C_5-CH_3), 27.4 (t, CH_2CH_2CHOO), 29.6 (t, CH_2CHOO), 32.7 (d, C_5), 41.6 (d, C_{3a}), 43.5 (d, C_4), 46.3 (d, C_{7a}), 60.6 (t, OCH_2CH_3), 64.9 (t, OCH_2CH_2O), 82.3 (d, C_1), 103.6 (d, OCHO), 122.0 (d, C_7), 135.7 (d, C_6), 171.1 (s, C=O), 173.8 (s, C=O); IR (film) 1730 (ester), 1780 (lactone) cm^{-1}.

1,3,3a,4,5,7a-Hexahydro-5-methyl-3-oxo-4-(ethoxycarbonyl)isobenzofuran-1-acetic Acid Ethyl Ester (4e). The crude product **3b** (6.9 g) was distilled in a Kugelrohr apparatus. The fraction boiling at 160–180 °C (0.2 mm) was treated with ether/hexane to give 1.9 g (31% over two steps) of the crystalline product **4e**: mp 108–110 °C; mass spectrum, *m/e* calcd for $C_{14}H_{17}O_5$ 265.107, found 265.115 [M^+ – OEt]; ^1H NMR ($CDCl_3$) δ 0.98 (d, 3, J = 7 Hz, $CHCH_3$), 1.23 (t, 3, J = 7.5 Hz, CH_3CH_3), 1.30 (t, 3, J = 7.5 Hz, CH_2CH_3), 2.5 (t, 1, J = 12.5 Hz, C_{7a}-H), 2.7–3.0 (m, 5, CH_2CO_2 + 3 CH), 4.15–4.3 (2 q, 4, 2 OCH_2), 4.5–4.65 (m, 1, C_1-H), 5.5–5.8 (m, 2, HC=CH); ^{13}C NMR ($CDCl_3$) δ 14.2 (q, 2 CH_2CH_3), 17.5 (q, $CHCH_3$), 32.7 (d, C_5), 38.3 (t, CH_2COOEt), 41.4 (d, C_{3a}), 43.5 (d, C_4), 46.2 (d, C_{7a}), 60.7 (t, OCH_2), 61.2 (t, OCH_2), 78.2 (d, C_1), 121.6 (d, C_7), 135.9 (d, C_6), 169.4 (C=O), 170.9 (C=O), 173.2 (C=O); IR (CH_2Cl_2) 1792 (lactone), 1736 (ester) cm^{-1}. Anal. Calcd for $C_{16}H_{22}O_6$ (310.4): C, 61.9; H, 7.1. Found: C, 61.8, H, 7.2.

Acknowledgment. We thank Dr. E. Fu for recording the mass spectra and Dr. M. Shapiro and his staff for providing the spectral data and for helpful discussions.

Synthesis of β-Arylvinyl Ethers by the Palladium-Catalyzed Reaction of Aroyl Chlorides with Vinyl Ethers

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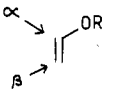
Reaction of aroyl chlorides with butyl vinyl ether in the presence of a palladium catalyst and an amine base affords β-arylvinyl ethers in 40–60% yield. Both with regard to regioselectivity and reaction rate, aroyl chlorides were superior to aryl bromides or iodides as starting materials. Thus, benzoyl chloride favored substitution at the terminal (β) carbon atom of the vinyl ether by a factor of about three, as compared to iodobenzene. Furthermore, the substituents in the aroyl chloride were found to have a profound influence on regioselectivity, with electron-withdrawing groups giving the best results. For example, a threefold improvement in β-selectivity was observed in going from benzoyl chloride to 4-nitrobenzoyl chloride.

Introduction

Interest in enol ethers, earlier regarded simply as derivatives of aldehydes and ketones, as synthetic intermediates has increased as a result of the development of new areas of application.[1] Although arylacetaldehyde enol ethers are valuable substrates in synthetic chemistry,[2] they have not been easily available, and recently a series of new approaches has been reported for the preparation of this class of compounds.[3]

The Heck arylation of olefins[4] has become an important, general method for the preparation of arylalkenes and would in principle be expected to provide a convenient entry to β-arylvinyl ethers. However, palladium-catalyzed arylations of electron-rich olefins, such as enol ethers, furnish mixtures of regioisomers and low yields have been reported.[5,6] Recent work in our laboratories has shown that the regiochemical outcome of these arylations is in fact to a great extent governed by the conditions and reactants employed and that a fair degree of regiochemical control can be achieved.



From this basic study[7] we anticipated that catalytic reactions involving arylpalladium chloride intermediates[8] would favor the desired β-arylation of alkyl vinyl ethers.

A valuable extension of the Heck reaction developed by Blaser and Spencer, introducing benzoyl chlorides as arylating agents,[9] gives indirect access to these interme-

(1) For some recent examples, see: (a) Torii, S.; Inokuchi, T.; Kondo, K. *J. Org. Chem.* **1985**, *50*, 4980. (b) Ousset, J. B.; Mioskowski, C.; Yang, Y. L.; Falck, J. R. *Tetrahedron Lett.* **1984**, *25*, 5903. (c) Franck, R. W.; Gupta, R. B. *J. Chem. Soc., Chem. Commun.* **1984**, 761. (d) Russel, C. E.; Hegedus, L. S. *J. Am. Chem. Soc.* **1983**, *105*, 943. (e) Huet, F.; Lechevallier, A.; Conia, J. M. *Synth. Commun.* **1980**, *10*, 83. (f) A short account of enol ether chemistry is given in: Earnshaw, C.; Wallis, C. J.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 3099.

(2) (a) Boit, H. G. *Ergebnisse der alkaloid-chemie*; Akademie Verlag: Berlin, 1961. (b) Chastanet, J.; Roussi, G. *J. Org. Chem.* **1985**, *50*, 2910. (c) Sakamoto, T.; Kondo, Y.; Yamanaka, H. *Chem. Pharm. Bull.* **1985**, *33*, 626. (d) Hallberg, A.; Westfelt, L.; Andersson, C.-M. *Synth. Commun.* **1985**, 1131. (e) Alonso, M. E.; Jano, P.; Hernandez, M. I.; Greenberg, R. S.; Wenkert, E. *J. Org. Chem.* **1983**, *48*, 3047. (f) Padwa, A.; Kumagai, T.; Woolhouse, A. D. *Ibid.* **1983**, *48*, 2330. (g) Matsumoto, M.; Kuroda, K. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 382. (h) Gray, T. I.; Pelter, A.; Ward, R. S. *Tetrahedron* **1979**, *35*, 2539. (i) Blondeau, D.; Sliwa, H. *J. Chem. Res., Synop.* **1979**, 2. (j) Kyba, E. P.; John, A. M.; *Tetrahedron. Lett.* **1977**, 2737.

(3) See for example: (a) From aryl halides via nickel-catalyzed coupling with (β-ethoxyalkenyl)zirconium derivatives: Negishi, E.; Van Horn, D. E. *J. Am. Chem. Soc.* **1977**, *99*, 3168. (b) From aryl halides by palladium-catalyzed cross-coupling with (2-ethoxyvinyl)boranes: Miyaura, N.; Maeda, K.; Suginome, H.; Suzuki, A. *J. Org. Chem.* **1982**, *47*, 2117. (c) From aryl Grignard reagents by nickel-catalyzed coupling with 2-bromovinyl ethyl ether: Tamao, K.; Zembayashi, M.; Kumada, M. *Chem. Lett.* **1976**, 1237. (d) From aldehydes via reaction with [methoxy(phenylthio)methyl]lithium and radical reductive elimination: Vatele, J.-M. *Tetrahedron Lett.* **1984**, 5997. (e) From benzyl alcohol, dimethyl sulfoxide, and potassium hydroxide: Langhals, H.; Julia, M.; Uguen, D. *Liebigs Ann. Chem.* **1982**, 2216. (f) From aldehydes through reaction with (phenylsulfonyl)methane followed by desulfonylation: Mandai, T.; Hara, K.; Nakajima, T.; Kawada, M.; Otera, J. *Tetrahedron Lett.* **1983**, 4993. (g) By Wittig–Horner olefination with (alkoxymethyl)phosphonate esters: Kluge, A. F.; Cloudsdale, I. S. *J. Org. Chem.* **1979**, *44*, 4847.

(4) (a) Heck, R. F. *Org. React. (N. Y.)* **1982**, *27*, 345. (b) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146. For an excellent survey of this and related reactions, see; Heck, R. F. *Palladium Reagents in Organic Syntheses*; Academic: London, 1985.

(5) See, for example; (a) Arai, I.; Daves, G. D., Jr. *J. Org. Chem.* **1979**, *44*, 21. (b) Ziegler, C. B.; Heck, R. F. *Ibid.* **1978**, *43*, 2949. (c) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5535.

(6) Cyclic enol ethers, e.g., dihydropyrans and glycals give exclusive α-arylation, and this has been applied to C-nucleoside syntheses. See: (a) Lee, T. D.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 399. (b) Hacksell, U.; Daves, G. D., Jr. *Ibid.* **1983**, *48*, 2870 and references cited therein. (c) Successful regiocontrolled arylation of vinyl sulfides has been demonstrated: Trost, B. M.; Tanigawa, Y. *J. Am. Chem. Soc.* **1979**, *101*, 4743.

(7) Andersson, C.-M.; Hallberg, A.; Daves, G. D., Jr. *J. Org. Chem.* **1987**, *52*, 3529.

(8) For a discussion of the mechanism, see ref 4a.

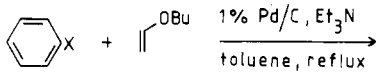
(9) (a) Blaser, H.-U.; Spencer, A. *J. Organomet. Chem.* **1982**, *233*, 267. (b) Spencer, A. *Ibid.* **1982**, *240*, 209; **1983**, *247*, 117; **1984**, *265*, 323.

0022-3263/88/1953-0235$01.50/0

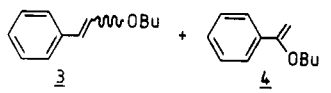
diates.[10] We have now successfully applied this modification in the arylation of butyl vinyl ether[11] and report here a simple synthesis of β-arylvinyl ethers from benzoic acids.

Results and Discussion

Initially, benzoyl chloride (**1a**) was reacted with butyl vinyl ether (**2**) in the presence of triethylamine and palladium on charcoal in refluxing toluene, as outlined in eq 1.



1 2



3 4 (1)

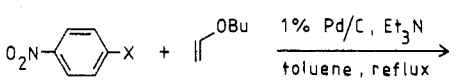
a; X = COCl	3	:	1
b; X = I	1	:	1

Analysis of the resulting reaction mixture revealed that the desired (*E*)- and (*Z*)-(2-butoxyethenyl)benzenes (**3**) had been formed in 40% yield, together with (1-butoxyethenyl)benzene (**4**, 14%) and an acylated enol ether, which was identified as (*E*)-3-butoxy-1-phenyl-2-propen-1-one (10%). A control experiment omitting the catalyst gave no arylation and only a trace of the acylated product. The reaction was carried out under conditions known to give the most favorable β/α ratio, starting from halobenzenes.[7,12]

However, a comparison of iodobenzene (**1b**) and benzoyl chloride as precursors for the arylpalladium intermediate revealed two important differences. First, the β/α ratio starting from benzoyl chloride (3:1) was much higher than that obtained from iodobenzene (1:1), under the same conditions. Second, the reaction was much faster starting from benzoyl chloride. The apparent dependence of regioselectivity on the nature of the halide, indicated in stoichiometric experiments,[7] was thus confirmed, and a more extensive study was undertaken.

We have previously found that a 4-nitro substituent in the aryl moiety exerts a strong directive effect toward the β-carbon atom of the enol ether in Heck arylations.[7,13] A comparison of the β/α ratios starting from 1-bromo-4-nitrobenzene, 1-iodo-4-nitrobenzene, and 4-nitrobenzoyl chloride (**5a–c**) was therefore made (eq 2). The conditions were identical with those given above. The acid chloride again gave the most favorable regioselectivity (**6**/**7** = 10:1), followed by the bromide (7:1) and the iodide (4:1).

The trend is in good agreement with that reported previously for stoichiometric experiments, starting from the corresponding (4-nitrophenyl)bis(triphenylphosphine)palladium halides.[7] Thus, apart from the directive effect due to the 4-nitro substituent, the choice of halo derivative clearly also affects the product distribution in a catalytic reaction. The yields decreased in the expected order COCl > I ≫ Br, with the acid chloride giving



5 2

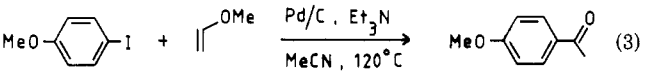
6 7 (2)

a; X = COCl	10	:	1
b; X = Br	7	:	1
c; X = I	4	:	1

a 60% total yield (**6** + **7**) after 24 h.

We attribute the differing regioselectivity to the halide counterions, although carbon monoxide might possibly occupy a ligand site on palladium throughout the reaction employing benzoyl chloride. The great resemblance between the results reported here and those obtained in stoichiometric experiments where no carbon monoxide was present suggest, however, that an effect from carbon monoxide is of minor importance.

The sensitivity of the arylation of enol ethers, via the Heck reaction, to conditions and arylating agent is interesting. Thus, starting from 4-iodoanisole (**8**) and performing the reaction in acetonitrile, the only isolable product was 4-methoxyacetophenone (**9**), formed from the 1-(alkoxyethenyl)-4-methoxybenzene upon hydrolysis (eq 3).



8 9 (3)

This compound was isolated in 55% yield;[13] the β-arylated isomers were not observed. In a palladium-mediated reaction starting from (4-methoxy-1-naphthyl)mercuric acetate and butyl vinyl ether, a 75% yield of 1-acetyl-4-methoxy-naphthalene was reported by Daves and coworkers.[6a] In light of this, the high selectivity for arylation at the terminal carbon atom reported here is remarkable (eq 2). We believe that this difference is due to the creation of an electron-deficient palladium center, under the conditions employed here.[7]

It should be stressed that the arylation of electron-rich substrates, such as enol ethers, is unique in its sensitivity to electronic effects. With the more frequently utilized activated olefins, the steric requirements are usually attributed greater importance.[4a] Thence, it could be anticipated that less electron-rich vinyloxy compounds should serve better as acetaldehyde equivalents. Our attempts in that direction have, however, been discouraging. It is well established that the reaction of vinyl acetate (**10**) with aryl halides with palladium catalysis gives mixtures of styrene (**11**) and stilbene (**12**),[5c,14] and no successful catalytic reaction with the acetate function intact has been reported so far. We found this to be the case also in reactions starting from acid chlorides. We tried to apply the same approach through the arylation of 1-(ethenyloxy)-4-nitrobenzene (**13**) (eq 4). However, also in this case comparable amounts of styrene and stilbene were the main

(10) In general, chlorobenzene is unreactive in the Heck arylation. A few exceptions have appeared; see: (a) Davison, J. B.; Simon, N. M.; Sojka, S. A. *J. Mol. Catal.* **1984**, *22*, 349. (b) Julia, M.; Duteil, M. *Bull. Soc. Chim. Fr.* **1973**, 2790. (c) Julia, M.; Duteil, M.; Grard, C.; Kuntz, E. *Ibid.* **1973**, 2791.

(11) Blaser and Spencer reported that no arylation was observed with butyl vinyl ether; ref 9a.

(12) Hallberg, A.; Westfelt, L. *J. Chem. Soc., Perkin Trans. 1* **1984**, 933.

(13) Hallberg, A.; Westfelt, L.; Holm, B. *J. Org. Chem.* **1981**, *46*, 5414.

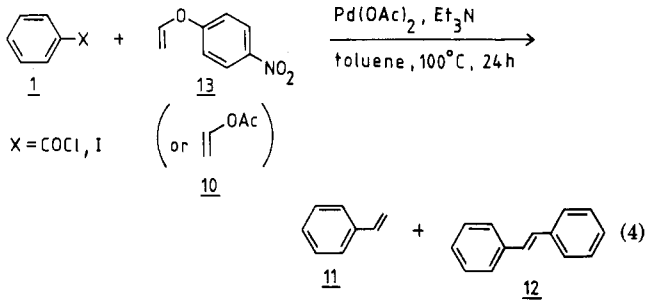
(14) A palladium-catalyzed synthesis of 5-vinylpyrimidines using vinyl acetate as an ethylene equivalent has been reported: Arai, I.; Daves, G. D., Jr. *J. Heterocycl. Chem.* **1978**, *15*, 351.

Table I. Palladium-Catalyzed Reaction of Benzoyl Chloride with Butyl Vinyl Ether under Various Conditions[k]

entry	base[a]	catal (%)[b]	amt of solv, mL	equiv of 2[c]	yield of (butoxyethenyl)benzenes after different reaction times,[d] % 1 h	2 h	3 h	4 h	5 h	8 h
1	BDA	Pd/C (1)	5	2		25				
2	BDA	Pd/C (5)	5	5	32		42			
3	BDA	$Pd(OAc)_2$ (5)	5	2	54		54			
4	BDA	$Pd(OAc)_2$ (10)	5	2		31			dec	
5	BDA	$Pd(OAc)_2$ (5)	*e*	2		27[f]				
6	NEM	$Pd(OAc)_2$ (1)	10	2	61		80		80	
7	NEM	$Pd(OAc)_2$ (1)	25	2	48	55		65[g]	67	
8	NEM	$Pd(OAc)_2$ (1)	50	2	24	34		38[h]		
9	NEM	$Pd(OAc)_2$ (1)	5	1.2	68[i]	65		63		
10	NEM	$Pd(OAc)_2$ (3)	25	5	44		52			67
11	NEM	Pd/C (3)	25	2			30		28	
12	NEM	Pd/C (1)	10[j]	2						68
13	EDA	$Pd(OAc)_2$ (1)	10	2		48				

[a] BDA is benzyldimethylamine, NEM is *N*-ethylmorpholine, and EDA is ethyldiisopropylamine. [b] Mol % relative to benzoyl chloride. [c] Molar equivalents relative to benzoyl chloride. [d] Determined by GLC. Total yield of isomers. The benzoylated product, (*E*)-3-butoxy-1-phenyl-2-propen-1-one, was formed in 5–10% yield in all cases. [e] 5 mL of BDA was used. [f] A large amount of unidentified material was detected. [g] Additional $Pd(OAc)_2$ (1%) was added after 2.5 h. [h] Additional $Pd(OAc)_2$ (1%) and olefin (2 equiv) were added after 2 h. [i] Selectivity was lost. [j] Toluene was used as the solvent. [k] Benzoyl chloride (10 mmol) was reacted with butyl vinyl ether in the presence of amine base (15 mmol) and the palladium catalyst at reflux temperature for the time indicated. Xylene was used as the solvent, unless stated.

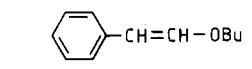
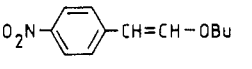
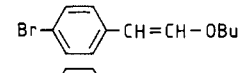
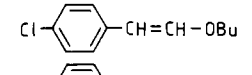
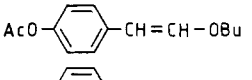
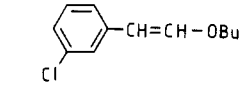
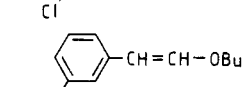
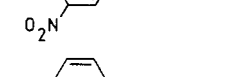
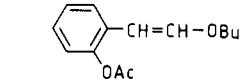
products, and only traces of the desired [β-(aryloxy)-ethenyl]benzenes were found.



Apparently, oxygen substituents with electron-accepting capacity are good enough leaving groups for palladium acetate or phenolate elimination to be facile; at the present time, manipulations in the aryl moiety appear most fruitful in attempts to achieve selective transformations.

Although the reactions presented in eq 1 and 2 gave favorable regioselectivity, the yields were modest and the long reaction time was unsatisfactory from a preparative point of view. Blaser and Spencer reported that best yields were generally achieved by using *p*-xylene as solvent and benzyldimethylamine as the base.[9a] Also in our case, refluxing *p*-xylene proved beneficial, in shortening the reaction time as well as suppressing the formation of 3-butoxy-1-phenyl-2-propen-1-one (vide supra). This solvent was used for an evaluation of reaction parameters. An account for the variables studied is given in Table I. The yields given are total yields of the three isomeric (butoxyethenyl)benzenes. The β/α ratio was found to be virtually independent of the base used, and also the two catalysts shown gave the same distribution. The presence of triphenylphosphine, 2 or 4 mol per mol of Pd, was found to inhibit the reaction totally. Catalyst activity was initially high, but decreased rapidly with time, possibly a result of catalyst agglomeration at the high temperature necessary to effect decarbonylation.[15] Longer reaction times than 5 to 8 h did not improve yields, and product decomposition sometimes occurred. Use of benzyl dimethylamine as the base and Pd/C as the catalyst gave only a 25% yield of the phenylated products (entry 1), although additional olefin and catalyst improved the yield somewhat (entry 2). $Pd(OAc)_2$ was more efficient than Pd/C (entries 2, 3). Very large amounts of catalyst depressed the yield markedly (entry 4), and we believe this to be due to agglomeration or metal formation. Reactions using the base as the solvent were unsuccessful, producing large amounts of unidentified byproducts (entry 5). Benzyldimethylamine did not seem to be more advantageous than the initially used triethylamine, and *N*-ethyl-

Table II. Isolated (Butoxyethenyl)benzenes (Equation 5)[e]

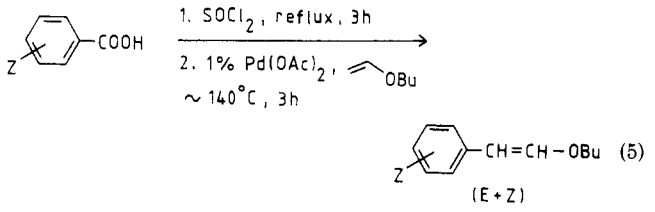
product		yield, %[a]	selectivity[b]
	3	53[c]	3.0
	6	60[d]	10
	14	55	2.5
	15	60	3.0
	16	40	2.7
	17	43	3.7
	18	44	4.1
		trace	
		trace	

[a] Isolated yield, based on the starting benzoic acid. [b] Ratio of β to α products in the crude product. [c] GLC yield, 60%. [d] GLC yield, 75%. [e] Butyl vinyl ether (40 mmol), the aroyl chloride (20 mmol), *N*-ethylmorpholine (24 mmol), and palladium acetate (0.2 mmol) were refluxed in 20 mL of xylene for 3 h.

(15) The amount of acylated product formed was in the range of 5–10%. Starting from activated olefins, Blaser and Spencer reported only traces of benzoylated products;[9a] the less efficient decarbonylation using butyl vinyl ether may be a result of partial blocking of coordination sites by the olefin.

morpholine, reported to be unreactive toward acid chlorides,[9a] was tested with much improved results. In these cases (entries 6–12) a good material balance was achieved, and few byproducts were produced. Best results were obtained when the reaction mixture was 1 M with respect to the aroyl chloride (80%, entry 6). A number of other amine bases also gave the reaction, e.g., tributylamine and the sterically hindered ethyldiisopropylamine (entry 13), but showed no advantages over *N*-ethylmorpholine.

The preparative results of this investigation are summarized in Table II. The yields are based on the starting benzoic acid and represent pure (2-butoxyethenyl)arenes, isolated by column chromatography. The *E*/*Z* ratios were approximately 2:1, although electron-withdrawing aryl substituents favored the formation of *E* products to some extent and vice versa. The overall transformation is outlined in eq 5.



(5)

The yields are comparable in the cases studied, except for the two ortho-substituted acids. The latter surprisingly failed to give the reaction, although ortho-substituted aryl halides are known to react normally in Heck arylations.[4] It is noteworthy that 4-nitrobenzoyl chloride, reported to give the poorest results with activated olefins,[9a] gave the best isolated yield with butyl vinyl ether. A comparison of the results obtained from the 3- and 4-chloro- and 3- and 4-nitrobenzoic acids, respectively, indicates that mesomeric effects are more important than inductive in governing the regioselectivity.

In conclusion, it seems that this new palladium-catalyzed transformation is a useful route for the preparation of β-arylvinyl ethers. The method merits attention due to the simplicity of the experimental procedure, the expected tolerance to a wide range of substituents in the aryl group,[4] and particularly the use of very simple and readily available starting materials. Although only moderate yields are obtained, it should provide an attractive complement to existing methods.[3]

Experimental Section

Instrumentation. Mass spectra were obtained on a Finnigan 4021 (Data System Incos 2100) gas chromatograph–mass spectrometer, operating at 70 eV. Elemental analyses were obtained from the Microanalytical Laboratory, University of Lund, Lund, Sweden. ^{1}H NMR spectra were recorded in deuteriochloroform on a Varian XL-300 spectrometer. Chemical shifts are given relative to internal Me_4Si. Gas chromatographic analyses were performed on a Varian 3300 instrument, equipped with a Varian 4270 integrator. A 2.5-m column of either 5% OV 17 on Chromosorb W or 5% Carbowax 20 M on Supelcoport 100/120 was used. Peak areas were determined relative to internal pentadecane. Silica gel 60 (0.040–0.064 mm, E Merck) was used for flash chromatography.

Materials. Palladium acetate and palladium-on-charcoal (10%) were obtained from Johnson-Matthey Chemicals and Riedel-de-Haën, respectively. Butyl vinyl ether was purchased from Fluka and used as received. Aroyl chlorides were prepared from commercially obtained acids by the standard procedure ($SOCl_2$, reflux). The crude acid chlorides were used directly in the preparative reactions. Amine bases were distilled and stored over molecular sieves (3 Å). Solvents were Janssen ACS grade, stored over molecular sieves. 1-(Ethenyloxy)-4-nitrobenzene (**13**) was prepared following the literature procedure.[16]

Small-Scale Experiments (Table I). The reactions were carried out in a 25-mL, dry, two-necked flask fitted with a reflux condenser and a mechanical stirrer. A slow stream of nitrogen was passed through the apparatus throughout the reaction. The following procedure is typical (entry 6, Table I): A mixture of palladium acetate (0.022 g, 0.1 mmol), *N*-ethylmorpholine (1.15 g, 12 mmol), and pentadecane (internal standard, 0.40 g) in 10 mL of *p*-xylene was stirred for 15 min. Benzoyl chloride (1.41 g, 10 mmol), dissolved in butyl vinyl ether (2.0 g, 20 mmol), was added through a syringe, and the reaction mixture was brought to reflux as quickly as possible, with vigorous stirring. The reaction was monitored by GLC on samples removed from the refluxing mixture by means of a syringe and diluted with diethyl ether.

Preparative Reactions (Table II). The reactions were generally performed in a 50-mL flask equipped with a condenser, fitted with a simple drying tube ($CaCl_2$), in a 20-mmol scale. Purification was accomplished by flash chromatography on a (5 × 15 cm) silica column. The butoxyethenyl aryls reported are unstable as neat liquid and should be stored in solution.[17] Samples for NMR and elemental analysis were removed directly upon isolation, and stored in nitrogen-flushed containers at −20 °C. Determination of the isomeric distribution of the products (Table II) was made on small samples of the crude material, removed prior to workup. The procedure given below is representative.

(*E*)-/(*Z*)-(2-Butoxyethenyl)benzene (3). A mixture of palladium acetate (0.045 g, 0.20 mmol) and *N*-ethylmorpholine (2.8 g, 24 mmol) in 20 mL of xylene was stirred until a homogeneous solution was obtained. To the orange solution were added butyl vinyl ether (4.0 g, 40 mmol) and benzoyl chloride (2.82 g, 20 mmol). The reaction mixture was heated to reflux with vigorous stirring, whereby it gradually darkened and grew turbid. Within minutes palladium black was observed in the vessel. After 3 h the solution was allowed to cool, and 50 mL of ether was added with stirring. This caused precipitation of the amine hydrochloride (2.9 g), which was removed by filtration. The filtrate was treated with two 25-mL portions of 1 M HCl (effecting selective decomposition of the α-isomer (**4**) into acetophenone; this practice served to simplify chromatography), and the combined aqueous phases were extracted twice with 25 mL of ether. The ethereal solution was washed with 50 mL of 1 M NaOH and 50 mL of water. After drying ($MgSO_4$), concentration under reduced pressure gave 3.7 g of crude material, which was subjected to flash chromatography using pentane/chloroform (5/1) as the eluent. The title substance was obtained as a colorless oil (1.7 g, 53%, $E/Z \approx 2/1$): ^{1}H NMR δ 7.6–7.1 (m, aryl), 6.98 (d, vinyl, J = 13 Hz, *E* isomer), 6.19 (d, vinyl, J = 7 Hz, *Z*), 5.81 (d, vinyl, J = 13 Hz, *E*), 5.19 (d, vinyl, J = 7 Hz, *Z*), 3.91 (t, J = 6 Hz, OCH_2, *Z*), 3.82 (t, J = 6 Hz, OCH_2, *E*), 1.68 (m, OCH_2CH_2, *E* + *Z*), 1.45 (m, $OCH_2CH_2CH_2$, *E* + *Z*), 0.96 (t, CH_3, *E* + *Z*). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.3; H, 8.96. A reaction was also performed starting from 0.1 mol (14.1 g) of benzoyl chloride. After filtration and concentration, distillation of the oily residue at reduced pressure gave 11.5 g (65%) of a colorless liquid boiling at 60–64 °C (0.02 mmHg). GLC analysis proved this to be a mixture of the title compound (**3**) (*E*/*Z* mixture, 9.2 g, 53%) and (1-butoxyethenyl)benzene (**4**) (2.3 g, 13%).

(*E*)-/(*Z*)-1-(2-Butoxyethenyl)-4-nitrobenzene (6): yellow oil (60%, $E/Z \approx 2/1$); eluent, pentane/chloroform, 2/1; ^{1}H NMR δ 8.2–7.2 (m, aryl), 7.19 (d, J = 13 Hz, *E*), 6.40 (d, J = 7 Hz, *Z*), 5.85 (d, J = 13 Hz, *E*), 5.27 (d, J = 7 Hz, *Z*), 4.02 (t, J = 6 Hz, *Z*), 3.90 (t, J = 6 Hz, *E*), 1.7 (m), 1.5 (m), 0.97 (t). Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83. Found: C, 65.0; H, 6.89.

(*E*)-/(*Z*)-1-(2-Butoxyethenyl)-4-bromobenzene (14): colorless oil (55%, $E/Z \approx 2/1$); eluent, pentane/chloroform, 10/1; ^{1}H NMR δ 7.5–7.0 (m, aryl), 6.98 (d, J = 13 Hz, *E*), 6.23 (d, J = 7 Hz, *Z*), 5.76 (d, J = 13 Hz, *E*), 5.14 (d, J = 7 Hz, *Z*), 3.94 (t, *Z*), 3.83 (t, *E*), 1.7 (m), 1.5 (m), 0.98 (t). Anal. Calcd for $C_{12}H_{15}BrO$: C, 56.49; H, 5.93. Found: C, 56.7; H, 6.08.

(*E*)-/(*Z*)-1-(2-Butoxyethenyl)-4-chlorobenzene (15): colorless oil (60%, $E/Z \approx 2/1$); eluent, pentane/chloroform, 95/5; ^{1}H NMR δ 7.6–7.1 (m, aryl), 6.96 (d, J = 13 Hz, *E*), 6.22 (d, J =

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7 Hz, Z), 5.78 (d, J = 13 Hz, E), 5.16 (d, J = 7 Hz, Z), 3.94 (t, Z), 3.83 (t, E), 1.7 (m), 1.5 (m), 0.97 (t). Anal. Calcd for $C_{12}H_{15}ClO$: C, 68.40; H, 7.18. Found: C, 68.5; H, 7.12.

(E)-/(Z)-1-(2-Butoxyethenyl)-4-acetoxybenzene (16): colorless oil (40%, $E/Z \approx 2/1$); eluent, pentane/methylene chloride, 1/1; ^1H NMR δ 8.1-7.0 (m, aryl), 6.20 (d, J = 7 Hz, Z), 5.82 (d, J = 13 Hz, E; the other component of the vinylic resonance was obscured by the aryl multiplet), 5.19 (d, J = 7 Hz, Z), 3.92 (t, Z), 3.83 (t, E), 2.28 (s, CH_3COO), 1.7 (m), 1.5 (m), 0.98 (t). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.4; H, 7.73.

(E)-/(Z)-1-(2-Butoxyethenyl)-3-chlorobenzene (17): colorless oil (43%, $E/Z \approx 2/1$); eluent, pentane; ^1H NMR δ 7.7-7.1 (m, aryl), 7.03 (d, J = 13 Hz, E), 6.25 (d, J = 7 Hz, Z), 5.78 (d, J = 13 Hz, E), 5.17 (d, J = 7 Hz, Z), 3.96 (t, Z), 3.85 (t, E), 1.7 (m), 1.5 (m), 1.0 (t). Anal. Calcd for $C_{12}H_{15}ClO$: C, 68.40; H, 7.18. Found: C, 68.4; H, 7.13.

(E)-/(Z)-1-(2-Butoxyethenyl)-3-nitrobenzene (18): colorless oil (44%, $E/Z \approx 2/1$); eluent, pentane/chloroform, 7/2; ^1H NMR δ 8.5-7.3 (m, aryl), 7.08 (d, J = 13 Hz, E), 6.31 (d, J = 7 Hz, Z), 5.80 (d, J = 13 Hz, E), 5.21 (d, J = 7 Hz, Z), 3.96 (t, Z), 3.83 (t, E), 1.7 (m), 1.4 (m), 0.95 (t). Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83. Found: C, 65.3; H, 6.75.

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Registry No. **1a**, 98-88-4; **1b**, 591-50-4; **2**, 111-34-2; (E)-**3**, 36586-17-1; (Z)-**3**, 36586-16-0; **4**, 56750-84-6; **5a**, 122-04-3; **5b**, 586-78-7; **5c**, 636-98-6; (E)-**6**, 97826-86-3; (Z)-**6**, 97826-85-2; **7**, 109125-23-7; **8**, 696-62-8; **9**, 100-06-1; **10**, 108-05-4; **11**, 100-42-5; **12**, 103-30-0; **13**, 940-14-7; (E)-**14**, 111615-85-1; (Z)-**14**, 111615-86-2; (E)-**15**, 111615-87-3; (Z)-**15**, 111615-88-4; (E)-**16**, 111615-89-5; (Z)-**16**, 111615-90-8; (E)-**17**, 111615-91-9; (Z)-**17**, 111615-92-0; (E)-**18**, 111615-93-1; (Z)-**18**, 111615-94-2; p-BrC_6H_4COCl, 586-75-4; p-ClC_6H_4COCl, 122-01-0; p-$AcOC_6H_4COCl$, 27914-73-4; m-ClC_6H_4COCl, 618-46-2; m-$NO_2C_6H_4COCl$, 121-90-4; o-$AcOC_6H_4COCl$, 5538-51-2; o-$NO_2C_6H_4COCl$, 610-14-0; CH_2=CHOMe, 107-25-5; (E)-BuOCH=CHCOPh, 111615-95-3.

Vinylic Organoboranes. 9. A General Stereospecific Synthesis of (Z)- and (E)-Disubstituted Alkenes via Organoboranes[1]

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A general and stereospecific synthesis of (Z)-disubstituted alkenes using mono- and dihaloboranes is presented. The hydridation of dialkylhaloboranes in the presence of 1-alkynes provides the corresponding dialkylvinylboranes (1), representing the first general synthesis of such derivatives. Treatment with iodine in the presence of sodium methoxide induces the migration of one of the alkyl groups from boron to the adjacent carbon, followed by a rapid deiodoboronation to afford (Z)-disubstituted alkenes (2) in high yields. Similarly, the hydroboration of 1-alkynes with alkylbromoboranes ($R^1BHBr\cdot SMe_2$, 4) followed by iodination in the presence of sodium methoxide in methanol affords (Z)-disubstituted alkenes (2) in good yields. Both procedures constitute a general one-pot synthesis of (Z)-disubstituted alkenes from an alkene and 1-alkyne. A simple synthesis of Muscalure (7), the sex pheromone of the housefly (*Musca domestica*), is achieved in good yields. An alternative general stereospecific synthesis of (Z)- and (E)-disubstituted alkenes based on alkenylboronic esters is also described.

The stereospecific synthesis of insect sex attractants is one of the most timely problems today in organic synthesis. Both (Z)- and (E)-disubstituted alkenes with hydroxy or acetate functionalities constitute a major segment of these insect pheromones.[3] Since the presence of minor isomers inhibits the biological activity in most cases,[4] the stereospecific synthesis of the most active isomer is of paramount importance, both scientifically and economically. Organoboranes play an important role in bringing latitude to organic synthesis.[5] The applications of organoboranes to carbon-carbon bond formation has been well documented, and a wide variety of synthetic methods for carbon skeletal assemblage is becoming available.[6] Now we report the stereospecific synthesis of (Z)-disubstituted alkenes using mono- and dihaloborane reagents and its application to the synthesis of Muscalure (7), the sex pheromone of the housefly (*Musca domestica*). We also herein report a general stereospecific synthesis of (Z)- and (E)-disubstituted alkenes utilizing alkenylboronic esters.

Results and Discussion

An elegant approach to the synthesis of both (Z)-[7] and (E)-[8]1,2-disubstituted olefins has been reported by Zweifel (eq 1 and 2).

However, the utility of this elegant Zweifel synthesis depends on the availability of dialkylboranes. Direct hydroboration leads cleanly to the formation of dialkylboranes only in the case of relatively hindered alkenes. More generally, hydroboration fails to stop cleanly at the

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