-(6′-methoxy)naphthyl]propanoic acid, 4-methoxyphenylacetic acid, bis(phenylacetic acid), and phenylacetic acid are commrcially available Aldrich products and were converted, for comparison, to the corresponding esters **3** with standard procedures (either treatment with diazomethane, or with alcohol and gaseous HCl). Methyl 2-(2′-naphthyl)propanoate (**3db**), methyl 2-(4-nitrophenylpropanoate (**3bb**), methyl 2-(4-methoxyphenyl)propanoate (**3cb**), ethyl 2-phenylbutanoate (**3bc**), methyl 2-(6-methoxynaphthyl)acetate (**3ea**), and/or their corresponding acids have been previously reported.[26-30] The catalytic runs were performed under nitrogen purified by passage through R3-11 BASF catalyst.

General Procedure for the Pd-Catalyzed Coupling Reaction. The preparations of methyl α-phenylpropanoate (**3ab**) starting either from phenyl triflate (A) or phenyl bromide (B) are reported as standard procedures.

(**A**) THF (15 mL) was added to a mixture of (η^3-C$_4$H$_7$PdOAc)$_2$ (0.010 g, 0.02 mmol), DPPF (0.050 g, 0.09 mmol), and lithium acetate (0.300 g, 4,5 mmol). The mixture was stirred for a few minutes, and then phenyl triflate (0.508 g, 2.25 mmol) and (*E*)-1-methoxy-1-(trimethylsiloxy)propane (0.360 g, 2.25 mmol) were added. The reaction mixture was refluxed for 6 h and then cooled at room temperature. THF was removed under reduced pressure. The residue was extracted with diethyl ether and passed through a silica gel column. Elution with hexane/ethyl acetate (95/5) yielded pure (**3ab**) (0.250 g, 67% yield). Acetoxy trimethylsilane was also isolated and compared with a pure sample.

(**B**) THF (20 mL) was added to a mixture of (η^3-C$_4$H$_7$PdOAc)$_2$ (0.010 g, 0.022 mmol), DPPF (0.050 g, 0.09 mmol), and TlOAc (0.250 g, 0.95 mmol). Bromobenzene (0.149 g, 0.95 mmol) and (*E*)-1-methoxy-1-(trimethylsiloxy)propane (0.153 g, 0.95 mmol) were then added. After being refluxed for 6 h the reaction mixture was cooled at room temperature and worked up as in A to yield **3ab** (0.095 g, 60% yield).

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Supplementary Material Available: Experimental data for compounds **3ab**, **3db**, **3bb**, **3cb**, **3eb**, **3ac**, **3bc**, **3ca**, **3ea**, **3ae**, and **3aa** (3 pages). Ordering information is given on any current masthead page.

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