Regiochemistry of Palladium-Catalyzed Arylation Reactions of Enol Ethers. Electronic Control of Selection for α- or β-Arylation

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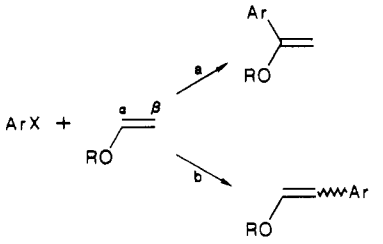
The regiochemistry of palladium-mediated arylation (Heck arylation) of enol ethers is sensitive to (a) the structure of the enol ether, (b) the arylating agent used, and (c) the reaction medium–catalyst system. By control of these parameters a 50-fold variation in regioselectivity for arylation at the olefinic α or β carbons of the enol ether was attained. Under catalytic conditions 3–9-fold variations in regiochemistry were typical. Using *n*-butyl vinyl ether as a reference, it was established that methyl substitution at either the α- or β-olefinic carbon of the enol ether favors α-arylation; incorporation of the enol ether system in a ring completely inhibits β-arylation. Electron-rich aryl systems (4-methoxyphenyl) favor α-arylation whereas electron-poor aryls (4-nitrophenyl) favor β-arylation. The choice of halogen for use in oxidative addition of palladium in forming the active arylpalladium reagent also affects arylation regiochemistry; a 10-fold increase in the ratio of β/α arylation occurred in going from I to Cl. β-Arylation is favored by use of poorly coordinated palladium catalyst systems (e.g., $Pd(OAc)_2$ in toluene) whereas a relatively electron-rich palladium catalyst (triphenylphosphine ligands, acetonitrile solvent) favors α-arylation. Mechanisms for α- and β-arylation of enol ethers in the presence of palladium catalysts are proposed.

The regiochemical outcome of palladium-mediated reactions of aryl halides with unsymmetrical olefins is of utmost importance in determining the synthetic utility of these procedures. A generalization has emerged that the regiochemistry of these organometallic reactions is primarily determined by steric factors although it is recognized that electronic factors play a role, particularly in conjugated olefins.[1] Of particular interest to us are arylation reactions of enol ethers in which the carbon–carbon double bond is highly polarized owing to conjugation with the ether oxygen π-electrons;[2] in such systems electronic effects are expected to be important.

For effective use of enol ether arylation in synthesis, the development of procedures for selective arylation at either the α- (reaction a) or the β-olefinic carbon (reaction b) is desirable. In recent reports from our laboratories, we have



described examples in which regioselective palladium-mediated arylations of both α[3-6] and β[7] carbons of enol ether double bonds have been accomplished. Earlier studies that report regioselectivity observed in palladium-catalyzed (mediated) reactions of enol ethers,[8] enamines,[9] enamides,[10] alkyl vinyl thiols,[11] and other related systems[12] are available. In the present report, we provide results of a systemmatic study that has significantly increased understanding of factors which determine the regiochemistry of palladium-mediated reactions of enol ethers. We have determined that by proper selection of experimental parameters, it is possible to achieve regioselective arylation of acyclic enol ethers at either the α- or β-olefinic carbon.

Results

Experiments were carried out using selected enol ethers and aryl iodides and bromides to assess the regiochemistry of palladium-mediated coupling reactions of enol ethers with aryl halides in the presence of catalytic palladium. Several palladium(0) and palladium(II) catalysts were used; similarly, solvents of differing coordinating ability were evaluated. Results obtained during these studies are

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Table I. Arylation of *n*-Butyl Vinyl Ether (2) with Halobenzenes in the Presence of Various Palladium Catalysts[a]

entry	halobenzene	catalyst	solvent	% unchanged 1	yield (%)[b] 3a	4a	5a + 6a	ratio β/α[e]	3a/4a
1	PhI (1a)	$Pd(OAc)_2$	CH_3CN	13	9	22	56	0.5	0.4
2	PhI (1a)	$PdCl_2$	CH_3CN	7	10	22	61	0.5	0.4
3	PhI (1a)	Li_2PdCl_4	CH_3CN	19	12	24	45	0.8	0.5
4	PhI (1a)	Pd/C	CH_3CN	12	11	23	52	0.6	0.5
5	PhI (1a)	$Pd(PPh_3)_4$	CH_3CN	0	19	23	53	0.8	0.8
6	PhI (1a)	$Pd(OAc)_2/2PPh_3$	CH_3CN	16	13	17	52	0.6	0.8
7	PhI (1a)	$Pd(OAc)_2/6PPh_3$	CH_3CN	0	17	21	60	0.6	0.8
8	PhI (1a)	$Pd/C/2PPh_3$	CH_3CN	10	16	20	53	0.7	0.8
9	PhI (1a)	$Pd(OAc)_2$	toluene	73	8	8	11	1.4	1.0
10	PhI (1a)	Pd/C	toluene	38	17	20	24	1.5	0.8
11	PhI (1a)	$Pd(OAc)_2/2PPh_3$	toluene	0	24	28	48	1.1	0.8
12	PhI (1a)	$Pd(PPh_3)_4$	toluene	0	22	26	50	1.0	0.8
13	PhI (1a)	$Pd(OAc)_2/2PPh_3$	none[c]	0	22	29	49	1.0	0.8
14	PhI (1a)	Pd/C	none[c]	55	18	9	18	1.5	2.0
15	PhI (1a)	Pd/C	DMF	11	17	23	49	0.8	0.7
16	PhBr (1b)	$Pd(OAc)_2/2PPh_3$	CH_3CN	34	16	6	34	0.6	2.5
17	PhBr (1b)	$Pd(OAc)_2/2PPh_3$	toluene	95	*d*	*d*	*d*	1.3[d]	2.8[d]

[a] The halobenzene (10 mmol), *n*-butyl vinyl ether (20 mmol), triethylamine (15 mmol), and the palladium catalyst (0.1 mmol of Pd) in 10 mL of solvent were heated for 16 h at 100 °C. [b] Based on halobenzene and determined by gas chromatographic analysis (see Experimental Section). [c] Additional *n*-butyl vinyl ether (10 mL) was used. [d] The relative yield of isomers was 5%; because of the low conversion isomer ratios could not be determined accurately. [e] Calculated as (3a + 4a)/(5a + 6a).

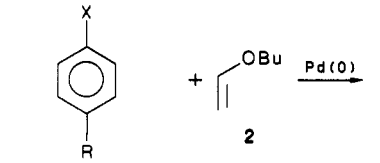
summarized in Tables I–III and in the accompanying text. Further studies involved (a) comparison of the reactivities of an acyclic and a cyclic enol ether under similar arylation conditions (Table IV), (b) arylation reactions of enol ethers with arylmercuric salts in the presence of stoichiometric palladium(II) salts (Table V), and (c) arylation reactions using preformed arylpalladium reagents (Table VI).

Catalytic Reactions. *n*-Butyl vinyl ether (2) was selected as a standard enol ether for use in experiments to assess the regioselectivity of arylation reactions. Three aryl iodides, iodobenzene (1a), 1-iodo-4-nitrobenzene (1c), and 1-iodo-4-methoxybenzene, were used in initial experiments since earlier studies[3,5] had established that the electron density of the aryl moiety has a major effect on the regiochemistry of arylation of enol ethers. Unfortunately, when 1-iodo-4-methoxybenzene was used, hydrolysis of products arising from β-arylation led to secondary reactions and tar formation which precluded accurate determination of the reaction regioselectivity. Therefore, only iodobenzene (1a), the electron-deficient 4-nitro analogue 1c, and the corresponding bromo compounds (1b and 1d) were used in the study. The reactions were carried out by using standard Heck arylation conditions with triethylamine as base.[1b] In addition to acetonitrile, commonly used as reaction solvent, toluene and dimethylformamide were used to assess the effect of coordinating and noncoordinating solvents on the regiochemistry of the reaction.

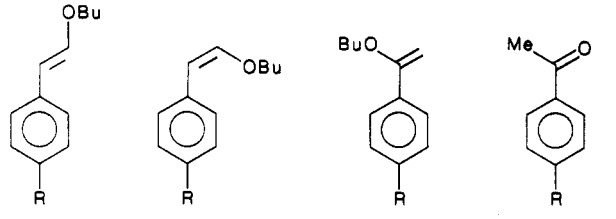
Arylation of *n*-Butyl Vinyl Ether with Iodo- or Bromobenzene. Results obtained in palladium-catalyzed arylations of *n*-butyl vinyl ether (2) using iodo- (1a) or bromobenzene (1b) are summarized in Table I. An initial screening of catalysts (Table I, entries 1–8) in reactions using acetonitrile as solvent produced good yields of arylated products in all cases and only minor differences in regioselectivity; in each case arylation at the α carbon of the enol ether was favored (β/α ratio 0.5–0.8). In a single experiment (entry 15) in which a different coordinating solvent (dimethylformamide) was used, similar results were obtained. In these reactions, the presence or absence of triphenylphosphine had little effect.

In contrast, when the arylation reaction was carried out in the noncoordinating solvent, toluene (Table I, entries 9–12), significant variation was observed. In this solvent, the absence of stabilizing triphenylphosphine ligands (entries 9 and 10) led to low yields of arylated products and modest regioselectivity for β-arylation (β/α = 1.4, 1.5). If triphenylphosphine was present (entries 11 and 12), yields were quantitative; however, no regioselectivity was attained (β/α = 1.0–1.1). When the enol ether reactant, *n*-butyl vinyl ether (2) was used as solvent (entries 13 and 14), the results were similar.

In the arylation reaction with *n*-butyl vinyl ether (2), bromobenzene (1b) reacted much more slowly than did iodobenzene (1a). In toluene, even when triphenylphosphine was present, the reaction proceeded to the extent of only about 5% in 16 h (entry 17). Reaction regioselectivities obtained in the experiments using bromobenzene (entries 16 and 17) accorded closely with those of corresponding reactions of iodobenzene (entries 6 and 11).



1a: X = I, R = H
1b: X = Br, R = H
1c: X = I, R = NO_2
1d: X = Br, R = NO_2



3a: R = H
3b: R = NO_2
4a: R = H
4b: R = NO_2
5a: R = H
5b: R = NO_2
6a: R = H
6b: R = NO_2

Arylation of *n*-Butyl Vinyl Ether with 1-Iodo- or 1-Bromo-4-nitrobenzene. Arylation reactions of *n*-butyl vinyl ether (2) with 4-nitrophenyl halides (1c, 1d) are summarized in Table II. An attempted direct comparison between the palladium-catalyzed reactions of iodobenzene (1a) and 1-iodo-4-nitrobenzene (1c) was unsuccessful because of the loss of material as a result of deiodination of 1c to nitrobenzene (entries 18–20, Table II). Therefore, 1-bromo-4-nitrobenzene (1d) was used to assess the effect of an electron-withdrawing group on the regiochemistry

Table II. Arylation of *n*-Butyl Vinyl Ether (2) with 1-Iodo-4-nitrobenzene (1c) or 1-Bromo-4-nitrobenzene (1d) in the Presence of Various Palladium Catalysts[a]

					yield (%)[b]			ratio	
entry	halobenzene	catalyst	solvent	% unchanged 1	3b	4b	5b	β/α[i]	3b/4b
18	1c	$Pd(OAc)_2/2PPh_3$	CH_3CN	0[h]	23	17	24	1.7	1.4
19	1c	$Pd(OAc)_2/2PPh_3$	toluene	10[h]	17	17	13	2.6	1.0
20	1c	Pd/C	toluene	24[h]	22	33	12	4.6	0.7
21	1d	$Pe(OAc)_2$	CH_3CN	0	46	38	17	5.0	1.2
22	1d	Pd/C	CH_3CN	0	45	39	16	5.2	1.2
23	1d	$Pd(OAc)_2/2\ PPh_3$	CH_3CN	0	49	22	21	3.4	2.2
24	1c	$Pd(PPh_3)_4$	CH_3CN	0	43	16	41	1.2	2.6
25	1d	$Pd/C/2\ PPh_3$	CH_3CN	2	49	21	28	2.5	2.3
26	1d	$Pd(OAc)_2$	toluene	68	24	8	0		3.0
27	1d	Pd/C	toluene	73	17	7	3	8.0	2.4
28	1d	Pd/C	toluene[c]	50	30	14	6	7.3	2.1
29	1d	Pd/C	toluene[d]	12	54	24	10	7.8	2.3
30	1d	$Pd(OAc)_2/2PPh_3$	toluene	0	48	20	18	3.8	2.4
31	1d	$Pd/C/2PPh_3$	toluene	97	*e*	*e*	*e*	3.6	2.0
32	1d	Pd/C	none[f]	76	14	7	3	7.8	2.2
33	1d	Pd/C	none[g]	44	31	17	8	6.0	1.8
34	1d	Pd/C	DMF	0	56	32	11	8.0	1.7

[a] The halobenzene (10 mmol), *n*-butyl vinyl ether (20 mmol), triethylamine (15 mmol), and the palladium catalyst (0.1 mmol of Pd) in 10 mL of solvent were heated for 16 h at 100 °C. [b] Based on halobenzene and determined by gas chromatographic analysis (see Experimental Section). [c] 5 mL of solvent was used. [d] 2 mL of solvent was used. [e] The relative yield of isomers was 3%. [f] Additional *n*-butyl vinyl ether (10 mL) was used. [g] Additional *n*-butyl vinyl ether (2 mL) was used. [h] Nitrobenzene formation accounted for remaining material. [i] Calculated as (3b + 4b)/5b.

Table III. Palladium-Catalyzed Arylation of Butyl 1(*Z*)-Propenyl Ether (7) with Halobenzenes in Acetonitrile[a]

			yield (%)[b]					
entry	halobenzene	catalyst	8	9	10	11	12	ratio β/α[e]
35	1a	Pd/C	13	4	25	19	40	0.20
36	1a	$Pd(PPh_3)_4$	4	8	34	21	29	0.14
37	1c	Pd/C	31	6	22	10	0	1.2[c,d]
38	1c	$Pd(PPh_3)_4$						*c, d*
39	1d	Pd/C	15	3	12	3	0	1.2[c]
40	1d	$Pd(PPh_3)_4$	2	9	8	2	0	1.1[c]

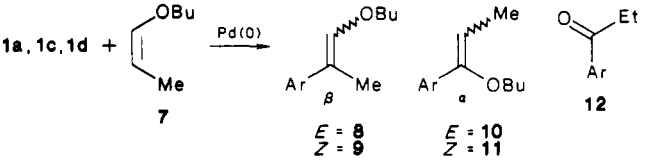
[a] The halobenzene (10 mmol), butyl 1(*Z*)-propenyl ether (20 mmol), triethylamine (15 mmol), and the palladium catalyst (0.1 mmol of Pd) in 10 mL of acetonitrile were heated for 24 h at 100 °C. [b] Based on halobenzene and determined by gas chromatographic analysis (see Experimental Section). The isomer distribution was confirmed by ^1H NMR analysis. [c] Unchanged halobenzene remained in the reaction mixture. [d] Nitrobenzene and 4,4′-dinitrobiphenyl were detected (GLC) after the reaction. [e] Calculated as (8 + 9)/(10 + 11 + 12).

of the palladium-catalyzed arylation reaction.

Comparison of data in Tables I and II reveals that introduction of an electron-withdrawing nitro group (a) greatly enhances the reaction regioselectivity and (b) increases sensitivity to differences in reaction conditions. In acetonitrile, a regioselectivity ratio of about 5 favoring β-arylation was observed (entries 21 and 22); when the solvent was toluene (entries 26–29), or when the enol ether served as solvent (entries 32, 33), β/α ratios of 6 or greater were obtained although, as observed in reactions of iodo- and bromobenzene (Table I), conversions were much lower. Surprisingly, reaction of 1-bromo-4-nitrobenzene (**1d**) with **2** in dimethylformamide (entry 34) yielded a β/α arylation ratio of 8, similar to the regioselectivity observed when toluene was used as solvent and significantly different from that obtained in acetonitrile. This result contrasts with that obtained by using iodobenzene for arylation (compare entries 4, 10, and 15, Table I).

Addition of triphenylphosphine increased α-arylation of **2** and significantly reduced the regioselectivity of the reaction (entries 18, 19, 23–25, 30, Table II). This effect of triphenylphosphine was particularly striking when $Pd(PPh_3)_4$ was used as catalyst; in this case (entry 24) the β/α ratio was only 1.2. Addition of triphenylphosphine to reaction mixtures in which palladium on carbon (Pd/C) was used as catalyst in acetonitrile also decreased the regioselectivity significantly (compare entries 22 and 25); when the solvent was toluene, the conversion was greatly diminished (compare entries 27 and 31). It is noteworthy that the low conversion rate observed in toluene were improved markedly by concentrating the reactants without adversely affecting reaction regiochemistry (compare entries 27–29).

Arylation of Butyl 1(*Z*)-Propenyl Ether with Halobenzenes. Arylation reactions of butyl 1(*Z*)-propenyl ether (**7**) were studied (Table III) to evaluate the effect of an alkyl substituent on the enol ether β-carbon. Both catalysts used, Pd/C and $Pd(PPh_3)_4$, gave good conversions when the arylating agent was iodobenzene (**1a**) and exhibited strong regioselectivities for α-arylation (β/α = 0.20, 0.14, Table III, entries 35, 36). When 4-nitrobenzene



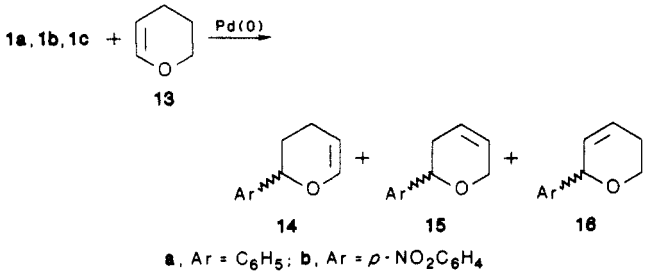
a, Ar = C_6H_5; **b**, Ar = *p*-$NO_2C_6H_4$

analogues **1c** or **1d** were used conversions were much poorer, especially when $Pd(PPh_3)_4$ was used as catalyst (entries 38, 40), and little regioselectivity (β/α = 1.1, 1.2) was attained. Comparison of data in Table III with those in Tables I and II indicates that (a) enol ether **7** is less reactive than **2** under similar conditions and (b) the presence of an electron-withdrawing nitro substituent on the aryl ring promotes β-arylation even when substitution at the β-carbon introduces an unfavorable steric factor.

It is noteworthy that products **10–12**, which result from α-arylation, are formed by regioselective β-palladium hy-

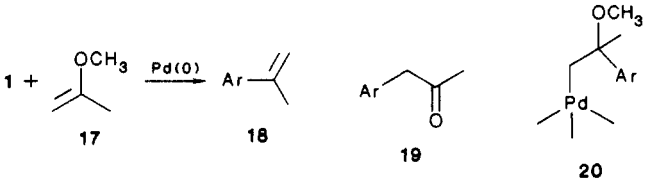
dride elimination; hydrogen loss is exclusively from the carbon bearing oxygen and aryl. No product arising from loss of palladium and methyl hydrogen was observed. This regiochemical preference for elimination of hydrogen on oxygen-bearing carbon accords with previous observations.[13]

Arylation of 3,4-Dihydro-2*H*-pyran. Arylation reactions of 3,4-dihydro-2*H*-pyran (**13**) were included in the study to provide data directly comparable to those obtained for other enol ethers and to extend previous studies.[4-6] The structural analogy between **13** and the β-substituted acyclic enol ether **7** provides a particularly interesting comparison. Catalytic arylation of **13** with iodobenzene (**1a**) in acetonitrile using either Pd/C or Pd(PPh$_3$)$_4$ proceeded smoothly, yielding the previously observed α-arylation product **14a**[5] in good yield; no product of β-arylation was observed. Reaction mixtures produced



by using either catalyst contained about 10% of a product of diarylation, presumably formed by arylation of **14a**. When Pd(PPh$_3$)$_4$ was used as catalyst, small amounts of double-bond isomers **15a** and **16a** and biphenyl were also detected. Reactions of 3,4-dihydro-2*H*-pyran (**13**) and 1-bromo-4-nitrobenzene (**1d**) similarly involved only α-arylation, producing **14b** (16%) with most starting material recovered. Corresponding reactions using iodo analogue **1c** gave no arylated products; nitrobenzene and 4,4′-dinitrobiphenyl were produced with accompanying tar formation. Attempted arylation reactions using toluene as solvent also were unsuccessful; regardless of the aryl halide used, starting material was recovered unchanged.

Arylation of Methyl 2-Propenyl Ether. Reaction of methyl 2-propenyl ether (**17**) with iodobenzene (**1a**) in acetonitrile or dimethylformamide in the presence of palladium on carbon or Pd(PPh$_3$)$_4$ as catalyst gave isopropenylbenzene (**18a**) and biphenyl in comparable yields as the only products formed. Arylation of **17** with the



4-nitrophenyl halides **1c** or **1d** proceeded similarly, yielding 1-isopropenyl-4-nitrobenzene (**18b**) and 4,4′-dinitrobiphenyl. Thus arylation of **17** occurred exclusively at the sterically hindered α-carbon; no evidence was obtained for the formation of the β-aryl regioisomer **19** (however, see below the discussion of the corresponding stoichiometric reaction). This result accords with those previously reported[14] in which arylation of 5-methyl-2,3-dihydrofuran, which is similarly substituted at the α-carbon, also exhibited only α-arylation.

Table IV. Comparison of Arylation Reaction Rates for Butyl 1(*Z*)-Propenyl Ether (7) and 3,4-Dihydro-2*H*-pyran (13)[a]

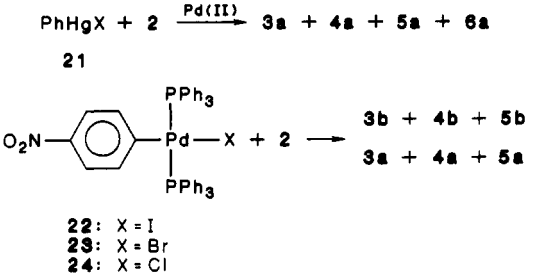
time (h)	conversion (%) 7	13
3	14	30
6	16	50
23	54	76
31	53	86

[a] Reactions utilized enol ethers (40 mmol), iodobenzene (10 mmol), triethylamine (15 mmol), and 1 mol % palladium on carbon in 20 mL of acetonitrile at 100 °C.

The formation of isopropenylbenzenes **18** deserves comment because, unlike the other arylation reactions, product formation involves loss of the enol ether oxygen function. In the intermediate σ-organopalladium adduct **20** which gives rise to **18**, the absence of hydrogens β to palladium precludes the facile β-hydride elimination reaction by which the other arylation products are formed. Adduct **20** decomposes with loss of palladium and β-methoxy; anti loss of palladium and acetoxy[14] or alkoxy[14] and syn loss of palladium and hydroxy[15] have been observed previously.

Relative Reactivities of Butyl 1(*Z*)-Propenyl Ether and 3,4-Dihydro-2*H*-pyran. The rates of conversion of the acyclic, β-substituted enol ether, butyl 1(*Z*)-propenyl ether (**7**) and the cyclic analogue, 3,4-dihydro-2*H*-pyran (**13**) are significantly different (Table IV). The cyclic enol ether (**13**) is more reactive, exhibiting 50% conversion to products in 6 h whereas the acyclic enol ether (**7**) requires 23 h to reach this level of conversion.

Stoichiometric Reactions. Arylations with Phenylmercuric Halides and Bis(triphenylphosphine)-(4-nitrophenyl)palladium Halides. Studies were made of arylation regiochemistries for reactions of *n*-butyl vinyl ether (**2**) and methyl 2-propenyl ether (**17**) with phenylmercuric salts (**21**) in the presence of stoichiometric palladium(II) salts and for reactions of **2** and bis(triphenylphosphine)-(4-nitrophenyl)palladium halides **22–24**. Results for reactions of *n*-butyl vinyl ether (**2**) are summarized in Tables V and VI, respectively.



Reaction of phenylmercuric chloride[16] (**21**, X = Cl) and *n*-butyl vinyl ether (**2**) in acetonitrile in the presence of an equimolar portion of palladium(II) chloride and triethylamine at 100 °C led to low yields of arylated products and did not exhibit regioselectivity (Table V, entry 41). When the reaction temperature was lowered to 25 °C,

(13) (a) Trost, B. M.; Chung, J. Y. L. *J. Am. Chem. Soc.* **1985**, *107*, 4586–4588. (b) Hirao, T.; Enda, J.; Ohshiro, Y.; Agawa, T. *Chem. Lett.* **1981**, 403–406. (c) Tamaru, Y.; Yamada, Y.; Yoshida, Z. *Tetrahedron* **1979**, *35*, 329–340. (d) Melpolder, J. B.; Heck, R. F. *J. Org. Chem.* **1976**, *41*, 265–272. (e) Chalk, A. J.; Magennis, S. A. *J. Org. Chem.* **1976**, *41*, 273–278.

(14) See, for example: (a) Arai, I.; Lee, T. D.; Hanna, R.; Daves, G. D., Jr. *Organometallics* **1982**, *1*, 742–747. (b) Arai, I.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1981**, *103*, 7683.

(15) Hacksell, U.; Daves, G. D., Jr. *Organometallics* **1983**, *2*, 772–775. Cheng, J. C. Y.; Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1986**, *51*, 3093–3098.

(16) Nenitzescu, C. D.; Isacescu, D. A.; Gruescu, C. *Bull. Soc. Chim. Romania* **1938**, *20*, 127; *Chem. Abstr.* **1940**, *34*, 1977.

Table V. Reaction of Phenylmercuric Salts 21 with *n*-Butyl Vinyl Ether in the Presence of Palladium(II) Salts[a]

entry	PhHgX, PdX_2 (X)	temp (°C)	time (h)	yield (%)[b] 3a	4a	5a	6a	ratio β/α[c]	3a/4a
41	Cl	100	2	14	7	0	22	1.0	2.0
42	Cl	25	1	6	3	41	0	0.2	2.0
43	Cl	25	4	8	5	53	0	0.2	1.6
44	OAc	25	1	29	21	51	0	1.0	1.4
45	OAc	25	4	26	18	50	0	0.9	1.4
46	OAc	50	2	26	17	39	5	1.0	1.5

[a] The phenylmercuric halide (PhHgX, 0.5 mmol), butyl vinyl ether (1.0 mmol), triethylamine (0.75 mmol), and palladium salt (PdX_2, 0.5 mmol) in acetonitrile (5 mL) was stirred for the time indicated. [b] Based on PhHgX and determined by gas chromatographic analysis (see Experimental Section). [c] Calculated as (**3a** + **4a**)/(**5a** + **6a**).

Table VI. Reaction of Bis(triphenylphosphine)(4-nitrophenyl)palladium(II) Halides 22–24 with *n*-Butyl Vinyl Ether in Toluene at 100 °C[a]

entry	complex	X	product distribution (%)[b] and ratios 3b	4b	5b	β/α[c]	3b/4b	3a	4a	5a	β/α[d]	3a/4a
47	22	I	10	10	21	1.0	1.0	5	7	47	0.2	0.7
48	23	Br	25	12	9	4.1	2.1	21	11	22	1.4	1.9
49	24	Cl	28	13	4	10.2	2.2	28	11	16	2.4	2.5

[a] The palladium complex (0.1 mmol) was heated with triethylamine (0.2 mmol) and butyl vinyl ether (0.5 mmol) in 3 mL of toluene for 4 h at 100 °C. The yields of arylated vinyl ethers were 40–20%, decreasing in the series I, Br, Cl. Nitrobenzene, 4-nitrobiphenyl, 4,4-dinitrobiphenyl, (4-nitrophenyl)diphenylphosphine oxide, triphenylphosphine oxide, and triphenylphosphine were also produced in the reaction. [b] Determined by gas chromatographic analysis. [c] Calculates as (**3b** + **4b**)/**5b**. [d] Calculated as (**3a** + **4a**)/**5a**.

yields improved and regioselective α-arylation was achieved (β/α ratio = 0.2, entries 42, 43). Change to acetate counterion (entries 44–46) greatly facilitates the reaction, but the regioselectivity was again lost.

Similar reaction of methyl 2-propenyl ether (**17**) with phenylmercuric chloride or acetate (**21**, X = Cl, OAc) in acetonitrile at room temperature yielded primarily biphenyl; trace amounts of isopropenylbenzene (**18a**) and phenylacetone (**19a**) were also detected.

A complex mixture of products was formed in reactions of bis(triphenylphosphine)(4-nitrophenyl)palladium iodide[17] (**22**), bromide (**23**), and chloride[17] (**24**) with *n*-butyl vinyl ether (**2**), Table VI, as a result of the migration of phenyl groups of triphenylphosphine ligands from phosphorus to palladium.[18] Yields of arylated products were modest, 20–40%, and were almost equally divided between products derived from the 4-nitrophenyl group of the palladium reagents (**22–24**) and phenylated products formed following rearrangement to a corresponding phenylpalladium species.[18] The arylated products in each of the series exhibited similar trends in arylation regioselectivity. In the nitrophenyl series the regioselectivity for arylation at the enol ether β-carbon by chloropalladium derivative **24** (β/α = 10.2) was 10-fold greater than that for the corresponding iodo derivative **22**, which exhibited no regioselectivity. The β/α ratios for the phenylated products were similar, 0.2 for the iodo compound **22** and 2.4 for chloro derivative **24**.

Trans–Cis Double-Bond Ratios of Olefins from β-Arylation. The trans/cis double-bond isomer ratios of β-arylation products resulting from the reactions included in the study are included in Tables I, II, V, and VI. The ratios vary from 0.4 to 2.6. The trans/cis ratios observed appear to be sensitive to (a) the electron density of the aryl moiety (compare data in Tables I and II), (b) the availability of ligands (Tables I, II, and V), and (c) the halide ion present (Table VI).

Because of the possibility of isomerization of enol ether double bonds by palladium(II)-catalyzed alcohol exchange[19] or simply as a result of complexation with Pd(II),[20] two control experiments were carried out. When *n*-butyl vinyl ether (**2**) was phenylated in the presence of a molar equivalent of methanol, no 2-methoxystyrene was formed. Two reactions were carried out under the conditions indicated in Table I, entry 4. To one of the reaction mixtures, in addition to the reactants, a 1:1 mixture of the trans/cis β-arylated product isomers (**3a** and **4a**) was also added in an amount equal to the expected reaction product yield. At the end of the experiment, the reaction mixture with added β-arylated products contained a total yield twice that of the companion mixture, indicating that no product degradation had occurred. The trans/cis product ratio of the control was 0.4 (0.5 in Table I, run 4). The corresponding ratio for the mixture to which product was added was 0.6; subtraction of the amounts of **3a** and **4a** produced in the control experiment restored the original 1:1 trans/cis ratio for added product. These data are indicative that the trans/cis ratios of β-arylation products observed in the various experiments result from the primary reaction and do not involve subsequent product isomerization. Spencer[21] found that trans/cis isomerization can occur during palladium-catalyzed arylation of olefins by readdition of palladium hydride formed in the reaction before decomplexation; our experiments did not determine whether such a process is occurring in the enol ether systems used in the present study.

Discussion

The goal of the present study is the elucidation of influences of reactant structure and reaction parameters on the regiochemistry of Heck arylation of enol ethers. In the study, three primary variables were considered: the enol ether, the arylating agent, and the reaction medium–catalyzed system.

(17) Fitton, P.; Rick, E. A. *J. Organomet. Chem.* **1971**, *28*, 287–291.
(18) (a) Goel, A. B.; Richards, H. J.; Kyung, J. H. *Tetrahedron Lett.* **1984**, *25*, 391–392. (b) Goel, A. B. *Inorg. Chim. Acta* **1984**, *86*, L77–L78. (c) Asano, R.; Moritani, I.; Fujiwara, Y.; Teranishi, S. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2910–2911. (d) Kikukawa, K.; Yamane, T.; Takagi, M.; Matsuda, T. *J. Chem. Soc., Chem. Commun.* **1972**, 695. (e) Yamane, T.; Kikukawa, K.; Takagi, M.; Matsuda, T. *Tetrahedron* **1973**, *29*, 955–962.
(19) (a) McKeon, J. E.; Fitton, P.; Griswold, A. A. *Tetrahedron* **1972**, *28*, 227–232. (b) McKeon, J. E.; Fitton, P. *Tetrahedron* **1972**, *28*, 233–238. (c) Divers, G. A.; Berchtold, G. A. *Synth. Commun.* **1977**, *7*, 43–48.
(20) Wakatsuki, Y.; Nozakura, S.; Murahashi, S. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3426–3429.
(21) Spencer, A. *J. Organomet. Chem.* **1982**, *240*, 209–216.

The Enol Ether. With *n*-butyl vinyl ether (**2**) as a reference, the effect of alkyl substitution on the regiochemistry of arylation was determined. Arylation of **2** (Tables I, II, V, VI) exhibited ratios of regioisomeric products that varied 50-fold (β/α = 0.2–10.2), depending on arylating agent and reaction conditions used. Direct comparison of arylation reactions of **2** with those of butyl 1(*Z*)-propenyl ether (**7**) indicated that methylation on the β-carbon significantly diminished, but did not completely inhibit, β-arylation; β/α ratios for arylation of **7** of 0.14–1.2 were observed (Table III). When the β-substituent was incorporated into a ring (see 3,4-dihydro-2*H*-pyran, **13**) discrimination against β-arylation was complete; only α-arylation was observed. These differences cannot be ascribed to a steric effect. Earlier, we noted[5] that the diminished conformational freedom of cyclic enol ethers serves to enhance the effectiveness of interaction of π electrons on oxygen with the carbon–carbon double bond and thereby accentuate electronic effects differentiating the olefinic carbons.[4] It is noteworthy that change from an acyclic β-alkyl substituted enol ether to a cyclic analogue also increases the rate of arylation (Table IV); this difference may be indicative of more effective complexation of the cyclic enol ether with palladium(II).[20]

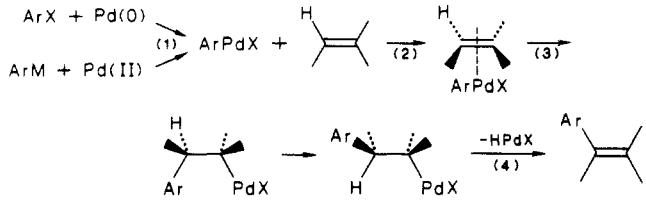
Substitution on the enol ether α-carbon (see methyl 2-propenyl ether, **17**) resulted in regiospecific α-arylation. This result, which accords with earlier observations,[4] provides even stronger evidence that steric effects in Heck arylation of enol ethers are secondary since, in **17**, the β-olefinic carbon is much more accessible than the α-carbon and yet no β-arylation product was observed.

Arylating Agent. The aryl precursor to the actual organopalladium arylating agent (see Mechanism below) strongly affected the observed regioselectivity of the reaction. Comparison of results from reactions in which the arylating reagent precursors are respectively a halobenzene and the corresponding 1-halo-4-nitrobenzene established that decreasing the electron density of the aryl ring by 4-nitro substitution increased the regioselectivity for β-arylation by a factor of 2 to 8, depending on other variables (Tables I–III, V, VI). This accords with earlier work[3,7] in which an increase in the electron density of the aryl moiety by 4-methoxy substitution led to an equally impressive preference for regioselective α-arylation.

Similarly, the halogen present in the arylating agent has an important effect on arylation regiochemistry. The effect is most evident in reactions of the bis(triphenylphosphine)(4-nitrophenyl)palladium(II) halides (Table VI) in which β/α regioselectivity ratios of 1.0, 4.1, and 10.2 for I, Br, and Cl, respectively, were observed. Differences were less pronounced in the catalytic reactions where preferences for β-arylation by bromo aryls of up to twice those for the corresponding iodo aryls were observed (Table II). Unfortunately, under the catalytic conditions used, formation of the arylpalladium reagent is sufficiently slow for bromobenzene (Table I) that use of aryl bromides and chlorides is impractical[1b,22] and precludes facile halogen selection for control of arylation regiochemistry. These data, and the related results (Table V) which indicate that acetate (as a ligand on palladium) is about 5 times more effective than chloride in selecting for β-arylation, correlate with the relative bond strengths of Pd(II)–X that are in the order I > Br > Cl ≫ OAc.[23]

(22) See, however, the recent work by Jeffery in which use of tetrabutylammonium chloride greatly facilitated arylpalladium reagent formation: Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287–1288. See also: ref 13e and Davison, J. B.; Simon, N. M.; Sojka, A. S. *J. Mol. Catal.* **1984**, *22*, 349.

Scheme I



Reaction Medium–Catalyst System. Activation of an aryl halide in the Heck arylation reaction involves oxidative addition to a Pd(0) center;[1] when a Pd(II) species is used as catalyst, an initial reduction is necessary before reaction with an aryl halide can occur. Catalytic activity may sometimes correlate with ease of reduction of the Pd(II) species,[24] but this process, which precedes π-complex formation (see below), is unlikely to affect reaction regiochemistry. A critical question is whether the catalytic reactions occur in solution or, in at least some instances, are heterogeneous. In these reactions, it is difficult to distinguish between processes occurring in solution and heterogeneous processes occurring on the surface of metal particles[24] and we have made no attempt to do so. For convenience in considering the effects of changes in reaction media on arylation regiochemistry, we assume that, in all cases, the key intermediate is Pd(II) with aryl and enol ether occupying adjacent ligand sites.

The choice of reaction solvent and the presence or absence of species that coordinate with Pd(II) affect the regiochemistry of arylation. A poorly coordinating solvent, toluene, is significantly more favorable toward β-arylation than acetonitrile, which effectively coordinates Pd(II). Inclusion of coordinating ligands, triphenylphosphine, in toluene-based reaction mixtures diminishes the preference for β-arylation (Tables I and II) and results in β/α arylation ratios more similar to those obtained in acetonitrile. Addition of triphenylphosphine to reaction mixtures in acetonitrile had little effect in arylations involving phenyl halides (Table I) but also decreased β-arylation when 4-nitrophenyl halides were used (Table II).

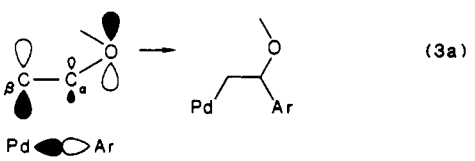
Mechanism of Heck Arylation. There is general agreement on the basic chemistry involved in Heck arylation of olefins.[1] It is convenient to consider the overall reaction as occurring in four discrete steps:[4,25] (1) arylpalladium reagent formation, usually by oxidative addition of Pd(0) to an aryl halide or by transmetalation of a metalloaryl derivative with Pd(II), (2) π-complex formation of the arylpalladium reagent with the olefinic double bond, (3) collapse of the π-complex to a σ-organopalladium adduct, and (4) decomposition of the σ-adduct with palladium elimination and product formation (Scheme I). Within this general scheme many mechanistic details remain obscure.

The regiochemistry of the arylation reaction is determined by the manner in which the π-complex collapses (Scheme I, step 3). Collapse of a π-complex of an unsymmetrical olefin, by syn addition of aryl and palladium to the two respective olefinic carbons,[1,26] can produce either of two σ-adducts or a mixture containing both. The mechanism of π-complex collapse to a σ-adduct (and its

(23) See reference 1d, pp 11–15.
(24) Andersson, C. M.; Karabelas, K.; Hallberg, A.; Andersson, C. *J. Org. Chem.* **1985**, *50*, 3891–3895.
(25) (a) Cacchi, S.; Arcadi, A. *J. Org. Chem.* **1983**, *48*, 4236–4240. (b) Kalinoski, H. T.; Hacksell, U.; Barofsky, E.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 6476–6482. (c) Cheng, J. C.-Y.; Daves, G. D., Jr. *Organometallics* **1986**, *5*, 1753–1755.
(26) Hacksell, U.; Kalinoski, H. T.; Barofsky, D. F.; Daves, G. D., Jr. *Acta Chem. Scand., Ser. B* **1985**, *39*, 469–476.

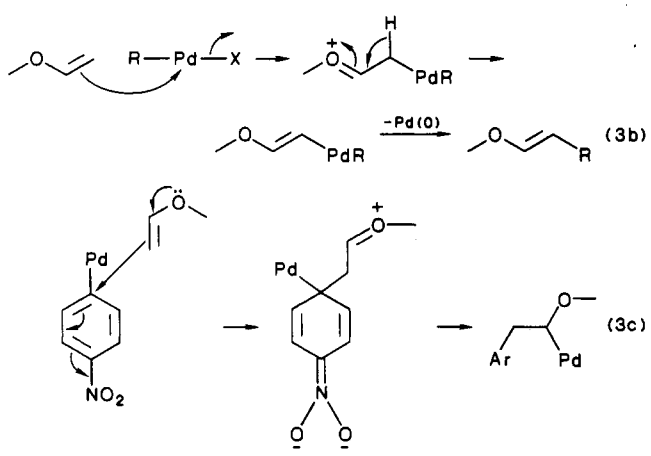
reverse) has attracted significant recent interest.[27] The reaction is viewed as involving a [2 + 2] cyclic interaction[27a] reached by "slipping"[27g] of the π-complexed olefin such that the palladium center approaches σ-bonding distance to one of the olefinic carbons with "migration" of a Pd-bonded group (e.g., aryl) to the other olefinic carbon. In this mechanism, the Pd(II) center is an electron acceptor and the migrating carbon is carbanionic, although, in general, little charge separation occurs as the reaction proceeds.[27d]

Mechanisms for α- and β-Arylations. The correlations delineated in this study establish that electronic factors determine the regiochemistry of palladium-catalyzed (mediated) enol ether arylation and that steric effects are of relatively minor importance. Further, the correlations indicate that an electron-deficient, poorly coordinated Pd(II) center favors β-arylation whereas an electron-rich palladium favors α-arylation. Within the general mechanism described, α-arylation is readily accounted for; the dominant interaction is that of the highest occupied molecular orbital of the enol ether with the antibonding (σ^*) Pd(II)-aryl orbital. This interaction leads to a (presumably) concerted reaction whereby the electron-deficient palladium forms a σ-bond with the β-carbon of the enol ether, which is the site of greatest electron density and the relatively electron-rich aryl carbon bonds to the α-carbon in a syn stereochemical sense (3a).[4]



(3a)

No similar mechanism leading to the β-arylation product is obvious. Alternatives that we believe merit consideration involve processes whereby the electron-rich enol ether attacks (3b) the poorly coordinated electropositive palladium center or (3c) the electron-deficient aryl carbon.[28] These processes (3b and 3c) accord with the correlation of increased β-arylation with increasing electron deficits of both the palladium center and the aryl ring.



(3b)

(3c)

(27) See, for example: (a) Fujimoto, H.; Yamasaki, T. *J. Am. Chem. Soc.* **1986**, *108*, 578–581. (b) Backvall, J. E.; Bjorkman, E. E.; Pettersson, L.; Siegbahn, P. *J. Am. Chem. Soc.* **1985**, *107*, 7265–7267. (c) Koga, N.; Obara, S.; Kitaura, K.; Morokuma, K. *J. Am. Chem. Soc.* **1985**, *107*, 7109–7116. (d) Doherty, N. M.; Bercaw, J. E. *J. Am. Chem. Soc.* **1985**, *107*, 2670–2682. (e) Bryndza, H. E. *J. Chem. Soc., Chem. Commun.* **1985**, 1696–1698. (f) Backvall, J. E.; Bjorkman, E. E.; Pettersson, L.; Siegbahn, P. *J. Am. Chem. Soc.* **1984**, *106*, 4369–4373. (g) Eisenstein, O.; Hoffmann, R. *J. Am. Chem. Soc.* **1981**, *103*, 4308–4320. (h) Thorn, D. L.; Hoffmann, R. *J. Am. Chem. Soc.* **1978**, *100*, 2079–2090.

(28) March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley-Interscience: New York, 1985; pp 576–578.

Experimental Section

Instrumentation. Mass spectra were obtained on a Finnigan 4021 (Data System Incos 2100) gas chromatograph–mass spectrometer, operating at 70 eV. ^{1}H NMR spectra were recorded on a Varian XL-300 spectrometer in deuteriochloroform. Chemical shifts are given relative to internal Me_4Si. Melting points were determined in capillary tubes and are uncorrected. Elemental analyses were obtained from Dornis u. Kolbe Mikroanalytisches Laboratorium, Mülheim, West Germany. Quantitative gas chromatographic analyses were performed on a Varian 3700 instrument equipped with a (2.5 m × 2 mm) glass column of either 5% OV 17 on Chromosorb W or 3% Carbowax 20 M on Supelcoport 100/120. A Varian 3400 instrument was used for capillary gas chromatography on an OV 1701 (25 m × 0.25 mm) column. Peak areas were determined by using a Varian 4270 integrator. Pentadecane was used as an internal standard. For flash chromatography silica gel 60 (0.040–0.0064 mm, E. Merck) was used. Catalytic experiments were performed in 50 mL, heavy-walled and thin-necked Pyrex tubes, sealed with a Teflon-brand stopcock.

Materials. Palladium salts were obtained from Johnson-Matthey Chemicals and were used as received. Tetrakis(triphenylphosphine)palladium(0) was prepared according to the method described by Coulson.[29] Palladium-on-charcoal (10%) was purchased from Riedel-de-Haën. Bis(triphenylphosphine)(4-nitrophenyl)palladium chloride and iodide were obtained by following the method of Fitton and Rick.[17] Bis(triphenylphosphine)(4-nitrophenyl)palladium bromide, a colorless solid, was obtained by the same procedure: mp 193–194 °C dec. Anal. Calcd for $C_{42}H_{34}BrNO_2PPd$: C, 60.6; H, 4.1; N, 1.68. Found: C, 60.5; H, 4.10; N, 1.65.

The aryl halides, butyl vinyl ether, methyl 2-propenyl ether, and 3,4-dihydro-2*H*-pyran were obtained from commercial sources and were purified by recrystallization or distillation before use. Phenylmercuric acetate and chloride were purchased from Sigma and EGA-Chemie, respectively, and were used as received. Butyl 1(*Z*)-propenyl ether was prepared, in about 70% yield, through isomerization of allyl butyl ether with potassium *tert*-butoxide at 160 °C[30] for 3 days followed by distillation. Triethylamine was distilled from potassium hydroxide and stored over (3 Å) molecular sieves until used. Solvents were stored over molecular sieves, but otherwise were used as received.

Catalytic Reactions. (A) Arylation of *n*-Butyl Vinyl Ether (Tables I and II). The aryl halide (10 mmol), triethylamine (15 mmol), and *n*-butyl vinyl ether (**2**, 20 mmol) were charged in the reaction vessel. The palladium catalyst (0.1 mmol) and (when present) phosphine ligand, dissolved/dispersed in 10 mL of solvent, were added to the mixture (see Tables I and II for details concerning catalyst systems and solvents). After thorough mixing of the components, the tube was closed and heated at 100 °C in an oil bath for 16 h. After cooling and dilution with diethyl ether, the internal standard (pentadecane, 250 mg) was added, and samples of ≈0.2 mL were removed. The samples were washed with a small amount of water and subjected to GC–MS analysis for determination of the yields of the separate isomers, and the amount of remaining starting material, relative to pentadecane (Tables I and II). Response factors were obtained by using pure compounds isolated from reaction mixtures and purified as described. Isomers were assumed to have the same response factor. Small amounts of acetophenone (**6a**) formed by hydrolysis of (1-butoxyethenyl)benzene (**5a**) were generally observed. Since the (1-butoxyethenyl)arenes (**5**) could not be isolated in a pure state (see below), they were quantified via complete hydrolysis to the acetophenone (**6**) with 1 M HCl, followed by a second gas chromatographic analysis. This careful hydrolysis proved to be selective, leaving the other isomers intact, whereas more concentrated acid caused decomposition of the (2-butoxyethenyl)arenes (**3**, **4**). The remaining crude product was partitioned between diethyl ether and water and the organic phase was washed with additional water. The organic layer was dried ($MgSO_4$) and concentrated, and the resulting oily residue was subjected to flash chromatography using pentane or pentane/

(29) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121.
(30) Prosser, T. J. *J. Am. Chem. Soc.* **1961**, *83*, 1701–1704.

chloroform as eluent. This practice afforded a mixture of the isomeric (2-butoxyethenyl)arenes (**3**, **4**), which was analyzed by NMR. Partial separation of the components was achieved. A second fractionation produced fractions of virtually isomerically pure material. The corresponding 1-aryl isomers (**5**), however, gradually decomposed to the acetophenone (**6**) on the column and were not isolated. NMR spectra were in good agreement with calculated and/or literature values. The instability of the (2-butoxyethenyl)benzenes[31] prevented elemental analysis.

(*E*)-(2-Butoxyethenyl)benzene (3a): colorless oil; ^{1}H NMR δ 7.0–7.4 (m, 5 H), 6.99 (d, 1 H, J = 13 Hz), 5.82 (d, 1 H, J = 13 Hz), 3.82 (t, 3 H), 1.4–1.6 (m, 4 H), 0.96 (t, 3 H); MS, m/e 176 ($M^{\bullet+}$), 120, 91.

(*Z*)-(2-Butoxyethenyl)benzene (4a): colorless oil; ^{1}H NMR δ 7.3–7.6 (m, 5 H), 6.19 (d, 1 H, J = 7 Hz), 5.19 (d, 1 H, J = 7 Hz), 3.91 (t, 2 H), 1.4–1.6 (m, 4 H), 0.96 (t, 3 H); MS, m/e 176 ($M^{\bullet+}$), 120, 91.

(1-Butoxyethenyl)benzene (5a): MS, m/e 176 ($M^{\bullet+}$), 161, 121, 105.

(*E*)-1-(2-Butoxyethenyl)-4-nitrobenzene (3b): yellow solid; mp 54–56 °C; ^{1}H NMR δ 7.2–8.2 (m, 4 H), 7.19 (d, 1 H, J = 13 Hz), 5.85 (d, 1 H, J = 13 Hz), 3.90 (t, 2 H), 1.45 (m, 4 H), 0.97 (t, 3 H); MS, m/e 221 ($M^{\bullet+}$), 165, 148, 135, 57.

Anal. (mixture of the E and Z isomers). Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83. Found: C, 65.09; H, 6.85.

(*Z*)-1-(2-Butoxyethenyl)-4-nitrobenzene (4b): yellow liquid; ^{1}H NMR δ 7.2–8.2 (m, 4 H), 6.40 (d, 1 H, J = 7.3 Hz), 5.27 (d, 1 H, J = 7.3 Hz), 4.02 (t, 2 H), 1.71 (m, 4 H), 0.97 (t, 3 H); MS, m/e 221 ($M^{\bullet+}$), 165, 148, 135, 57.

1-(1-Butoxyethenyl)-4-nitrobenzene (5b): MS, m/e 206, 166, 150, 56.

(B) Arylation of Butyl 1(*Z*)-Propenyl Ether (Table III). To a mixture of the aryl halide (10 mmol) and butyl 1(*Z*)-propenyl ether (**7**, 20 mmol) were added triethylamine (15 mmol) and the palladium catalyst (0.1 mmol), dissolved/dispersed in 10 mL of acetonitrile (see Table III for details), and the mixture was thoroughly agitated. The tube was sealed and heated at 100 °C for 24 h. After cooling, the crude reaction mixture was diluted with diethyl ether and internal standard (pentadecane, 250 mg) was added. The solution was washed with water and, from a small sample, the isomeric distribution was determined by GC analysis (see Table III). Attempted separation of the isomers by column chromatography and HPLC failed. NMR spectra were therefore recorded on the oily mixtures of isomers obtained by flash chromatography of the concentrated crude product using pentane/chloroform as eluent. Structures were assigned with the aid of decoupling experiments. Elemental analysis of the butoxyphenylpropenes was not obtained, owing to their instability.[31]

(*E*)-1-Butoxy-2-phenylpropene (8a): ^{1}H NMR δ 7.2–7.5 (m, 5 H, aryl), 6.48 (q, 1 H, J = 1 Hz), 3.86 (t, 2 H), 2.0 (d, 3 H, J = 1 Hz), 1.6–1.8 (m, 2 H), 1.4–1.5 (m, 2 H), 0.95 (m, 6 H); MS, m/e 190 ($M^{\bullet+}$), 134, 115, 105.

(*Z*)-1-Butoxy-2-phenylpropene (9a): ^{1}H NMR δ 7.2–7.5 (m, 5 H, aryl), 6.20 (q, 1 H, J = 1 Hz), 3.82 (t, 2 H), 1.9 (d, 3 H, J = 1 Hz), 1.6–1.8 (m, 2 H), 1.4–1.5 (m, 2 H), 0.95 (m, 6 H); MS, m/e 190 ($M^{\bullet+}$), 134, 115, 105.

(*E*)-1-Butoxy-1-phenylpropene (10a): ^{1}H NMR δ 7.2–7.5 (m, 5 H, aryl), 5.37 (q, 1 H, J = 7 Hz), 3.61 (t, 2 H), 1.8 (d, 3 H, J = 7 Hz), 1.6–1.8 (m, 2 H), 1.4–1.5 (m, 2 H), 0.95 (m, 6 H); MS, m/e 190 ($M^{\bullet+}$), 134, 115, 105.

(*Z*)-1-Butoxy-1-phenylpropene (11a): ^{1}H NMR δ 7.2–7.5 (m, 5 H, aryl), 4.82 (q, 1 H, J = 7 Hz), 3.73 (t, 2 H), 1.7 (d, 3 H, J = 7 Hz), 1.6–1.8 (m, 2 H), 1.4–1.5 (m, 2 H), 0.95 (m, 6 H); MS, m/e 190 ($M^{\bullet+}$), 161, 133, 115, 105.

(*E*)-1-Butoxy-2-(4-nitrophenyl)propene (8b): ^{1}H NMR δ 7.2–8.2 (m, 4 H, aryl), 6.74 (q, 1 H, J = 1 Hz), 3.46 (t, 2 H), 1.6–1.8 (m, 2 H), 1.4–1.5 (m, 2 H), 0.9–1.0 (m, 6 H); MS, m/e 235 ($M^{\bullet+}$), 179, 162, 132, 57.

Anal. (mixture of four isomers). Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28. Found: C, 66.40; H, 7.31.

(*Z*)-1-Butoxy-2-(4-nitrophenyl)propene (9b): ^{1}H NMR δ 7.2–8.2 (m, 4 H, aryl), 6.38 (q, 1 H, J = 1 Hz), 3.72 (t, 2 H), 1.6–1.8 (m, 2 H), 1.4–1.5 (m, 2 H), 0.9–1.0 (m, 6 H); MS, m/e 235 ($M^{\bullet+}$), 179, 162, 132, 57.

(*E*)-1-Butoxy-1-(4-nitrophenyl)propene (10b): ^{1}H NMR δ 7.2–8.2 (m, 4 H, aryl), 4.96 (q, 1 H, J = 7 Hz), 3.42 (t, 2 H), 1.6–1.8 (m, 2 H), 1.4–1.5 (m, 2 H), 0.9–1.0 (m, 6 H); MS, m/e 235 ($M^{\bullet+}$), 206, 179, 162, 150, 132, 57.

(*Z*)-1-Butoxy-1-(4-nitrophenyl)propene (11b): ^{1}H NMR δ 7.2–8.2 (m, 4 H, aryl), 5.64 (q, 1 H, J = 7 Hz), 3.62 (t, 2 H), 1.6–1.8 (m, 2 H), 1.4–1.5 (m, 2 H), 0.9–1.0 (m, 6 H); MS, m/e 235, ($M^{\bullet+}$), 206, 179, 162, 150, 132, 57.

(C) Arylation of 3,4-Dihydro-2*H*-pyran (13). The experiments were performed by following the procedure given in A, with 3,4-dihydro-2*H*-pyran (**13**) replacing *n*-butyl vinyl ether. The spectral data for 2-phenyl-3,4-dihydro-2*H*-pyran (**14a**) were in accord with those reported earlier.[5] From the reaction starting from 4-nitrobromobenzene (**1d**), standard workup afforded 2-(4-nitrophenyl)-3,4-dihydro-2*H*-pyran (**14b**, 16%): ^{1}H NMR δ 7.48–8.26 (m, 4 H), 6.53 (dt, 1 H, J = 6 Hz, 2 Hz), 4.93 (dd, 1 H, J = 10 Hz, 2 Hz), 4.82 (m, 1 H), 1.8–2.3 (m, 4 H).

Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40. Found: C, 64.42; H, 5.45.

(D) Arylation of Methyl 2-Propenyl Ether (17). Attempted arylation of methyl 2-propenyl ether (**17**) was conducted at conditions identical with those reported in A. A single reaction was also performed in dimethylformamide as solvent with sodium acetate replacing triethylamine.[32]

(E) Comparison of the Reactivities of 3,4-Dihydro-2*H*-pyran (13) and Butyl 1(*Z*)-Propenyl Ether (7) toward Arylation with Iodobenzene (Table IV). To a solution of iodobenzene (10 mmol), triethylamine (15 mmol), and internal standard in 20 mL of acetonitrile was added a suspension of Pd/C (0.1 mmol) in the enol ether (40 mmol), and the solution was heated at 100 °C in an oil bath. The consumption of iodobenzene was periodically monitored by GC analyses. The use of 4 equiv of enol ether[13] supressed the formation of diarylated product of 3,4-dihydro-2*H*-pyran.

Stoichiometric Reactions. (F) Arylation of *n*-Butyl Vinyl Ether (2) with Phenylmercuric Salts (Table V). Phenylmercuric salt (**21**, chloride or acetate, 0.5 mmol) and the corresponding palladium salt (0.5 mmol) were placed in a 10-mL flask. A solution of *n*-butyl vinyl ether (**2**, 1.0 mmol) and triethylamine (0.75 mmol) in 5 mL of acetonitrile was added with stirring. After heating at the appropriate temperature, for the time indicated (see Table V for details), diethyl ether and water were added to the black mixture. Internal standard was added and the organic layer removed and filtered. The product distribution was obtained by GC–MS analysis (see A).

(G) Arylation of Methyl 2-Propenyl Ether (17) with Phenylmercuric Salts. The reactions were run according to procedure F.

(H) Arylation of *n*-Butyl Vinyl Ether (2) with Bis(triphenylphosphine)(4-nitrophenyl)palladium Halides (Table VI). The appropriate palladium complex (**22–24**, 0.1 mmol) was charged together with *n*-butyl vinyl ether (**2**, 0.5 mmol) and triethylamine (0.2 mmol) in a 10-mL heavy-walled ampule. Three milliliters of dry, degassed toluene was added, and the ampule was flushed with nitrogen and sealed through melting. After thorough mixing, the ampule was heated, with occasional shaking, at 100 °C in an oil bath for 4 h. The solution gradually darkened, and after the reaction was complete a palladium mirror was observed in the vessel. Internal standard was added to the cold reaction mixture and after filtration, capillary GC–MS analysis was performed.

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