α-Regioselectivity in Palladium-Catalyzed Arylation of Acyclic Enol Ethers

Walter Cabri,* Ilaria Candiani, Angelo Bedeschi, and Sergio Penco

Farmitalia Carlo-Erba S.r.l. (Erbamont Group), R & D, via Dei Gracchi, 35 20146-Milano, Italy

Roberto Santi

Istituto Guido Donegani S.p.a., via Fauser, 4 28100-Novara, Italy

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Regioselective α-arylation of acyclic enol ethers by aryl trifluoromethanesulfonates, aryl bromide, aryl iodides, and aroyl chlorides is described. The outcome of the reaction proved to be dependent from the relationship between ligand and counterion in the oxidative addition complex.

Introduction

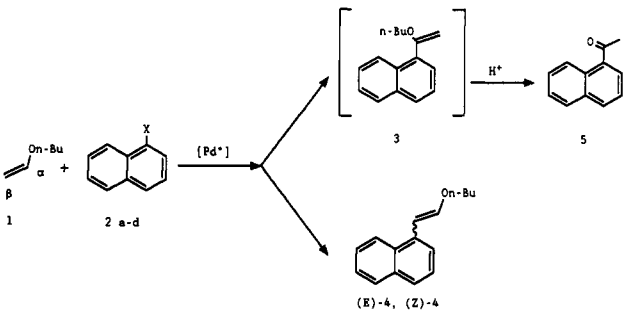
The direct functionalization of olefins with aryl and heterocyclic derivatives (Heck reaction) is one of the more interesting and important palladium-catalyzed reactions because of the compatibility of several functionalities, the mild conditions, and the simplicity of the procedure.[1] However, the low degree of regioselectivity observed with some classes of olefins is the major drawback. During the last decade this limitation has been circumvented by the development of methodologies requiring the functionalization of the olefin as an organometallic derivative.[2]

Considerable effort has been devoted to improving the regioselectivity of the arylation of enol ether,[3] and recently Hallberg and co-workers have described a method for the regioselective β arylation of modified acyclic enol ethers.[4] Herein we report our results on the direct arylation of acyclic enol ethers, focusing attention on the relationship between ligands and leaving groups and on their influence on the reactivity of the catalytic system.[5] An important goal of these studies has been the development of a general method for the regioselective α-arylation of acyclic enol ethers by aryl trifluoromethanesulfonates (triflates), aryl bromides, aryl iodides, and aroyl chlorides.

Results and Discussion

Palladium-catalyzed reactions were carried out in the presence of a catalyst generated in situ from $Pd(OAc)_2$ and the ligand.

Scheme I[a]



[a] X: **a**, OTf; **b**, Br; **c**, I; **d**, COCl.

Table I. Palladium-Catalyzed Reaction between Butyl Vinyl Ether 1 and 1-Naphthyl Triflate (2a). Phosphine Ligand Effect[a]

entry	ligand (L/Pd)[b]	cone angle θ,[c] deg	T, °C	t, h	conv, %	3/4[d]	E/Z[d]
1	none		100	24	8	55/45	71/29
2	PPh_3 (2)	145	100	1.5	100	63/37	80/20
3	$P(p\text{-tolyl})_3$ (2)	145	100	5	100	61/39	72/28
4	$P(o\text{-tolyl})_3$ (2)	194	100	5	100	63/37	76/24
5	PCH_3Ph_2 (3)	136	80	5	100	>99/1	
6	$P(CH_3)_2Ph$ (3)	122	80	6	100	>99/1	
7	DPPM (2)	121	100	24	60	80/20	74/26
8	DPPE (2)	125	80	24	95	>99/1	
9	DpTE (2)	125	80	24	93	>99/1	
10	DPPP (1.1)	127	60	0.5	100	>99/1	
11	DPPB (2)		60	1.5	100	>99/1	
12	DPPF (1.1)		60	2	100	>99/1	
13	c-DPPET (2)		80	12	100	>99/1	

[a] Reactions were run under an argon atmosphere with 1 equiv of **2a**, 5 equiv of 1, 1.2 equiv of Et_3N, and 2.5 mol % of $Pd(OAc)_2$ in DMF. The only products of the reactions were **3** and **4**. [b] Molar ratio between ligand and $Pd(OAc)_2$. [c] See ref 7. [d] Determined by GC.

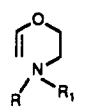
Aryl Trifluoromethanesulfonates. Ligand Effect. The effect that the nature of the ligand has on the regioselectivity of the reaction between butyl vinyl ether **1** and 1-naphthyl triflate (**2a**) in DMF as solvent (Scheme I) was investigated.[6] The results obtained are reported in Table I. In the absence of ligands, the conversion was

(1) (a) Heck, R. F. *Palladium Reagents in Organic Syntheses*; Academic Press: London, 1985. (b) Heck, R. F. *Org. React.* **1982**, *27*, 345. (c) Heck, R. F. *Pure Appl. Chem.* **1981**, *53*, 2323. (d) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146.

(2) In particular, several organometallic derivatives with a metal on the α position of vinyl ethers have been used in palladium-catalyzed reaction with aryl or vinyl derivatives. For reaction of zinc derivatives see: (a) Neghishi, E.; Luo, F.-T. *J. Org. Chem.* **1983**, *48*, 1560. (b) Russell, C. E.; Hegedus, L. S. *J. Am. Chem. Soc.* **1983**, *105*, 943. For reaction of tin derivatives see: (c) Kosugi, M.; Sumiya, T.; Obara, Y.; Suzuki, M.; Sano, M.; Migita, T. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 767. (d) Kwon, H. B.; McKee, B. H.; Stille, J. K. *J. Org. Chem.* **1990**, *55*, 3114. For reaction of silicon derivatives see: (a) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918.

(3) Daves, G. D., Jr.; Hallberg, A. *Chem. Rev.* **1989**, *89*, 1433 and references cited therein.

(4) Andersson, C.-M.; Larsson, J.; Hallberg, A. *J. Org. Chem.* **1990**, *55*, 5757. In this paper in order to obtain selective β arylation the enol ethers were modified as described below.

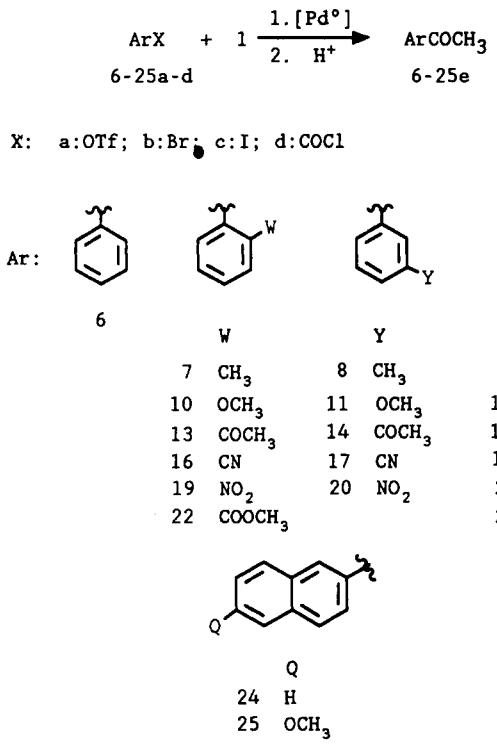


(5) For previous accounts on this work see: (a) Cabri, W.; Candiani, I.; Bedeschi, A.; Santi, R. *Tetrahedron Lett.* **1991**, *32*, 1753. (b) Cabri, W.; Candiani, I.; Bedeschi, A.; Santi, R. *J. Org. Chem.* **1990**, *55*, 3654.

(6) For palladium-catalyzed reaction between olefins and aryl trifluoromethanesulfonates see: (a) Cabri, W.; Candiani, I.; DeBernardinis, S.; Francalanci, F.; Penco, S.; Santi, R. *J. Org. Chem.*, in press. (b) Ozawa, F.; Kubo, A.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 1417. (c) Tilley, J. W.; Sarabu, R.; Wagner, R.; Mulkerins, K. *J. Org. Chem.* **1990**, *55*, 906. (d) Chen, Q.-Y.; He, Y. B. *Syntheses* **1988**, 896. (e) Andersson, C.-M.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 2112. (f) Tilley, J. W.; Zawoiski, S. *J. Org. Chem.* **1988**, *53*, 386. (g) Chen, Q.-Y.; Yang, Z.-Y. *Tetrahedron Lett.* **1986**, *27*, 1171.

0022-3263/92/1957-1481$03.00/0

Scheme II



only 8%, and the arylation afforded a mixture of **3**, (*E*)-**4**, and (*Z*)-**4** (entry 1). In the presence of phosphine ligands, with a few exceptions, the conversion was complete and the regioselectivity was greatly affected by the nature of the ligand. With PPh_3 the regioselectivity (**3**/**4** ratio) was only 1.7 (entry 2). An increase of the basicity and/or the cone angle θ of the monodentate phosphine,[7] with the use of P(*o*-tolyl)$_3$ or P(*p*-tolyl)$_3$, did not alter the ratio appreciably (entries 3 and 4). On the contrary, with phosphines like PCH_3Ph_2 or $P(CH_3)_2Ph$ having cone angle $\theta \leq 136°$,[7] regioselective α-arylation of **1** leading to **3** was observed (entries 5 and 6).[8]

The α regioselectivity seems to increase with the tendency of the ligand to be linked to the palladium metal. In fact, the coordinating ability of monodentate phosphines is correlated with the cone angle and increases in the order P(*o*-tolyl)$_3$ $\ll$ PPh_3 $\cong$ P(*p*-tolyl)$_3$ $\ll$ PCH_3Ph_2 $\cong$ $P(CH_3)_2Ph$.[7]

These results suggested that a higher selectivity toward **3** could be obtained by using bidentate phosphines. In practice, all chelating bidentate ligands,[9] except DPPM[10] (entry 7), afforded only **3** (entries 8–13). In the bidentate series, steric and electronic factors appear to play a minor role in determining the regioselectivity.

The use of 2 equiv of phosphines was sometimes required in order to avoid catalyst decomposition. However, DPPP promotes the reaction at 60 °C, and only a slight excess is necessary in order to have a stable and effective catalyst. Therefore, we decided to use $Pd(OAc)_2$/DPPP as catalyst for further study.

Table II. Palladium-Catalyzed α-Arylation of Vinyl Butyl Ether 1 and Aryltriflates 6–21a[a]

entry	ArOTf	T, °C	t, h	α/β[b]	product (yields, %)[c]
1	**6a**	80	3	>99/1	**6e** (90)[d]
2	**7a**	80	3	>99/1	**7e** (90)
3	**8a**	80	1	>99/1	**8e** (90)
4	**9a**	80	0.5	>99/1	**9e** (91)
5	**10a**	80	4	>99/1	**19e** (91)
6	**11a**	80	2	>99/1	**11e** (86)
7	**12a**	80	1.5	>99/1	**12e** (93)
8	**13a**	80	2.5	>99/1	**13e** (72)
9	**14a**	80	7	>99/1	**14e** (90)
10	**15a**	80	5	>99/1	**15e** (96)
11	**16a**	80	2.5	>99/1	**16e** (87)
12	**17a**	80	4.5	>99/1	**17e** (85)
13	**18a**	80	3	>99/1	**18e** (92)
14	**19a**	100	6	>99/1	**19e** (40)
15	**20a**	100	3	95/5[e]	**20e** (64)
16	**21a**	100	3.5	99/1[f]	**21e** (54)

[a] Reactions were run under an argon atmosphere with 1 equiv of **2a**, 5 equiv of 1, 1.2 equiv of Et_3N, 2.5 mol % of $Pd(OAc)_2$, and 2.75 mol % of DPPP in DMF, until the conversion was complete. [b] Determined by GC of the crude before the acidic treatment. [c] Isolated yields of the corresponding aryl methyl ketones. [d] Determined by GC. [e] The *E*/*Z* ratio of the β-arylated products was 55/45. [f] The *E*/*Z* ratio of the β-arylated products was 80/20.

Temperature and Solvent Effect. The regioselectivity of the reaction was unaffected by the temperature and solvent. Only a decrease of the reaction rate was observed at lower temperature or using less dissociating solvents. The reaction of **2a** carried out under standard conditions in DMF at 40 °C was complete in 12.5 h. In dioxane and toluene at 80 °C the reaction times were, respectively, 1.5 and 2 h.

Substrate Effect. The electronic effect exerted by the substituents on the aromatic ring has been reported to affect the regioselectivity of the arylation of **1** using $Pd(OAc)_2$ or Pd/C as catalyst.[11] Triflates **6–21a** were synthesized (Scheme II) in order to study electronic and steric effects on the reaction. The catalyst generated from $Pd(OAc)_2$ and DPPP controls the α-regioselectivity of the reaction independently from the aryl substituents. With a few exceptions, after acidic treatment the corresponding aryl methyl ketones **6–21e** were isolated in high yields (Table II). The reaction of benzene triflate **6a** was complete within a few hours at 80 °C (entry 1). An acceleration of the arylation was observed when an electron-donating group, such as methyl or methoxy, was present in the meta or para positions (entries 3, 4, 6, and 7). The reaction of the corresponding ortho derivatives was slower, due probably to an increase of the steric hindrance near the reactive site (entries 2 and 5). The presence of an electron-withdrawing group, such as nitrile or acetyl, decreases the efficiency of the catalytic cycle requiring longer reaction times (entries 8–13). Interestingly, among these substrates, the ortho derivatives **13a** and **16a** reacted faster than the corresponding meta and para isomers (cf. entries 8 and 11 with entries 9, 10, 12, and 13). The reactivity is probably affected by the coordinating ability of the carbonyl and the nitrile groups.[12]

Although the presence of the nitro group should favor the oxidative addition step, the reactions of **19–21a** had to be carried out at 100 °C, and the yields of the corre-

(7) Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313.
(8) The notation α/β >99/1 has been used when, after aqueous workup, the β arylated product was not detected by both capillary GLC and ^1H NMR (200 MHz) of the crude.
(9) DPPM = 1,1-bis(diphenylphosphino)methane; DPPE = 1,2-bis(diphenylphosphino)ethane; DpTE = 1,2-bis(di-*p*-tolylphosphino)ethane; DPPP = 1,3-bis(diphenylphosphino)propane; DPPB = 1,4-bis(diphenylphosphino)butane; DPPF = 1,1'-bis(diphenylphosphino)ferrocene; *c*-DPPET = *c*-1,2-bis(diphenylphosphino)ethylene.
(10) The result obtained with DPPM is not easily explained, because this phosphine generates bridged binuclear complexes Puddephatt, R. J. *J. Chem. Soc. Rev.* **1983**, 99.
(11) Andersson, C.-M.; Hallberg, A.; Daves, G. D., Jr. *J. Org. Chem.* **1987**, *52*, 3529.
(12) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*, 2nd ed.; University Science Books: Mill Valley, CA, 1987.

Table III. Palladium-Catalyzed Reactions between Vinyl Butyl Ether (1) and Naphthyl Derivatives 2a–e. Leaving Group and Salt Effects[a]

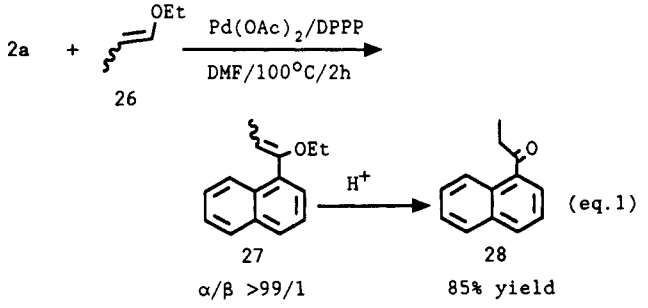
entry	substrate	salt	T, °C	t, h	conv,[b] %	3/4[b]	E/Z[b]	products (yield, %)[c]
1	**2b**[d]		100	18	100	61/39	77/23	**5** (54) + **4** (32)
2	**2b**[d]	$AgNO_3$	100	24	48	>99/1		**5** (42)
3	**2b**[d]	AgOTf	100	24	68	>99/1		**5** (61)
4	**2b**	TlOAc	100	0.8	100	>99/1		**5** (86)
5	**2b**	TlOAc	80	1	100	>99/1		**5** (92)
6	**2b**	TlOAc	60	12	100	>99/1		**5** (97)
7	**2c**[d]		100	20	100	67/33	67/33	**5** (63) + **4** (28)
8	**2c**	TlOAc	100	0.7	100	88/12	65/35	**5** (81) + **4** (11)
9	**2c**	TlOAc	80	0.7	100	>99/1		**5** (99)
10	**2c**	TlOAc	60	24	78	>99/1		**5** (70)
11	**2d**[d]		100	24				
12	**2a**[d]	LiCl[e]	100	24				
13	**2d**	TlOAc	100	4	100	>99/1		**5** (60)

[a] Reactions were run under an argon atmosphere with 1 equiv of **2a**, 5 equiv of 1, 2.5 mol % of $Pd(OAc)_2$, and 2.75 mol % of DPPP in DMF. When present 1.1 equiv of salt was added. [b] Determined by GC of the crude before the acidic treatment. [c] Isolated yields after the acidic treatment. [d] 1.2 equiv of Et_3N have been added. [e] 2 equiv of LiCl have been added.

sponding aryl methyl ketones **19–21e** were low (entries 14–16). Furthermore, in the case of the meta isomer **20a** 5% of the β arylated products were detected. Although a few percent of nitrobenzene was found in the reaction mixture, the quantity was not enough to justify the low yields.[13] Blank experiments revealed that the β-isomers were stable under the reaction condition excluding their formation and decomposition.

The results presented in Table II seem to point out that the rate-determining step is not the oxidative addition or the double-bond coordination, but probably the migration of the aromatic ring on the π system. In fact, the reactivity of the para isomers, unaffected by steric and coordinating factors, was higher in the presence of electron-donating groups.[14]

The regioselectivity of the reaction was maintained using β-substituted enol ethers. When 1-ethoxy-1-propene (**26**), as a mixture of isomers, and triflate **2** reacted in the presence of the DPPP containing catalyst at 100 °C, the β-arylated products were not detected; after acidic workup the corresponding ethyl ketone **28** was isolated in 85% yield (eq 1).



Aryl Bromides, Aryl Iodides, and Aroyl Chlorides. The arylations of 1 with bromide **2b** and iodide **2c** catalyzed by $Pd(OAc)_2$/DPPP were slow, and the α/β ratios were 1.6 and 2, respectively (Table III, entries 1 and 7). On the other hand, it is worth noting that under decarbonylative conditions[15] 1-naphthoyl chloride **2d** was completely unreactive (entry 11). The outcome of these reactions was related to the presence of halide anions as palladium ligands in the oxidative addition intermediate. In fact, the arylation of 1 with triflate **2a** was inhibited by using the Stille protocol for the generation in situ of the aryl–$Pd^{(II)}$–Cl complex (entry 12).[16]

Silver(I)[17] and thallium(I)[18] salts were added in order to eliminate the halide anions from the solution. As expected, in the presence of $AgNO_3$ or AgOTf, bromide **2b** afforded product **3** selectively (entries 2 and 3). The use of TlOAc caused, in addition to complete regioselectivity, a consistent acceleration of the reaction rate (entry 4). The effectiveness of TlOAc with respect to the silver(I) salts, is probably attributable to an increase of the catalyst stability under the reaction conditions. Furthermore, the organic base was not necessary and the regioselective outcome was independent of the reaction temperature (entries 4, 5 and 6).

The addition of TlOAc to the reactions of iodide **2c** increased the amount of the α-isomer (entries 8, 9, and 10). The critical parameter proved to be the temperature; at 80 °C, the conversion was complete without any trace amounts of β-isomer (entry 9). At 100 °C the decomposed catalyst is able to catalyze nonregioselective arylation of the enol ether by aryl iodides;[19] on the other hand, at 60 °C after 24 h the conversion was only 78%. TlOAc was effective even with 1-naphthoyl chloride (**2d**). In fact, the reaction carried out under decarbonylative conditions at 100 °C gave **3** selectively (entry 13).

The procedure developed for **2b**, **2c**, and **2d** proved to be general and compatible with the several functional groups (Table IV). Sometimes, the use of 2 equiv of DPPP and/or an organic base was necessary in order to increase the stability of the catalytic system. The yields of the corresponding aryl methyl ketones were generally high, except for the nitro derivatives (entries 6 and 12) and the aroyl chlorides (entries 14 and 15).

Reaction Mechanism.[20] Our results suggest that the combination of ligands and counterion in the oxidative addition complex control the coordination–insertion step

(13) Hallberg observed the presence of bifenil derivatives, in reaction catalyzed by $Pd(OAc)_2$.[4] In the presence of phosphines this side reaction is suppressed.

(14) Cawse, J. N.; Fiato, R. A.; Pruett, R. L. *J. Organomet. Chem.* **1979**, *172*, 405.

(15) Blaser, H.-U.; Spencer, A. *J. Organomet. Chem.* **1982**, *233*, 267.

(16) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478.

(17) For examples of silver(I) salts as sequestrating agents of halide anions see: (a) Jeffery, T. *Tetrahedron Lett.* **1990**, *31*, 6641. (b) Reference 4. (c) Larock, R. C.; Gong, W. H. *J. Org. Chem.* **1990**, *55*, 407. (d) Abelman, M. M.; Oh, T.; Overman, L. E. *J. Org. Chem.* **1987**, *52*, 4130.

(18) For examples of thallium(I) salts as sequestrating agents of halide anions see: (a) Reference 5a. (b) Carfagna, C.; Musco, A.; Sallese, G.; Santi, R. *J. Org. Chem.* **1991**, *56*, 261. (c) Grigg, R.; Loganathan, V.; Santhakumar, V.; Sridharan, V.; Teasdale, A. *Tetrahedron Lett.* **1991**, *32*, 687.

(19) Bromide **2b** was practically unreactive in the presence of $Pd(OAc)_2$ in DMF at 100 °C. On the contrary, under the same conditions, iodide **2c** gave a mixture of **3** and **4** (56/44 ratio) with a 90% conversion after 24 h.

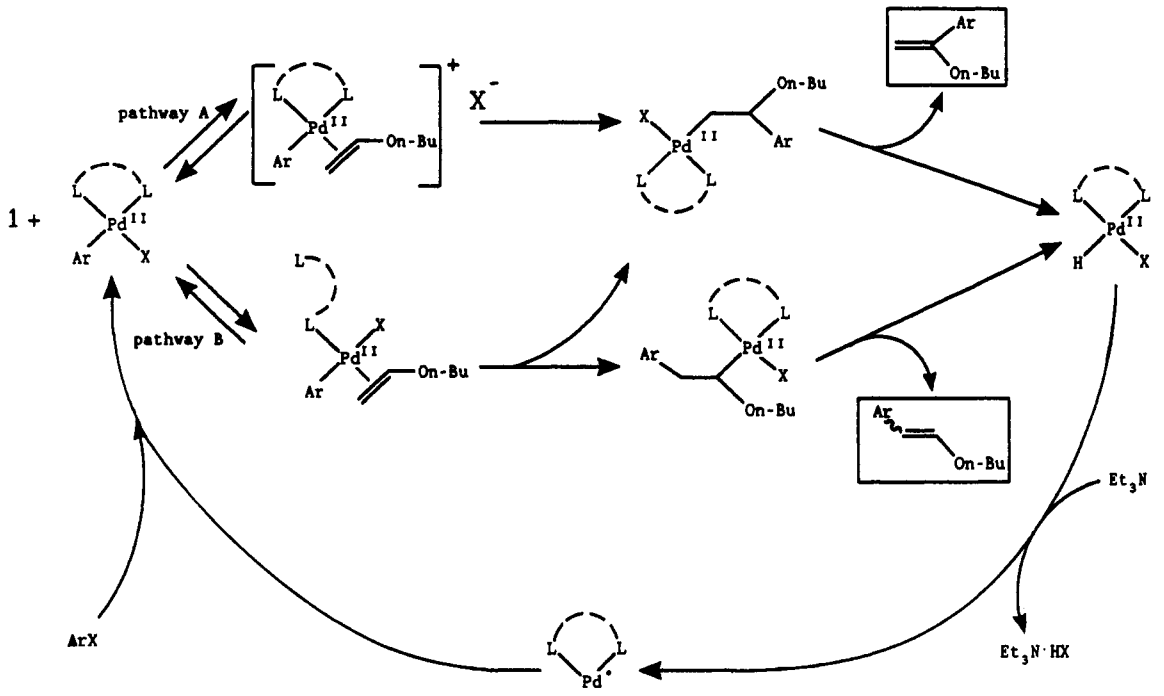
(20) For a mechanistic hypothesis in the absence of palladium ligands see ref 11.

Table IV. Palladium-Catalyzed Reactions between Vinyl Butyl Ether (1) and Aryl Halides in the Presence of TlOAc[a]

entry	substrate	base	mol % (L/Pd)[b]	T, °C	t, h	α/β[c]	product (yield, %)[d]
1	**6b**		2.5 (2)	80	7	>99/1	**6e** (91)[e]
2	**9b**	Et_3N	2.5 (2)	80	8	>99/1	**9e** (88)
3	**12b**	Et_3N	5 (2)	100	5	>99/1	**12e** (86)
4	**14b**		2.5 (1.1)	80	5.5	>99/1	**14e** (87)
5	**17b**		2.5 (1.1)	80	12	>99/1	**17e** (83)
6	**21b**	Et_3N	5 (2)	100	36	>99/1	**21e** (47)
7	**24b**		2.5 (1.1)	80	1	>99/1	**24e** (90)
8	**25b**		2.5 (1.1)	80	5.5	>99/1	**25e** (87)
9	**6c**		2.5 (1.1)	80	4.5	>99/1	**6e** (81)[e]
10	**9c**	Et_3N	2.5 (1.1)	80	2	>99/1	**9e** (88)
11	**12c**	Et_3N	2.5 (1.1)	80	2	>99/1	**12e** (82)
12	**21c**	Et_3N	5 (2)	100	26	>99/1	**21e** (60)
13	**22c**		2.5 (1.1)	80	4	>99/1	**22e** (92)
14	**6d**	DIPEA[f]	2.5 (2)	100	5	>99/1	**6e** (27)[e]
15	**23d**	DIPEA[f]	2.5 (2)	100	5	>99/1	**23e** (42)

[a] Reactions were run under an argon atmosphere with 1 equiv of the substrate, in the presence of 5 equiv of 1 and 1.1 equiv of TlOAc in DMF, until the conversion was complete. When Et_3N or DIPEA were present, 1.2 equiv have been added. [b] mol % of $Pd(OAc)_2$ and ratio between DPPP and $Pd(OAc)_2$. [c] Determined by GC of the crude before the acidic treatment. [d] Isolated yields of the corresponding aryl methyl ketones. [e] Determined by GC. [f] DIPEA = *N,N*-diisopropylethylamine.

Scheme III



and consequently the regioselectivity of the reaction. The coordination of the olefin can follow two pathways:[21] (a) dissociation of the anion present in the $Pd^{(II)}$ complex (Scheme III, pathway A), and (b) dissociation of the phosphine ligand (Scheme III, pathway B). Taking in consideration pathway A, the coordination of the olefin in a cationic complex increases the polarization of the π system favoring the migration of the aryl moiety onto the α carbon because of the lower charge density respect to the β one. In contrast, if the reaction follows pathway B, consistent amounts of β arylated products should be expected, as a consequence of the reduced polarization of the double bond. Therefore, the α/β ratio is a monitor of the reaction mechanism. When the triflate anion, a labile palladium(II) ligand,[22] is present in the oxidative addition complex and the phosphine ligand is strongly coordinated to the metal, only pathway A is allowed. In fact, in the presence of PCH_3Ph_2, $P(CH_3)_2Ph$, DPPE, DpTE, DPPP, DPPB, DPPF, and *c*-DPPET the α/β ratio was always >99/1. On the contrary, with weak ligands like PPh_3, P(*o*-Tol)$_3$, or P(p-Tol)$_3$ both pathways are allowed and the α/β ratio decreases. The low regioselectivity observed using the DPPP-containing catalyst in the reactions of 1-naphthyl bromide **2b** and 1-naphthyl iodide **2c** or the inactivity of 1-naphthoyl chloride **2d** indicates that the strong association of the halide anions with palladium(II)[23] blocks pathway A. On the other hand, the high trans effect of bromide and iodide anions[12] favors the dissociation of one of the two phosphorous atoms in the oxidative addition complex and the reaction follows pathway B. Chloride anion exerts a lower trans effect, and both coordination pathways are hampered because of the stability of the square planar palladium(II) complex.[24]

(21) A similar dualistic mechanism for the coordination of olefins by palladium(II) complexes was proposed on the basis of completely different results by us[6a] and Hayashi.[6b]

(22) (a) Hinkle, R. J.; Stang, P. J.; Kowalsky, M. H. *J. Org. Chem.* **1990**, *55*, 5033. (b) Lawrence, G. A. *Chem. Rev.* **1986**, *90*, 17. (c) Rimml, H.; Venanzi, L. M. *J. Organomet. Chem.* **1984**, *260*, C52-C54.

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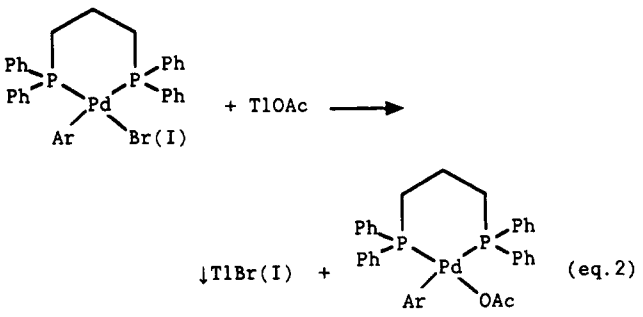
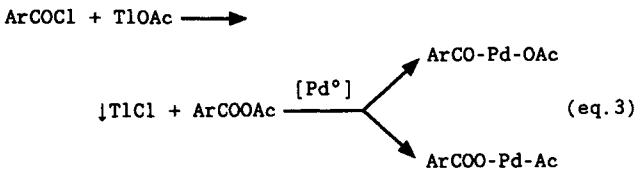
In the case of aryl bromides or iodides, the addition of TlOAc determines the substitution of bromide or iodide, linked to palladium(II) in the oxidative addition complex, with the acetate anion (eq 2). The acetate can easily



(eq. 2)

dissociate and the coordination can occur via dissociation of the counterion (pathway A). The effectiveness of TlOAc relies on the fact that the elimination of the halide anions is faster than the coordination–insertion step via pathway B (Scheme III). With aroyl chlorides the role of the thallium(I) salt is completely different. 1-Naphthoyl chloride **2d** afforded the corresponding mixed anhydride under these reaction conditions. The low regioselectivity of the palladium(0) complex attack to the mixed anhydride determines the low yields observed (eq 3).[25]



(eq. 3)

Conclusion

The foregoing results demonstrate that the relationship of ligands and counterions in the oxidative addition complex controls the regioselective outcome of the Heck reaction. The methodologies developed proved to be of general use.

The specific reactivity of enol ethers allowed us to study in detail the coordination-insertion step of the reaction and gave indication of the general mechanism of the Heck reaction.[20] Further studies on the application of bidentate phosphines containing catalysts are under way.

Experimental Section

All compounds were identified and characterized through their 200-MHz ^{1}H NMR spectra in $CDCl_3$, mass spectra, mp (Kofler apparatus and uncorrected), and/or oven temperature (ot) from bulb to bulb distillation conducted with a Büchi Kugelrohr. GC analyses were carried out with a Nordibond OV-1 column (25 m length, i.d. 0.32 mm) and a flame ionization detector.

1,4-Dioxane and toluene were distilled from Na and stored over activated 4A molecular sieves. DMF and Et_3N were distilled over CaH_2 and stored over activated 4A molecular sieves.

Aryl iodides, aryl bromides, aroyl chlorides, butyl vinyl ether (1), (*E*/*Z*)-1-ethoxy-1-propene (**26**), $Pd(OAc)_2$, PPh_3, P(*o*-Tol)$_3$, P(*p*-Tol)$_3$, PCH_3Ph_2, $P(CH_3)_2Ph$, DPPE, DpTE, DPPP, DPPB, and DPPF were Aldrich products and used as received. *c*-DPPET was a Strem product and used as received. Aryl triflates **2a** and **6–21a** were prepared from the corresponding phenols by a standard procedure in 74–95% yields.[16] Triflates **2a**, **12a**, **15a**, and **21a** are known compounds, and their structures were determined by comparison of their physical and spectroscopic data with the reported values.[16]

Phenyl trifluoromethanesulfonate (6a): colorless oil; ot 84–86 °C (2.0 mmHg); IR (neat) 3070, 1490, 1425 cm^{-1}; ^{1}H NMR δ 7.52–7.33 (m, 3 H), 7.32–7.20 (m, 2 H). Anal. Calcd for $C_7H_5F_3O_3S$: C, 37.18; H, 2.23. Found: C, 37.22; H, 2.20.

2-Methylphenyl trifluoromethanesulfonate (7a): colorless oil; ot 80–82 °C (1.5 mmHg); IR (neat) 3070, 1495, 1435 cm^{-1}; ^{1}H NMR δ 7.38–7.12 (m, 4 H), 2.38 (s, 3 H). Anal. Calcd for $C_8H_7F_3O_3S$: C, 40.00; H, 2.94. Found: C, 40.00; H, 2.91.

3-Methylphenyl trifluoromethanesulfonate (8a): colorless oil; ot 81–83 °C (1.3 mmHg); IR (neat) 3080, 1620, 1585, 1490 cm^{-1}; ^{1}H NMR δ 7.40–6.97 (m, 4 H), 2.39 (s, 3 H). Anal. Calcd for $C_8H_7F_3O_3S$: C, 40.00; H, 2.94. Found: C, 40.02; H, 2.92.

4-Methylphenyl trifluoromethanesulfonate (9a): colorless oil; ot 85–87 °C (1.5 mmHg); IR (neat) 3080, 1580, 1490 cm^{-1}; ^{1}H NMR δ 7.30–7.00 (m, 4 H), 2.37 (s, 3 H). Anal. Calcd for $C_8H_7F_3O_3S$: C, 40.00; H, 2.94. Found: C, 40.02; H, 2.93.

2-Methoxyphenyl trifluoromethanesulfonate (10a): colorless oil; ot 131–133 °C (1.9 mmHg); IR (neat) 2955, 1620, 1510 cm^{-1}; ^{1}H NMR δ 7.38–7.17 (m, 2 H), 7.09–6.91 (m, 2 H), 3.90 (s, 3 H). Anal. Calcd for $C_8H_7F_3O_4S$: C, 37.51; H, 2.75. Found: C, 37.49; H, 2.78.

3-Methoxyphenyl trifluoromethanesulfonate (11a): colorless oil; ot 135–137 °C (2.0 mmHg); IR (neat) 2955, 1615, 1510 cm^{-1}; ^{1}H NMR δ 7.40–7.27 (m, 1 H), 6.97–6.75 (m, 3 H), 3.86 (s, 3 H). Anal. Calcd for $C_8H_7F_3O_4S$: C, 37.51; H, 2.75. Found: C, 37.49; H, 2.75.

2-Acetylphenyl trifluoromethanesulfonate (13a); colorless oil; ot 151–153 °C (2.0 mmHg); IR (neat) 1700, 1610, 1430 cm^{-1}; ^{1}H NMR δ 7.82 (dd, *J* = 7.6, 1.8 Hz, 1 H), 7.70–7.42 (m, 2 H), 7.34 (dd, *J* = 8.1, 1.1 Hz, 1 H), 2.63 (s, 3 H). Anal. Calcd for $C_9H_7F_3O_4S$: C, 40.31; H, 2.63. Found: C, 40.28; H, 2.64.

3-Acetylphenyl trifluoromethanesulfonate (14a): colorless oil; ot 150–152 °C (1.7 mmHg); IR (neat) 3080, 1700, 1575, 1430 cm^{-1}; ^{1}H NMR δ 7.96 (bd, *J* = 7.5 Hz, 1 H), 7.81 (bs, 1 H), 7.62–7.34 (m, 2 H), 2.59 (s, 3 H). Anal. Calcd for $C_9H_7F_3O_4S$: C, 40.31; H, 2.63. Found: C, 40.33; H, 2.66.

2-[(Trifluoromethanesulfonyl)oxy]benzonitrile (16a): colorless oil; ot 151–153 °C (2.0 mmHg); IR (neat) 3110, 2240, 1610, 1490 cm^{-1}; ^{1}H NMR δ 7.87–7.64 (m, 2 H), 7.60–7.37 (m, 2 H). Anal. Calcd for $C_8H_4F_3NO_3S$: C, 38.26; H, 1.61. Found: C, 38.30; H, 1.60.

3-[(Trifluoromethanesulfonyl)oxy]benzonitrile (17a): colorless oil; ot 157–159 °C (2.0 mmHg); IR (neat) 3090, 2240, 1560 cm^{-1}; ^{1}H NMR δ 7.84–7.42 (m, 4 H). Anal. Calcd for $C_8H_4F_3NO_3S$: C, 38.26; H, 1.61. Found: C, 38.23; H, 1.60.

4-[(Trifluoromethanesulfonyl)oxy]benzonitrile (18a): colorless oil; ot 160–162 °C (2.0 mmHg); IR (neat) 3105, 2240, 1605, 1500, cm^{-1}; ^{1}H NMR δ 7.77 (d, *J* = 9.0 Hz, 2 H), 7.40 (d, *J* = 9.0 Hz, 2 H). Anal. Calcd for $C_8H_4F_3NO_3S$: C, 38.26; H, 1.61. Found: C, 38.30; H, 1.65.

2-Nitrophenyl trifluoromethanesulfonate (19a): pale yellow oil; ot 145–147 °C (1.3 mmHg); IR (neat) 3100, 1610, 1540, 1435 cm^{-1}; ^{1}H NMR δ 8.17 (d, *J* = 8.2 Hz, 1 H), 7.76 (t, *J* = 8.2 Hz, 1 H), 7.59 (t, *J* = 8.3 Hz, 1 H), 7.47 (d, *J* = 8.2 Hz, 1 H). Anal. Calcd for $C_7H_4F_3NO_5S$: C, 31.01; H, 1.49. Found: C, 31.00; H, 1.53.

3-Nitrophenyl trifluoromethanesulfonate (20a): pale yellow solid; mp 62–64 °C; ot 146–148 (1.2 mmHg); IR (neat) 3105, 1600, 1540 cm^{-1}; ^{1}H NMR δ 8.40–8.23 (m, 1 H), 8.21–8.07 (m, 1 H), 7.77–7.52 (m, 2 H). Anal. Calcd for $C_7H_4F_3NO_5S$: C, 31.01; H, 1.49. Found: C, 30.98; H, 1.50.

Palladium-Catalyzed Reaction. Compounds (*E*)-**4** and (*Z*)-**4** were previously characterized.[5b]

General Procedure for Table I (Table I, entry 2). To a stirred solution of **2a** (1 g, 3.62 mmol) in DMF (10 mL) under Ar at rt were sequentially added Et_3N (0.438 g, 0.6 mL, 4.34 mmol), **1** (1.810 g, 2.3 mL, 18.1 mmol), PPh_3 (0.044 g, 0.1 mmol), and $Pd(OAc)_2$ (0.0203 g, 0.090 mmol). The reaction temperature was raised to 100 °C. Periodical GLC analyses of the reaction mixture were performed on small amounts of the solution diluted with CH_2Cl_2 and washed with water.

Aryl ketones **5**, **6–15e**, and **17–24e** are known compounds, and their structures were determined by comparison of their physical and spectroscopic data with the reported values.[26]

(24) We have already observed the inhibition effect of chloride anions in the Heck reaction catalyzed by $Pd(OAc)_2$/DPPP. See ref 6a.

(25) The anhydride generated in DMF at 100 °C by the reaction between benzoyl chloride and TlOAc was treated with benzyl amine. The corresponding acetamide was isolated.

General Procedure for Table II (Table II, entry 1). To a stirred solution of **7a** (0.869 g, 3.62 mmol) in DMF (10 mL) under Ar at rt were sequentially added Et_3N (0.731 g, 0.6 mL, 4.34 mmol), I (1.81, 2.3 mL, 18.1 mmol), DPPP (0.044 g, 0.1 mmol), and $Pd(OAc)_2$ (0.0203 g, 0.090 mmol). The reaction temperature was raised to 80 °C. After 3 h the conversion was complete (GLC), and the reaction mixture was cooled to rt. HCl (5%, 15 mL) was added and after another 0.5 h of stirring the mixture was poured into CH_2Cl_2 (40 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL), and the combined organic layers were washed with water until neutrality, dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product was purified by flash chromatography[27] (hexane/ethyl acetate 9/1 by volume), affording **7e** (0.436 g, 90%).

2-Acetylbenzonitrile (16e): pale yellow solid; mp 46–48 °C (CH_3OH) (lit.[28] mp 48 °C); IR (Nujol) 2215, 1695 cm^{-1}; ^1H NMR δ 7.94 (dd, J = 6.9, 1.7 Hz, 1 H), 7.80–7.51 (m, 3 H), 2.64 (s, 3 H). Anal. Calcd for C_9H_7NO: C, 74.47; H, 4.86. Found: C, 74.43; H, 4.90.

The reaction described in eq 1 was carried out as described above with 5 equiv of **(E/Z)-1-ethoxy-1-propene (26)**. A sample of the crude product was analyzed before acidic treatment. **(E/Z)-1-Ethoxy-1-(1'-naphthyl)propene (27)**: colorless oil; H^1 NMR δ 8.10–7.31 (m, 7 H), 5.18–4.95 (m, 2 H), 3.90 (q, J = 7.0 Hz, 1.6 H, E isomer), 3.50 (q, J = 7.0 Hz, 0.4 H, Z isomer), 1.33 (t, J = 7.0 Hz, 2.4 H, E isomer), 1.17 (t, J = 7.0 Hz, 0.6 H, Z isomer); GLC-MS (Z)-**27** m/e 212 (M^+), 183, 155 (100). (E)-**27** m/e 212 (M^+), 183, 155 (100).

General Procedure for Table III and Table IV (Table III, entry 4). To a stirred solution of **2b** (0.3 g, 1.46 mmol) in DMF (3.5 mL) under Ar at rt were sequentially added TlOAc (0.420 g, 1.6 mmol), I (0.726 g, 0.938 mL, 7.26 mmol), DPPP (0.0166 g, 0.040 mmol), and $Pd(OAc)_2$ (0.008 g, 0.036 mmol). The reaction temperature was raised to 100 °C. After 0.8 h the conversion was complete (GLC) and the reaction mixture was cooled to rt, filtered, and treated with HCl (5%, 15 mL). After another 0.5 h of stirring the mixture was diluted with CH_2Cl_2 (35 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL), and the combined organic layers were washed with water until neutrality, dried (Na_2SO_4), filtered and concentrated in vacuo. The crude product was purified by flash chromatography (hexane/ethyl acetate 9/1 by volume), affording **5** (0.214 g, 86%).

2-Acetyl-6-methoxynaphthalene (25e): white solid; mp 106–108 °C (CH_3OH) (lit.[29] mp 108 °C (CH_3OH)); IR (Nujol) 1685, 1620 cm^{-1}; ^1H NMR δ 8.37 (bs, 1 H), 8.02–7.75 (m, 3 H), 7.28–7.02 (m, 2 H), 3.93 (s, 3 H), 2.68 (s, 3 H). Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.96; H, 6.07.

Registry No. 1, 111-34-2; **2a**, 99747-74-7; **2b**, 90-11-9; **2c**, 90-14-2; **2d**, 879-18-5; **3**, 134576-01-5; **Z-4**, 127087-65-4; **E-4**, 127087-64-3; **5**, 941-98-0; **6a**, 17763-67-6; **6b**, 108-86-1; **6c**, 591-50-4; **6d**, 98-88-4; **6e**, 98-86-2; **7a**, 66107-34-4; **7e**, 577-16-2; **8a**, 32578-31-7; **8e**, 585-74-0; **9a**, 29540-83-8; **9b**, 106-38-7; **9c**, 624-31-7; **9e**, 122-00-9; **10a**, 59099-58-0; **10e**, 579-74-8; **11a**, 66107-33-3; **11e**, 586-37-8; **12a**, 66107-29-7; **12b**, 104-92-7; **12c**, 696-62-8; **12e**, 100-06-1; **13a**, 129849-05-4; **13e**, 704-00-7; **14a**, 138313-22-1; **14b**, 2142-63-4; **14e**, 6781-42-6; **15a**, 109613-00-5; **15e**, 1009-61-6; **16a**, 138313-23-2; **16e**, 91054-33-0; **17a**, 66152-74-7; **17b**, 6952-59-6; **17e**, 6136-68-1; **18a**, 66107-32-2; **18e**, 1443-80-7; **19a**, 132993-22-7; **19e**, 577-59-3; **20a**, 32578-25-9; **20e**, 121-89-1; **21a**, 17763-80-3; **21b**, 586-78-7; **21c**, 636-98-6; **21e**, 100-19-6; **22a**, 17763-70-1; **22c**, 610-97-9; **22e**, 1077-79-8; **23a**, 29540-84-9; **23d**, 122-01-0; **23e**, 99-91-2; **24a**, 3857-83-8; **24b**, 580-13-2; **24e**, 93-08-3; **25a**, 129731-74-4; **25b**, 5111-65-9; **25e**, 3900-45-6; **26**, 928-55-2; **27**, 138313-24-3; **28**, 2876-63-3; DPPM, 2071-20-7; DPPE, 1663-45-2; DpTE, 138313-25-4; DPPP, 6737-42-4; DPPB, 7688-25-7; DPPF, 12150-46-8; c-DPPET, 983-80-2; PPh_3, 603-35-0; P(p-tolyl)$_3$, 1038-95-5; P(o-tolyl)$_3$, 6163-58-2; PCH_3Ph_2, 1486-28-8; $P(CH_3)_2Ph$, 672-66-2; $Pd(OAc)_2$, 3375-31-3; HOC_6H_4-o-Me, 95-48-7.

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Selective Solid-State Photorearrangement through the Less Stable of Two Possible Biradical Intermediates

Phani Raj Pokkuluri, John R. Scheffer,* James Trotter,* and Melvin Yap

Department of Chemistry, University of British Columbia, Vancouver, British Columbia, Canada V6T 1Z1

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The photochemistry of methyl 2-benzoyl-1,4-dihydro-1,4-ethenonaphthalene-3-carboxylate is completely medium-dependent. In solution, two primary di-π-methane-type photoproducts are formed. Neither of these products is produced when the photolysis is carried out in the solid state; instead, three new photoproducts are formed. The results are interpreted as being due to reaction through 1,3-biradical intermediates, the more stable of which are preferred in solution whereas the less stable ones are formed in the solid state as a result of topochemical restrictions of molecular motion. X-ray crystallographic evidence in support of these ideas is presented and discussed.

Most organic reactions are carried out in solution. It is becoming increasingly apparent, however, that chemical studies in organic solids and other "organized media" offer several advantages over studies in liquid media.[1] Key among these is the interesting situation that arises when liquid- and solid-phase reactions give entirely different products. New reactions are discovered that offer new possibilities for organic synthesis, and fresh insights are provided into reaction mechanisms. Solid/liquid reactivity differences can arise, for example, when the reaction in solution occurs through a conformational isomer that is not present in the solid state.[2] Another source of sol-

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