experiments samples of 5 were added to a 10-fold excess of tributylstannane in benzene (1.62 or 3.24 M), and the solutions were degassed, heated at 80 °C for 3 h, and then analyzed for 11 and 12 by GC. The results are given in the text.

**Reaction of 8 with Tributylstannane.** The bromide 8 (10.2 mg, 0.046 mmol) was dissolved in benzene (2.0 mL). Tributylstannane (6.2 μL, 0.023 mmol) and a trace of AIBN were added to an aliquot (0.50 mL) of this solution, which was then heated in a sealed tube at 80 °C for 17 h. After distillation (bath 60 °C (50 mm)), the mixture was analyzed by GC-MS analysis (40 °C isothermal). Varying amounts of tributylstannane were added to other aliquots, which were then heated and analyzed in the same way for 11 and 12. Within experimental error the results obtained were the same as those from reactions of 5.

**Acknowledgment.** We thank Mr. A. Wallner for preparing compound 12 and for other technical assistance. One of us (J.Z.) gratefully acknowledges the award of a Postdoctoral Fellowship from the Swiss National Foundation.

**Registry No.** 2, 34680-83-6; 3, 135561-11-4; 4, 135561-12-5; 5, 135561-13-6; 6, 50635-65-9; 7, 135561-14-7; 8, 135561-15-8; 9, 135561-16-9; 11, 135561-17-0; *cis*-12, 13398-31-7; *trans*-12, 14671-83-1; 16a, 16183-00-9; 16b, 75375-38-1; 19a, 23907-66-6; *cis*-19b, 100649-36-3; *cis*-19c, 135561-18-1; $HO(CH_2)_2CH(t\text{-}Bu)(CH_2)_2CO_2Me$, 135561-19-2; $MeP(Ph)_3^+ \cdot Br^-$, 1779-49-3; $H_2C{=}CHCH_2CH(t\text{-}Bu)(CH_2)_2CO_2Me$, 135561-20-5; $HO_2C(CH_2)_2CH(t\text{-}Bu)CH_2CO_2H$, 10347-88-3; $Bu_3Sn$, 688-73-3; $p\text{-}O_2NC_6H_4COCl$, 122-04-3; $o\text{-}O_2NC_6H_4C(O)O(CH_2)_2CH(t\text{-}Bu)(CH_2)_2OH$, 135561-21-6; $o\text{-}O_2NC_6H_4C(O)O(CH_2)_2CH(t\text{-}Bu)CH_2CHO$, 135561-22-7; $H_2C{=}CHCH_2CH(t\text{-}Bu)CH_2C(O)OC_6H_4NO_2\text{-}p$, 135561-23-8; *N*-hydroxypyridine-2-thione, sodium salt, 15922-78-8; 3-*tert*-butylcyclopentanone, 5581-94-2; 1-*tert*-butyl-3-methylenecyclopentane, 69217-81-8.

**Supplementary Material Available:** Experimental procedures for the four-step conversion of 6 to 7; $^1H$ NMR spectra of 7, 8, and intermediates between 6 and 7; and the 0.60–0.95 ppm region of the 500-MHz $^1H$ NMR spectrum of a 3:2 mixture of *cis*- and *trans*-12 (9 pages). Ordering information is given on any current masthead page.

# Heck Reaction on Anthraquinone Derivatives: Ligand, Solvent, and Salt Effects

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The palladium-catalyzed Heck reaction of trifluoromethanesulfonates of anthraquinoid systems is described. The outcome of the reaction between methyl acrylate 4 and 1-(9,10-anthraquinoyl)trifluoromethanesulfonate 7 (reduction versus arylation) is strongly correlated to the choice of ligand, solvent, and added salt. The results are explained in terms of different coordination-insertion pathways as a function of the reaction conditions. Best conditions have been transferred to the synthesis of novel anthracyclinone, 4-demethoxy-4-(2'-methoxycarbonyl)ethenyl-13-dioxolanyldaunomycinone 5.

## Introduction

During our studies of structure–activity relationships of antitumor anthracyclines,[1] we needed to prepare substantial quantities of novel 4-substituted anthracyclinones for glycosidation and biological evaluation.[2]

In this context, we have recently developed a new process for the preparation of 4-demethoxydaunomycinone 3, based on the palladium-catalyzed reduction of the key intermediate ketal triflate 2,[3] readily available from the natural daunomycinone 1 (Scheme I).[4] Accordingly, we decided to extend palladium catalysis to carbon–carbon bond formation by exploiting the Heck reaction (arylation of olefin by palladium catalyst).[5]

Unfortunately, the reported procedure for aryl triflates ($Pd(PPh_3)_2Cl_2$, methyl acrylate 4, $Et_3N$, in DMF at 90 °C) failed when 2 was used as substrate.[6] The desired acrylate 5 was not formed, and the only product present in the reaction mixture after 24 h was 6 (Scheme II).

This result prompted us to study in some detail the mechanism of the Heck reaction on anthraquinoid systems, in order to understand the main factors affecting the reaction course.

## Results and Discussion

In our previous work on the palladium-catalyzed reduction of aryl sulfonates in the presence of triethylammonium formate,[3,7] we reported that catalytic systems generated in situ from $Pd(OAc)_2$ and bidentate phosphine ligands like 1,3-bis(diphenylphosphino)propane (DPPP) or 1,1'-bis(diphenylphosphino)ferrocene (DPPF) were much more effective than the $PPh_3$-based one.

These results are in agreement with a recent paper by Dolle and co-workers on palladium-catalyzed alkoxycarbonylation of aryl triflates, where the use of DPPP

(1) Arcamone, F. *Anticancer Agents Based on Natural Product Models*; eds. Cassidy, J. M., Douros, J. D., Eds.; Academic Press: New York, 1980.

(2) (a) Krohn, K. *Tetrahedron* **1990**, *46*, 291. (b) Krohn, K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 790. (c) Kelly, T. R. *Tetrahedron* **1984**, *40*, 4539; Tetrahedron Symposia-in-Print no. 17.

(3) Cabri, W.; DeBernardinis, S.; Francalanci, F.; Penco, S. *J. Chem. Soc., Perkin Trans. 1* **1990**, 428.

(4) Arcamone, F.; Cassinelli, G.; Franceschi, G.; Mondelli, R.; Orezzi, P.; Penco, S. *Gazz. Chim. Ital.* **1970**, *100*, 949.

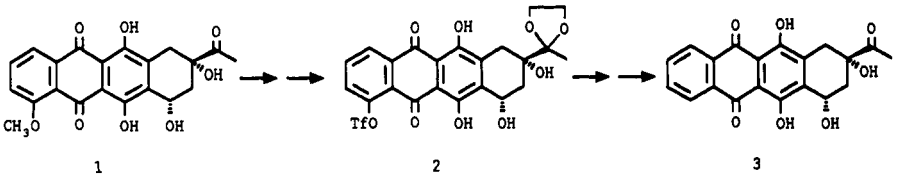
(5) (a) Heck, R. *Org. React.* **1982**, *27*, 345. (b) Heck, R. *Pure Appl. Chem.* **1981**, *53*, 2323. (c) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146.

(6) (a) Tilley, J. W.; Sarabu, R.; Wagner, R.; Mulkerins, K. *J. Org. Chem.* **1990**, *55*, 906. (b) Chen, Q.-Y.; He, Y.-B. *Synthesis* **1988**, 896. (c) Andersson, C. M.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 2112. (d) Tilley, J. W.; Zawoiski, S. *Ibid.* **1988**, *53*, 386. (e) Chen, Q.-Y.; Yang, Z.-Y. *Tetrahedron Lett.* **1986**, *27*, 1171.

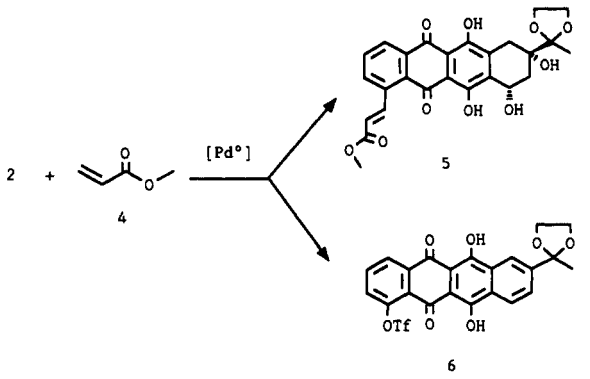
(7) Cabri, W.; DeBernardinis, S.; Francalanci, F.; Penco, S.; Santi, R. *J. Org. Chem.* **1990**, *55*, 350.

0022-3263/91/1956-5796$02.50/0 

**Scheme I**



**Scheme II**



allowed a 500-fold increase in the reaction rate with respect to $PPh_3$.[8]

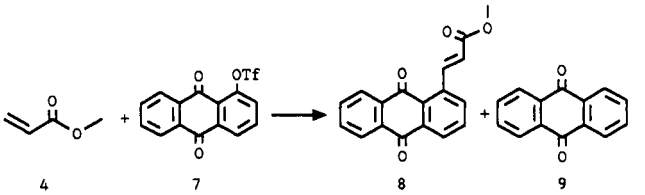
However, both the DPPP- and the DPPF-containing catalyst were ineffective in promoting the reaction of **2** with methyl acrylate **4**.[9] The failure of the Heck reaction is not related to a slow oxidative addition of **2** to the palladium catalyst, which proved to be a very efficient process, as deduced by the results of the catalytic reduction (Scheme III, part a), but is probably attributable either to an inefficient olefin coordination or to a high-energy migration of the aryl moiety onto the coordinated double bond (Scheme III, part b).

In order to find better conditions for the coordination–insertion process, we investigated the reaction between **4** and the model triflate **7**.

A comparative study of different catalysts is reported in Table I. Bis(triphenylphosphine)palladium dichloride in the presence of 10 equiv of **4** at 90 °C gave the arylated product **8** in good yield (entry 1), but was ineffective at 60 °C (entry 2). On the other hand, with the DPPP-containing catalyst the reaction was complete at 60 °C within 1.5 h (entry 3). With DPPF as ligand, we observed a longer reaction time and a mixture of **8** and the reduction product **9** was obtained (entry 4).

Although the model **7** showed different reactivity from compound **2**, the outcome of the reaction with DPPF as ligand suggested that the coordination–insertion step was the major problem in this case too. The **8**/**9** ratio could be used to monitor the effectiveness of the catalytic system for the arylation process. With the catalyst generated in situ from $Pd(OAc)_2$ and DPPP, the molar ratio **4**/**7** had no influence on rate or selectivity (Table II, entries 1 and 2). In contrast, in the presence of DPPF the reaction became slower and less selective for the arylated product **8** be decreasing the olefin excess (entries 3–6). The nature of the solvent affects the selectivity of the reaction significantly using $Pd(OAc)_2$/DPPF as catalyst. When the reaction was carried out in dioxane or DMF, similar results were observed (entries 3 and 7), while in toluene only 4% of 9,10-anthraquinone **9** was formed (entry 8). Complete selectivity for **8** was achieved in DMF using $NaHCO_3$ as base (entry 9).

**Table I. Palladium-Catalyzed Reaction between Methyl Acrylate 4 and Triflate 7. Ligand Effect[a]**



| entry | catalyst (mol %) | $T$, °C | $t$, h | product (yield,[b] %) |
|---|---|---|---|---|
| 1 | $Pd(PPh_3)_2Cl_2$ (10) | 90 | 16 | **8** (91) |
| 2 | $Pd(PPh_3)_2Cl_2$ (10) | 60 | 24 | |
| 3 | $Pd(OAc)_2$/DPPP (5) | 60 | 1.5 | **8** (94) |
| 4 | $Pd(OAc)_2$/DPPF (5) | 60 | 22 | **8** (65) + **9** (24) |

[a] All reactions were run under an argon atmosphere using 0.5 mmol of **7** in the presence of the reported catalytic system, 5 mmol of **4**, and 1 mmol of $Et_3N$ in DMF (0.6 M). [b] Isolated yield.

**Table II. Palladium-Catalyzed Reaction between 4 and 7. Base, Solvent, and Olefin's Equivalent Effect[a]**

| entry | ligand | base | solvent | **4**/**7**[b] | $t$, h | **8**/**9**[c] |
|---|---|---|---|---|---|---|
| 1 | DPPP | $Et_3N$ | DMF | 10 | 1.5 | 100/0 |
| 2 | DPPP | $Et_3N$ | DMF | 5 | 1.7 | 100/0 |
| 3 | DPPF | $Et_3N$ | DMF | 10 | 22 | 71/29 |
| 4 | DPPF | $Et_3N$ | DMF | 5 | 38 | 43/57 |
| 5 | DPPF | $Et_3N$ | DMF | 3 | 48 | 20/80 |
| 6 | DPPF | $Et_3N$ | DMF | | 50 | 0/100 |
| 7 | DPPF | $Et_3N$ | dioxane | 10 | 24 | 66/34 |
| 8 | DPPF | $Et_3N$ | toluene | 10 | 24 | 96/4 |
| 9 | DPPF | $NaHCO_3$ | DMF | 10 | 16 | 100/0 |

[a] All reactions were run under an argon atmosphere using 0.5 mmol of **7** in the presence of 5 mol % of $Pd(OAc)_2$, 5.5 mol % of the ligand, and 1 mmol of the base at 60 °C until the conversion was complete. [b] Molar ratio. [c] Molar ratio determined by HPLC using 1-(9,10-antraquinoyl)tosilate as external standard; the yields, determined by HPLC, were always better then 95%.

These results can be rationalized on the basis of the charge distribution in the oxidative addition complex, in which the palladium atom is linked to the following: (i) an electron-poor carbon atom, due to the presence of the anthraquinoid system; (ii) a trifluoromethanesulfonate counterion strongly dissociated from the metal;[10] (iii) a bidentate phosphine ligand.

If an associative mechanism is ruled out for steric reasons, the coordination of the double bond can occur by displacement of the counterion (Scheme IV, path A) or by displacement of one of the two phosphorus atoms (Scheme IV, path B).

Stang[11] has noted the "exceptional lability" of the $Pt^{(II)}$–OTf bond in the oxidative addition intermediate generated in the reaction between platinum(0) complexes

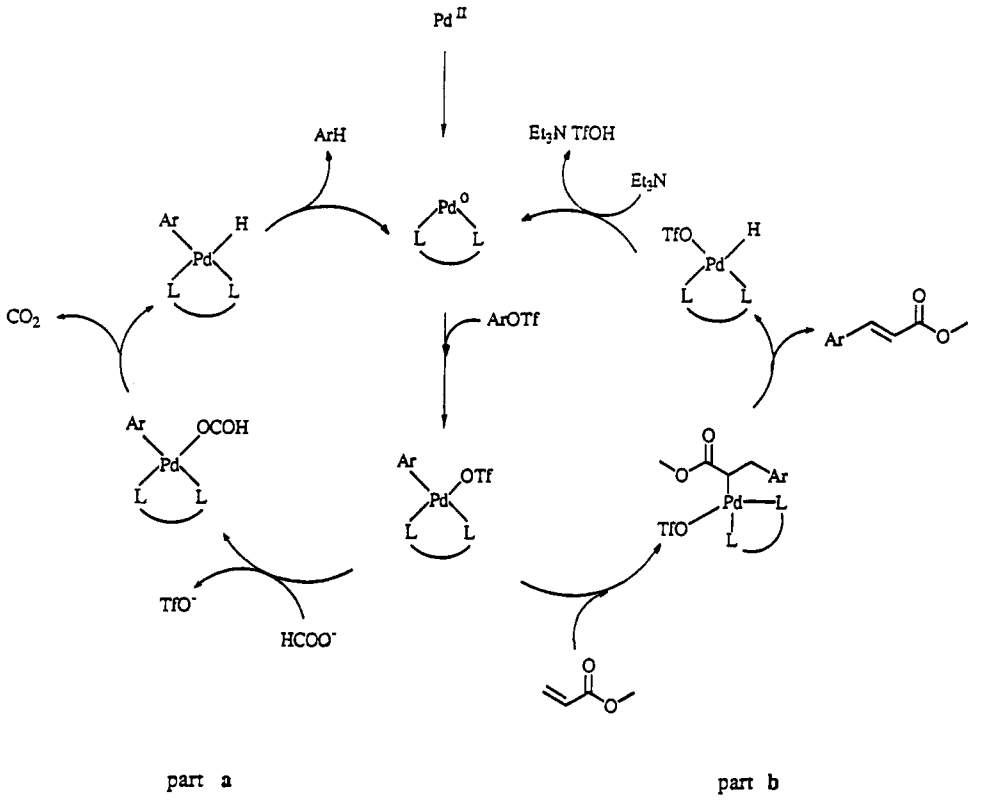
(8) Dolle, R. E.; Schmidt, S. J.; Kruse, L. I. *J. Chem. Soc., Chem. Commun.* **1987**, 904.

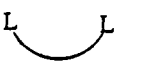
(9) After 24 h at 60 °C in DMF only trace amounts of **6** have been detected.

(10) (a) Lawrence, G. A. *Chem. Rev.* **1986**, *86*, 17. (b) Rimml, H.; Venanzi, L. M. *J. Organomet. Chem.* **1984**, *260*, C52–C54.

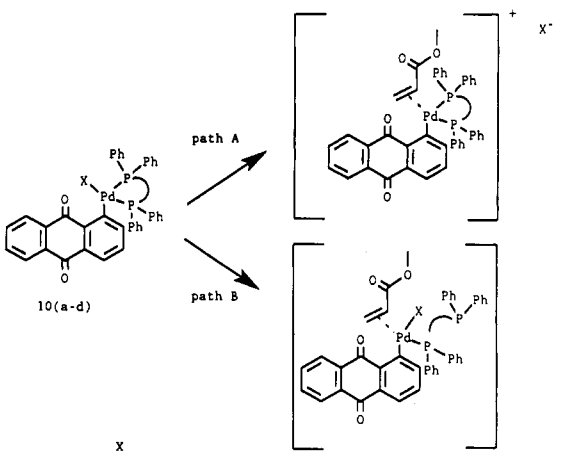
(11) (a) Stang, P. J.; Kowalski, M. H.; Schiavelli, M. D.; Longford, D. *J. Am. Chem. Soc.* **1989**, *111*, 3347. (b) Stang, P. J.; Kowalski, M. H. *Ibid.* **1989**, *111*, 3356.

**Scheme III**



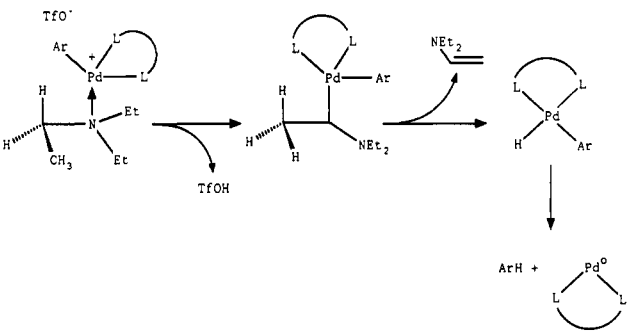

**Scheme IV**




| | X | |
|---|---|---|
| $-(CH_2)_3-$ | TfO | 10a |
| $-(CH_2)_3-$ | Cl | 10b |
| Fe | TfO | 10c |
| Fe | Cl | 10d |

and vinyl triflates. The capability of the trifluoromethanesulfonate anion to be easily exchanged in the oxidative addition complex by neutral ligands has been postulated for the corresponding palladium complexes,[12]

**Scheme V**




and it is reasonable to extend it to our intermediate. According to this hypothesis for triflate **7** in DMF, the coordination occurs preferentially via path A. When the two phosphorus atoms are linked by an alkyl chain, as in **10a**, the charge density on the metal is sufficient to favor the coordination of **4**, and compound **8** is obtained selectively. On the other hand, if a ferrocenyl moiety is present, as in **10c**, the charge density on the metal is reduced and

(12) The same intermediate isolated in platinum-catalyzed reaction of vinyl triflates (see ref 11a) was supposed to be formed in palladium-catalyzed vinylation of triphenylphosphine. See: Hinkle, R. J.; Stang, P. J.; Kowalski, M. H. *J. Org. Chem.* **1990**, *55*, 5033.

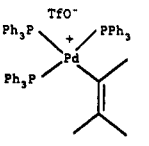


**Table III. Palladium-Catalyzed Reaction between 4 and 7. Salt Effect[a]**

| entry | ligand | salt | t, h | 8/9[b] |
|---|---|---|---|---|
| 1 | DPPF | | 38 | 43/57 |
| 2 | DPPF | LiCl | 20 | 100/0 |
| 3 | DPPF | LiBr | 22 | 100/0 |
| 4 | DPPF | LiI | 21 | 100/0 |
| 5 | DPPF | $Et_4NCl$ | 19 | 100/0 |
| 6 | DPPF | AcOLi | 40 | 80/20 |
| 7 | DPPP | | 1.5 | 100/0 |
| 8 | DPPP | AcOLi | 24 | 100/0 |
| 9 | DPPP | LiCl | 24 | |

[a] All reactions were run under an argon atmosphere using 0.5 mmol of 7, in the presence of 5 mol % of $Pd(OAc)_2$, 5.5 mol % of the ligand, 5 mmol of 4, 1 mmol of $Et_3N$ and 1.5 mmol of the salt in DMF (0.6 M) at 60 °C. When present 3 equiv of salt have been added. [b] Molar ratio determined by HPLC using 1-(9,10-antraquinoyl)tosilate as external standard; the yields, determined by HPLC, were always better then 95%.

there is a competition between the coordination of methyl acrylate (good $\pi$ acceptor and poor donor) and the lone pair of the nitrogen of triethylamine (good $\sigma$ donor).[13]

The coordination of $Et_3N$ by the palladium(II) complex followed by metal insertion and $\beta$-hydride elimination gives the Pd–H intermediate that after reductive elimination affords the reduction product **9** (Scheme V).[14,15] This suggestion is supported by the complete suppression of the reduction product when $NaHCO_3$ was used as base; in this case no source of hydride was present in the reaction mixture and the arylation product **8** was formed selectively (Table II, entry 9).

The solvent effect can be explained on the basis of the solvation of ion pairs; toluene, a poorly coordinating and dissociating solvent, increases the electrostatic interaction in the Pd(II)–OTf bond, and the coordination step proceeds perferentially through displacement of the ligand (Scheme IV, path B). The charge density on the metal is higher than it is when coordination takes place via dissociation of the anion (Scheme IV, path A), the overlap between the d orbital of the metal and the $\pi^*$ orbital of the olefin is more effective, and triethylamine is unable to coordinate to the metal. This resulted in a higher selectivity toward **8**.

These considerations suggest that another way to increase the charge density on palladium can be devised, namely the replacement of $CF_3SO_3^-$ by a less easily dissociated counterion. It is well-known from Stille's work[16] on the palladium-catalyzed cross-coupling reaction between aryltriflates and tin derivatives that addition of LiCl results in exchange between $CF_3SO_3^-$ and $Cl^-$ in the oxidative addition complex. In our system, intermediate **10d** should, via dissociation of the ligand (Scheme IV, path B), efficiently afford **8** even when DPPF is the ligand. The results obtained with added salts, reported in Table III, are in agreement with this hypothesis. In fact, with DPPF as ligand, the addition of halide anions resulted in a complete selectivity toward **8** and an increase of the reaction rate regardless of the counterion employed, either $Li^+$ or $Et_4N^+$ (entries 1–5). When AcOLi was used as added salt, only moderate enhancement of the selectivity was observed according to the intermediate-dissociating ability of $AcO^-$ with respect to triflate and halides (entry 6).[17]

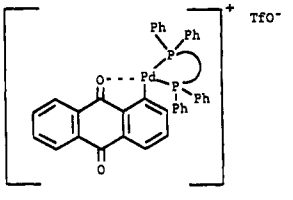
It is worth noting that completely different behavior was observed using DPPP as ligand. In this case the reaction rate was decreased in the presence of $AcO^-$ (entry 8) and the reaction was completely suppressed in the presence of LiCl (entry 9). The different behavior of the two ligands can be ascribed to the greater tendency of DPPF compared to DPPP to dissociate from the metal.[18] DPPP is not prone to dissociation (path B in Scheme IV), and since in the presence of $Cl^-$ also path A is hampered, the oxidative addition intermediate **10b** is unable to coordinate **4**.[19] These results allowed us to perform the Heck reaction on substrate **2**. In fact, using $Pd(OAc)_2$/DPPF as the catalytic system in dioxane, the presence of added chloride or acetate anions allowed the synthesis of the novel anthracyclinone **5** in 50–62% yield.

Our procedure failed with electron-rich enol ethers[20] because back-donation from the metal to the olefin is useless with poor $\pi$ acceptors.

The use of acetate[21] or halide[22] salts has been a subject of interest in the Heck reaction. These salts were added mainly as bases or phase-transfer cataysts, but there is no evidence that their addition modifies the mechanism of the coordination insertion step when aryl or aroyl halides are used as substrates.[23] The easy exchange of the counterion in the oxidative addition complex is peculiar to the trifluoromethanesulfonate anion.

It should be added that, although this work has been carried out on one particular substrate, the proposed

(13) Unfortunately, any attempt to isolate the oxidative addition complexes **10a** and **10c** failed. The possibility that the carbonyl group in peri position in respect to the metal takes part in the coordination cannot be ruled out.




(14) (a) McCrindle, R.; Ferguson, G.; Arsenault, G. J.; McAlees, A. J.; Stephenson, D. K. *J. Chem. Res., Symp.* **1984**, 360. *J. Chem. Res., Miniprin* **1984**, 3301. (b) McCrindle, R.; Ferguson, G.; Arsenault, G. J.; McAlees, A. J. *J. Chem. Soc., Chem. Commun.* **1983**, 571. (c) Murahashi, S.-I.; Watanabe, T. *J. Am. Chem. Soc.* **1979**, *101*, 7429. (d) Murahashi, S.-I.; Hirano, T.; Yano, T. *Ibid.* **1978**, *100*, 348.

(15) For examples of palladium-catalyzed reductions using trialkylamino as hydride source, see: (a) Saa, J. M.; Dopico, M.; Martorell, G.; Garcia-Raso, A. *J. Org. Chem.* **1990**, *55*, 991. (b) Stokker, G. E. *Tetrahedron Lett.* **1987**, *28*, 3179.

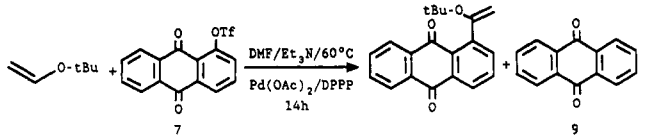
(16) (a) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 1557. (b) Echavarren, A. M.; Stille, J. K. *Ibid.* **1984**, *107*, 5478 and reference cited therein.

(17) Henry, P. M. *Palladium Catalyzed Oxidation of Hydrocarbons*; D. Riedel: Dordrecht, Holland, 1980.

(18) Hayashi, T.; Konishi, M.; Kobori, Y; Kumada, M.; Higuchi, T.; Hiritsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158.

(19) We have already observed the negative effect of LiCl on the arylation of olefins by simple aryl triflates in the presence of Pd(OAc)$_2$/DPPP as catalytic system. See: Cabri, W.; Candiani, I.; Bedeschi, A.; Santi, R. *Tetrahedron Lett.* **1991**, *32*, 1753.

(20) The arylation of butyl vinyl ether (5 equiv) with **7** in the presence of $Pd(OAc)_2$/DPPP (5 mol %) at 60 °C in DMF gave after 14 h a mixture of arylated olefin and reduction product **9**; the two compounds were isolated after purification, respectively, in 81% and 17% yield.




(21) Spencer, A. *J. Organomet. Chem.* **1983**, *258*, 101.

(22) Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287.

(23) Ag(I) and Tl(I) salts have been added in the reactions of aryl halides and olefin in order to eliminate from the solution the halide anions. See for Ag(I) salts: (a) Jeffery, T. *Tetrahedron Lett.* **1990**, *31*, 6641. (b) Abelman, M. M.; Overman, L. E.; Tran, V. D. *J. Am. Chem. Soc.* **1990**, *112*, 6959. (c) Andersson, C.-M.; Larsson, J.; Hallberg, A. *J. Org. Chem.* **1990**, *55*, 5757. (d) Larock, R. C.; Gong, W. H. *Ibid.* **1990**, *55*, 407. See for Tl(I) salts: (a) reference 19. (b) Carfagna, C.; Musco, A.; Sallese, G.; Santi, R. *Ibid.* **1991**, *56*, 261. (c) Grigg, R.; Loganathan, V.; Santhakumar, V.; Sridharan, V.; Teasdale, A. *Tetrahedron Lett.* **1991**, *32*, 687.

mechanism seems to be a general one in the presence of bidentate phosphine ligands. In fact, in a very recent paper Ozawa and Hayashi invoked a similar mechanistic hypothesis in order to explain the outcome of the asymmetric Heck reaction of simple aryl triflates and aryl iodides with dihydrofuran in the presence of the $Pd(OAc)_2$/(R)-BINAP complex.[24a]

## Conclusion

DPPP and DPPF have shown to be good ligands in the Heck reaction; this work represents the first example in which bidentate phosphines have been used with success in the reaction between aryl triflates and an electron-deficient olefin.[24]

The particular reactivity of the anthraquinoid system allowed us to study, under controlled conditions, the coordination-insertion step of the olefin onto the palladium(II) complex, and the effectiveness of the reaction resulted from a subtle balance between ligand and counterion in the oxidative addition intermediate.

The mechanism proposed is in agreement with the hypothesis of Ozawa and Hayashi and allows the clarification, to some extent, of the general mechanism of the arylation of olefin catalyzed by palladium complex in the presence of bidentate phosphine ligands. The procedure developed made possible the synthesis of the first anthracyclinone substituted at carbon 4 with a vinyl derivative. However, in anthracycline chemistry the Heck reaction is limited to the use of olefins able to accept electron back-donating from the metal.

## Experimental Section

Melting points were determined on a Kofler apparatus and are uncorrected. $^1H$ NMR spectra were recorded at 200 MHz in $CDCl_3$. HPLC analyses were performed with a LiChrosorb RP-18 (7-$\mu$m) column using $CH_3CN/CH_3OH/H_2O$ (51/15/33 by volume) as eluent. Purifications by flash chromatography were carried out on Merck silica gel 60 (230-400 mesh), as described by Still.[25] 4-Demethyl-4-(trifluoromethanesulfonyl)-13-dioxolanyldaunomycinone (2),[3] 1-(9,10-anthraquinoyl) triflate 7,[7] and $Pd(PPh_3)_2Cl_2$[26] were prepared according to published procedures. $Pd(OAc)_2$, DPPP, DPPF were purchased from Aldrich.

**Representative Procedure for Palladium-Catalyzed Reaction with Methyl Acrylate (4). Methyl [1-(9,10-Anthraquinoyl)]propenoate (8) (Table I, Entry 3).** To a stirred solution of triflate 7 (0.178 g, 0.5 mmol) in 8.4 mL of DMF under Ar at rt were sequentially added $Et_3N$ (0.139 mL, 1.0 mmol), 4 (0.45 mL, 5.0 mmol), DPPP (0.0113 g, 0.0275 mmol), and $Pd(OAc)_2$ (0.0056 g, 0.025 mmol). The solution was stirred and heated at 60 °C for 1.5 h then cooled to rt. $CH_2Cl_2$ (40 mL) was added, and the resulting mixture was sequentially washed with 5% HCl (3 × 5 mL) and water until neutral. The solution was dried ($Na_2SO_4$), filtered, and evaporated. The crude product was purified by flash chromatography (hexane/ethyl acetate (8/2) by volume) affording quinone 8 (0.137 g, 94%): yellow solid; mp 195-197 °C (MeOH); IR (Nujol) 1720, 1690, 1340, 1290 $cm^{-1}$; $^1H$ NMR $\delta$ 3.86 (s, 3 H), 6.27 (d, 1 H, $J$ = 15.9 Hz), 7.65-7.90 (m, 4 H), 8.16-8.48 (m, 3 H), 8.69 (d, 1 H, $J$ = 15.9 Hz). Anal. Calcd for $C_{18}H_{12}O_4$: C, 73.94; H, 4.14. Found: C, 73.91; H, 4.11.

The procedures for the palladium-catalyzed reactions of Table III and for triflate 2 were the same as described above with the exception that 3 equiv of the indicated salt were added just before the phosphine.

The reaction of 2 was carried out using the procedure described above in the presence of AcOLi and DPPF as ligand.

**4-Demethoxy-4-[2'-(methoxycarbonyl)ethenyl]-13-dioxolanyldaunomycinone (5):** 0.154 g, 62%; red solid; mp 214-216 °C dec; IR (KBr) 3470, 1716, 1610, 1575 $cm^{-1}$; UV (EtOH) 527, 492, 347, 264, 213 nm; $\lambda_{max}$ 264 nm; $^1H$ NMR ($CDCl_3$) $\delta$ 1.48 (3 H, s), 1.98 (1 H, dd, $J$ = 5.1, 14.7 Hz), 2.46 (1 H, dt, $J$ = 2.0, 14.7 Hz), 2.79 (1 H, d, $J$ = 18.9 Hz), 3.24 (1 H, dd, $J$ = 2.1, 18.9 Hz), 3.34 (2 H, s), 3.80 (1 H, br s), 3.87 (3 H, s), 4.08 (4 H, s), 5.26 (1 H, dd, $J$ = 1.5, 4.9 Hz), 6.24 (1 H, d, $J$ = 15.9 Hz, 7.75-7.80 (2 H, m), 8.36-8.44 (1 H, m), 8.72 (1 H, d, $J$ = 15.9 Hz), 13.35 (1 H, s), 13.54 (1 H, s); $[\alpha]_D$ = 195.0° ($c$ 0.1 in dioxane). Anal. Calcd for $C_{26}H_{24}O_{10}$: C, 62.90; H, 4.87. Found: C, 62.85; H, 4.91.

By use of the same procedure in the presence of 3 equiv of LiCl instead of $Et_3N$ and AcOH, compound 5 was isolated in 50% yield.

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**Registry No.** 2, 128065-73-6; 4, 96-33-3; 7, 123412-36-2; 8, 135340-33-9; 9, 84-65-1; DPPP, 6737-42-4; DPPF, 12150-46-8; $Pd(PPh_3)_2Cl_2$, 13965-03-2; $Pd(OAc)_2$, 3375-31-3; LiCl, 7447-41-8; LiBr, 7550-35-8; LiI, 10377-51-2; $Et_4NCl$, 56-34-8; AcOLi, 546-89-4; $CH_2$=CHO-$t$-Bu, 926-02-3; 1-(1-*tert*-butoxyethenyl)-9,10-anthracenedione, 135340-35-1.

(24) Bidentate phosphines were reported not to form effective catalyst for the Heck reaction, ref 5c. There are only two examples in the literature of arylation of olefins by aryltriflates. Interestingly, in both papers were used electron-rich olefins, enol ethers. See: (a) Ozawa, F.; Kubo, A.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 1417. (b) Cabri, W.; Candiani, I.; Bedeschi, A.; Santi, R. *J. Org. Chem.* **1990**, *55*, 3654. For aryl iodides see: (c) Reference 19. (d) Karabellas, K.; Westerlund, C.; Hallberg, A. *Ibid.* **1985**, *50*, 3896.

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# Lewis Acid Induced Ene Cyclization of $\omega$-Olefinic Trifluoromethyl Ketones: Access to Bicyclic Compounds Bearing a $CF_3$ Group

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Lewis acid induced ene cyclization of $\omega$-olefinic trifluoromethyl ketones provides (trifluoromethyl)decalins and (trifluoromethyl)hydrindans in high yield. $\delta$-(1-Cyclohexenyl) trifluoromethyl ketone **1a** leads stereoselectively to 1-(trifluoromethyl)-1-hydroxy-$\Delta^{5,10}$-octalin **3a** or 10-chloro-1-(trifluoromethyl)-1-hydroxydecalin **6a**, depending on the choice of Lewis acid. $\gamma$-(1-Cyclohexenyl) trifluoromethyl ketone **2a** leads to a mixture of 9-chloro-1-(trifluoromethyl)-1-hydroxyhydrindans **10a** and **11a**. Similar reactions were performed successfully with the corresponding $\beta$-keto esters **1b** and **2b**.

Much attention has been focused on trifluoromethyl-substituted compounds because of the remarkable effect of such fluorinated groups on biological activity.[1a-c] The selective introduction of a $CF_3$ group into bioactive mol-

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