Chelation-Controlled, Palladium-Catalyzed Arylation of Vinyl Ethers

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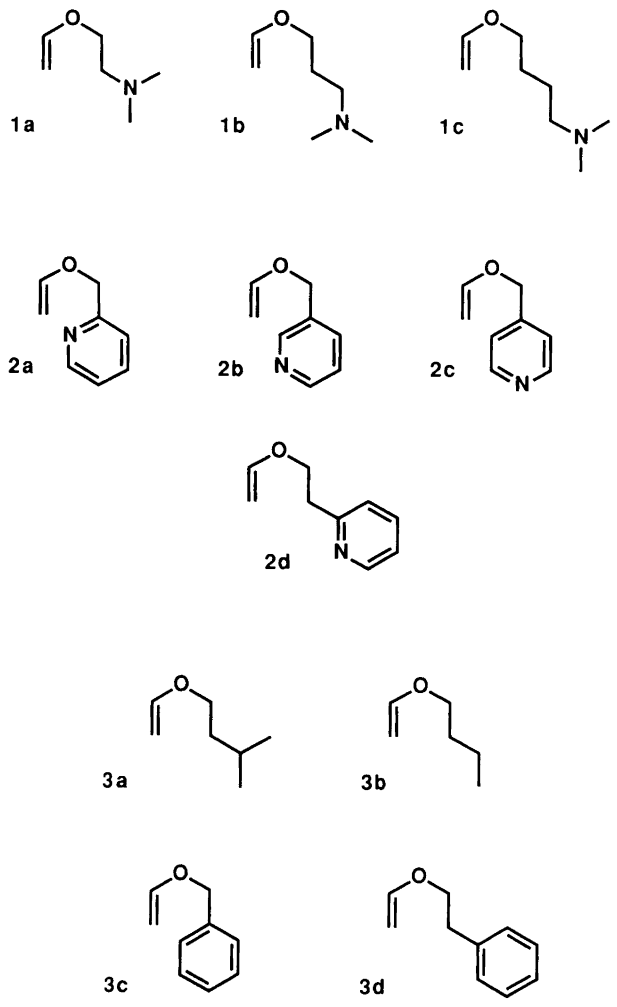
Chelation-controlled, palladium-catalyzed arylation of vinyl ethers with nitrogen-containing directing groups has been studied. Ethenyloxyalkylamines **1a–c** and pyridines **2a–d**, representing different carbon tethers were reacted with iodobenzene **4a** and 1-iodonaphthalene **4b** under phase-transfer conditions. The regioselectivity achieved is compared with the outcome from reactions with sterically similar vinyl ethers **3a–d**. Arylations of the dimethylamine derivative **1a** and the pyridine derivative **2a** occurred at the terminal position of the olefins and were highly regioselective. A catalytic cycle for the regioselective, chelation-controlled vinylic substitution, involving a six-membered chelate ring, is proposed.

Dedicated to Professor Salo Gronowitz on the occasion of his 65th birthday.

The Heck arylation reaction has developed into a very useful method for carbon–carbon bond formation under practical conditions, but has mostly been useful for vinylic reactants having three or more carbon atoms.[1–4] Attachment of functionalized two-carbon fragments often has associated complications, such as elimination of the hetero substituent and low regioselectivity.[5] For example, attempted reactions utilizing enol ethers as the olefinic reactant have been complicated by the formation of regioisomeric mixtures.[6–10] In spite of this, highly regioselective α-arylation[11,12] and α-vinylation[13] procedures have recently been reported, and, under specific conditions, moderate β-selectivity can be achieved.[14,15] However, no general procedure for β-arylation based on direct vinylic substitution of simple enol ethers has emerged. The fact that such a procedure should be a useful entry into arylethylamines or arylacetic acids, compounds of considerable pharmaceutical importance, encouraged us to search for alternative methods of regio-control. In an initial study,[16] we communicated that chelation-controlled palladium-catalyzed arylation of **1a** constitutes an entry into 2-aryl-ethanals. We herein report an extended investigation of the impact of some nitrogen-containing directing groups in ethenyloxyalkylamines and ethenyloxyalkylpyridines.

The directing effect of the nitrogen functionality in the dimethylamines, **1a–c**, and pyridines, **2a–d**, representing different carbon tethers, was studied. The tertiary amines and pyridines were compared with sterically similar enol ethers, **3a–d**.



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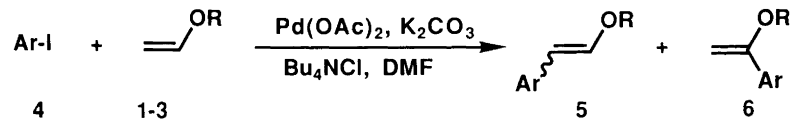


Scheme 1.

Results

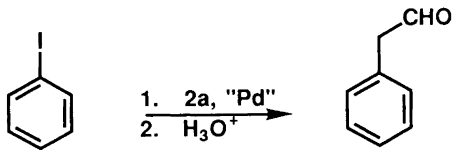
Reactions of iodobenzene (**4a**) and 1-iodonaphthalene (**4b**) with **1–3** were performed in DMF under the phase-transfer conditions developed by Jeffery,[17] using potassium carbonate as the base and palladium acetate as the catalyst (Scheme 1). The results are summarized in Table 1. The product distribution (**5–6**) was estimated using a combination of GLC and NMR and was determined on crude samples removed prior to product purification. The reactions were generally complete after 18 h at 80°C but reactions employing **2a** and reactions of **4b** with **1b** and **2d** required 40 h for complete conversion. Vinyl ethers **3** all gave a similar β:α ratio, with only a very weak preference for the terminally substituted product **5**, in accordance with earlier findings.[10]

Several characteristic features are obvious from Table 1. First, a highly regioselective β-arylation, β:α > 95:5, of both the tertiary amine **1a** and the pyridine derivative **2a** was achieved. Thus, the two substrates having a two-carbon tether between the vinylic oxygen and the nitrogen atom were apparently equally efficient at directing the regiochemistry of arylation, although **2a** reacted much more sluggishly. The large capacity of the pyridine to direct the arylation is also obvious from a comparison of **1b** and **2d**. A moderately selective arylation was observed with **2d** while the outcome with alkylamine **1b** was similar to that observed with the alkyl vinyl ethers. The β-selectivity experienced with **2d** seems not to be of steric origin since reactions of **3d** with **4a** or **4b** exhibited no or only little preference for the β-position. Second, a very weak predominance of α-arylation was noted for reactions of the nitrogen-containing vinyl ethers **1b–c** and **2b–c** with iodonaphthalene. Third, in non-selective arylations **4a** gives slightly more β-product than does **4b**. Fourth, olefins which display chelation control (**1a**, **2a** and **2d**) give rise to an *E*:*Z* value of about 50:50, while **3** favors formation of *trans* products, *E*:*Z* about 80:20. Finally, we confirmed that **5g** provided 2-phenylethanals upon treatment with hydrochloric acid, although more sophisticated methods for this transformation are available (Scheme 2).[9,16]

Table 1. Arylation of **1**, **2** and **3** with iodobenzene (**4a**) or 1-iodonaphthalene (**4b**).[a]

Enol ether	Aryl halide	β:α[b]	*E*:*Z*[c]	Product	Yield (%)[d]
1a	**4a**	97:3	41:59	**5a**	82
1a	**4b**	97:3	41:59	**5b**	80
1b	**4a**	52:48	58:42	**5c**	48
1b	**4b**	45:55	48:52	**5d**	42[e]
1c	**4a**	48:52	73:27	**5e**	35[g]
1c	**4b**	41:59	75:25	**5f**	29[g]
2a	**4a**	95:5	50:50	**5g**	87
2a	**4b**	97:3	58:42	**5h** + **6h**	84[f]
2b	**4a**	50:50	73:27	**5i** + **6i**	92
2b	**4b**	41:59	79:21	**5j** + **6j**	92
2c	**4a**	50:50	75:25	**5k** + **6k**	88[e]
2c	**4b**	41:59	77:23	**5l** + **6l**	84[e]
2d	**4a**	77:23	55:45	**5m**	68[f]
2d	**4b**	81:19	50:50	**5n**	76
3a	**4a**	58:42	80:20	**5o** + **6o**	79[e]
3a	**4b**	52:48	83:17	**5p** + **6p**	76
3b	**4a**	57:43	81:19	**5q** + **6q**	76
3b	**4b**	50:50	80:20	**5r** + **6r**	76
3c	**4a**	66:34	81:19	**5s** + **6s**	79
3c	**4b**	55:45	80:20	**5t** + **6t**	80[e]
3d	**4a**	63:37	81:19	**5u** + **6u**	64
3d	**4b**	50:50	80:20	**5v** + **6v**	84

[a] The reactions were performed as described in the general procedure for preparative arylation reactions. [b] Calculated as **5**:**6** as determined by GLC. [c] (*E*)-**5**/(*Z*)-**5** as determined by GLC. [d] Yield of pure (>95% by GLC) isolated arylated product. [e] >89% by GLC. [f] The reaction was performed on a 5.0 mmol scale. [g] The reaction was performed on a 1.75 mmol scale.

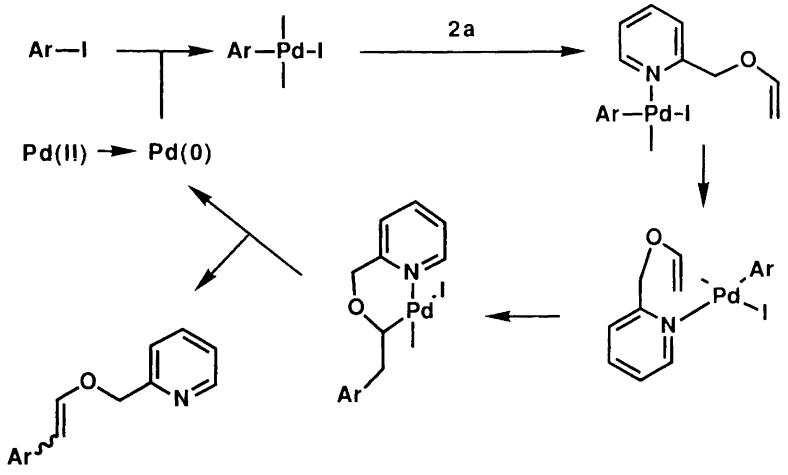


Scheme 2.

Discussion

For the chelation-controlled vinylic substitution reactions, the catalytic cycle exemplified for the pyridine derivative **2a** seems reasonable (Scheme 3). After initial reduction of Pd(II)[18,19] followed by oxidative addition we believe that the arylpalladium iodide is trapped by the pyridine nitrogen and after a second ligand exchange a π-complex chelate is formed. Insertion of the olefin results in formation of a, presumably, relatively stable six-membered σ-complex. The β-selectivity observed with **1a** and **2a**, is clearly a result of palladium–nitrogen coordination.[20–27] The collapse of the π-complex, governed by steric constraints, apparently favors the six-membered derivative over the seven-membered alternative.

The fact that the pyridine olefin **2a** reacts considerably more slowly than the alkylamine analog **1a**, we believe is a result of the formation of more stable intermediate



Scheme 3.

complexes rendering regeneration of the catalyst rate-determining. It has been reported that a stable 5-membered intermediate is formed after reaction of 2-vinylpyridine with 'phenylpalladium chloride'.[28] With the intention of obtaining support for our suggestion, we performed a competitive experiment with **1a** and **2a**. Interestingly, **1a** was now consumed more slowly than **2a**, finally yielding a 60:40 ratio of **5g** to **5a**. Moreover, the conversion of **1a** was slower than in the absence of **2a** and the β-selectivity decreased in the presence of **2a** (**5a**:**6a** = 90:10). The β-selectivity with regard to arylation of **2a** was unaffected. This further loss of regiochemical control is presumably due to intermolecular complexation involving **2a**. These results corroborate a mechanism involving product formation rather than complexation as the slow step. The competitive behavior of the two substrates **1a** and **2a** observed in this experiment further suggests that the pyridine **2a** is, in fact, a more powerful chelating ligand. In a separate experiment, the presence of pyridine (equimolar to the substrate) was shown almost completely to counteract the directing effect in **1a**, the β:α ratio going from 97:3 to about 67:33, whereas triethylamine did not effect a coupling utilizing **2a**. The somewhat higher preference for α-arylation observed with the two non-chelating pyridine analogs **2b** and **2c** probably reflects the effect of intermolecular complexation.

Accordingly, in an experiment in which **3c** was reacted with iodobenzene in the presence of equimolar amounts of pyridine, the β:α ratio decreased from 65:35 to 47:53. Triethylamine, on the other hand, seemed instead to promote β-arylation, the ratio increasing from 65:35 to 70:30. Highly regioselective α-arylations starting from aryl triflates, bromides and iodides have been reported by Cabri *et al.*[11,12] These have been suggested to follow an alternative pathway facilitated by the formation of cationic intermediate complexes in the presence of strongly coordinating ligands. It is possible that a similar mechanism becomes favorable in the presence of pyridine.

Conclusion

For the use as an ethanal equivalent the directing group attached to the oxygen atom must (*a*) provide high β-selectivity, (*b*) permit regeneration of the catalyst and (*c*) be easily cleaved. Both **1a** and **2a** fulfil these prerequisites. Although olefin **1a** is perhaps most attractive for preparative purposes, the fact that **2a** also exhibits powerful chelation control may be useful. For example, **2a** should allow the study of electronic effects from substituents in the pyridine ring. The chelation-controlled reaction discussed here constitutes an alternative to the cross-coupling procedures[9] previously used for the preparation of β-aryl enol ethers. An extension to other chelating substrates, targeting regio- and stereo-selective aspects of the Heck reaction promises to be worthwhile.

Experimental

General. ^{1}H NMR spectra were recorded on a Jeol EX 270 spectrometer at 270.05 MHz and on a Jeol FX90Q spectrometer at 89.5 MHz. Chemical shifts are reported as δ values (ppm) relative to internal tetramethylsilane. Low-resolution electron-impact mass spectral data (70 eV) were obtained on a Hewlett–Packard mass spectrometer HP5971A MSD connected to a gas chromatograph HP GC5890 Series 2, equipped with a HP-1 (25 m × 0.2 mm) column. Capillary gas chromatographic analyses were carried out on a Shimadzu GC-14A, using a HP-1 (50 m × 0.32 mm) column, and on a Carlo Erba GC 6000 Vega series, using a DB-5 (25 m × 0.32 mm) column. The column temperature was 50–260°C (gradient, 10°C min^{-1}). Both gas chromatographs were equipped with a flame ionization detector. Isomers were assumed to have the same response factor. Elemental analyses were performed by Mikro Kemi AB, Uppsala, Sweden. Column chromatography was performed on silica gel 60 (0.040–0.063 mm, Merck) or on aluminum oxide 90 (0.063–0.200 mm, Merck). All arylation experiments were carried out in heavy-walled and

thin-necked Pyrex tubes, sealed with a screw-cap fitted with a Teflon gasket.

Materials. Palladium(II) acetate was obtained from Merck. Aryl halides were purchased from Janssen and used without further purification. The pyridyl alcohols were used as received from Fluka. The amino alcohols were commercially available except 4-dimethylamino-1-butanol, which was prepared from 4-(dimethylamino)-butanoic acid hydrochloride (Janssen) by reduction with lithium aluminum hydride. THF and triethylamine (from potassium hydroxide) were distilled prior to use. DMF was stored over 4 Å molecular sieves. All other reagents were commercially obtained and used as received.

Vinyl ethers. The vinyl ethers **1a**, **2a** and **3c** were prepared from the corresponding alcohols as described elsewhere.[16] The remaining vinyl ethers **1b**,[29] **2b**,[30] **2c**,[30] **2d**,[31] **3a**,[32] and **3d**,[33] with the exception of **3b** (purchased from Janssen), were obtained analogously, using a mercury(II)-catalyzed transetherification procedure.[31, 34]

General procedure for preparative arylation reactions (Table 1). Palladium acetate (0.07 g, 0.3 mmol), potassium carbonate (2.8 g, 20 mmol) and tetrabutylammonium chloride (2.8 g, 10 mmol) were stirred in 15 ml of DMF for 5 min. To the yellow suspension was added a mixture of aryl halide (10 mmol) and vinyl ether (12 mmol) in 15 ml of DMF. The tube was capped and heated with stirring at 80°C in an oil bath for 16–40 h. The reaction solution turned black within 3 h. After cooling, a sample was withdrawn, diluted with ether, washed with water, dried with potassium carbonate and subjected to GLC analysis. The remaining crude reaction mixture was diluted with 100 ml of light petroleum or *n*-pentane, transferred to a separatory funnel and washed with 50 ml of 0.1 M sodium hydroxide and 2 × 50 ml of water. Drying (magnesium sulfate), filtration and concentration gave a black, viscous oil. The crude arylated products **5** and **6** were analyzed as the isomeric mixtures, using ^{1}H NMR spectroscopy to confirm the *E*:*Z* ratio, and the regioselectivity. Distillation at aspirator pressure or purification by column chromatography afforded the pure product as a mixture of isomers **5** and **6**. Further purification, for elemental analysis, was achieved by column chromatography (aluminum oxide, pentane–ethyl acetate 9:1) and repeated distillation in a Kugelrohr apparatus. Alternatively, acidic aqueous work-up was performed affording exclusively the β-arylated products (**5a–g, m, n**). The cool reaction mixture was diluted with 100 ml of light petroleum or *n*-pentane and washed twice with 50 ml of water. The organic layer was then extracted 4–8 times with 50 ml of 0.1 M HCl (0.3 M HCl in the case of **5g**). The aqueous extracts were combined, treated with 50 ml of light petroleum or *n*-pentane and poured into a beaker containing 1.0 M NaOH and 100 ml of light petroleum or *n*-pentane. After being stirred for 10 min, the phases were separated and the aqueous layer extracted with an additional 100 ml of light petroleum or *n*-pentane. After washing with brine and drying (magnesium sulfate), evaporation of the combined organic solutions afforded the pure β-arylated products **5**. This work-up method takes advantage of the fact that compounds **6** are more labile towards acid, and hence become selectively cleaved to the corresponding acetyl arenes. Enol ether products **5a**,[16] **5b**[16] and **5q**[10] have previously been characterized by us and **5r**[11] was recently described by Cabri. **5o**[35] and **5s**[36] are known. The remaining enol ether products exhibited physical data as summarized below. The *E*:*Z* ratios are given in Table 1.

N,N-*Dimethyl-3-(2-phenylethenyloxy)propanamine* (**5c**). Isolated yield 48%. Anal. $C_{13}H_{19}NO$: C, H. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.58 (d, J = 8 Hz), 7.30–7.05 (m, aryl), 7.00 (d, J = 13 Hz) *E*, 6.21 (d, J = 7 Hz) *Z*, 5.84 (d, J = 13 Hz) *E*, 5.21 (d, J = 7 Hz) *Z*, 3.98 (t, J = 6 Hz) *Z*, 3.89 (t, J = 6 Hz) *E*, 2.41 (dt, J = 7 Hz), 2.24 (s), 1.95–1.80 (m). MS [IP 70 eV; *m/z* (% rel. int.)]: 205 (11, *M*), 86 (14), 71 (19), 58 (100).

N,N-*Dimethyl-3-[2-(1-naphthyl)ethenyloxy]propanamine* (**5d**). Isolated yield 42%. Anal. $C_{17}H_{21}NO$: C, H. ^{1}H NMR (270 MHz, $CDCl_3$): δ 8.10–7.35 (m, aryl), 6.93 (d, J = 13 Hz) *E*, 6.50 (d, J = 13 Hz) *E*, 6.44 (d, J = 7 Hz) *Z*, 5.89 (d, J = 7 Hz) *Z*, 3.99 (dt), 2.47–2.36 (m), 2.26 (s), 2.22 (s), 1.96–1.82 (m). MS [IP 70 eV; *m/z* (% rel. int.)]: 255 (10, *M*), 141 (7), 86 (36), 71 (18), 58 (100).

N,N-*Dimethyl-4-(2-phenylethenyloxy)butanamine* (**5e**). Isolated yield 35%. Anal. $C_{14}H_{21}NO$: C, H. ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.58 (d, J = 9 Hz), 7.30–7.05 (m, aryl), 7.00 (d, J = 13 Hz) *E*, 6.20 (d, J = 7 Hz) *Z*, 5.83 (d, J = 13 Hz) *E*, 5.21 (d, J = 7 Hz) *Z*, 3.94 (t, J = 6 Hz) *Z*, 3.85 (t, J = 6 Hz) *E*, 2.30 (dt), 2.23 (s), 2.22 (s), 1.80–1.55 (m). MS [IP 70 eV; *m/z* (% rel. int.)]: 219 (1, *M*), 100 (53), 58 (100).

N,N-*Dimethyl-4-[2-(1-naphthyl)ethenyloxy]butanamine* (**5f**). Isolated yield 29%. Anal. $C_{18}H_{23}NO$: C, H. ^{1}H NMR (270 MHz, $CDCl_3$): δ 8.10–7.35 (m, aryl), 6.93 (d, J = 13 Hz) *E*, 6.50 (d, J = 13 Hz) *E*, 6.43 (d, J = 7 Hz) *Z*, 5.89 (d, J = 7 Hz) *Z*, 3.95 (dt, J = 6 Hz), 2.33 (dt, J = 7 Hz), 2.24 (s), 2.20 (s), 1.81–1.58 (m). MS [IP 70 eV; *m/z* (% rel. int.)]: 269 (0.4, *M*), 141 (7), 100 (100), 58 (90).

2-(2-Phenylethenyloxymethyl)pyridine (**5g**). Isolated yield 87%. Anal. $C_{14}H_{13}NO$: C, H. ^{1}H NMR (270 MHz, $CDCl_3$): δ 8.61–8.56 (m, aryl), 7.80–7.05 (m, aryl), 7.11 (d, J = 13 Hz) *E*, 6.31 (d, J = 7 Hz) *Z*, 5.98 (d, J = 13 Hz) *E*, 5.32 (d, J = 7 Hz) *Z*, 5.12 (s), 5.04 (s). MS [IP 70 eV; *m/z* (% rel. int.)]: 211 (37, *M*), 194 (22), 182 (97), 168 (16), 92 (100).

2-[2-(1-Naphthyl)ethenyloxymethyl]pyridine (**5h**). Isolated yield 84%. Anal. $C_{18}H_{15}NO$: C, H. ^{1}H NMR

(270 MHz, $CDCl_3$): δ 8.56–8.48 (m, aryl), 8.10–7.10 (m, aryl), 6.97 (d, $J = 13$ Hz) *E*, 6.56 (d, $J = 13$ Hz) *E*, 6.48 (d, $J = 7$ Hz) *Z*, 5.93 (d, $J = 7$ Hz) *Z*, 5.07 (s) *E*, 5.05 (s) *Z*. MS [IP 70 eV; *m/z* (% rel. int.)]: 261 (50, *M*), 232 (44), 169 (43), 141 (100).

3-(2-Phenylethenyloxymethyl)pyridine (**5i**) *and 3-(1-phenylethenyloxymethyl)pyridine* (**6i**). Isolated yield 92%. Anal. $C_{14}H_{13}NO$: C, H. The ^1H NMR spectrum was recorded on the isomeric mixture of the α- and β-arylated products (270 MHz, $CDCl_3$): δ 8.72–8.55 (m, aryl), 7.80–7.10 (m, aryl), 7.07 (d, $J = 13$ Hz) **5i***E*, 6.26 (d, $J = 7$ Hz) **5i***Z*, 5.97 (d, $J = 13$ Hz) **5i***E*, 5.32 (d, $J = 7$ Hz) **5i***Z*, 5.00 (s) **5i***Z*, 4.98 (s) **6i**, 4.91 (s) **5i***E*, 4.79 (d, $J = 3$ Hz) **6i**, 4.34 (d, $J = 3$ Hz) **6i**. MS [IP 70 eV; *m/z* (% rel. int.)]: **5i**; 211 (31, *M*), 182 (27), 92 (100), 65 (36). **6i**; 211 (7, *M*), 210 (12), 182 (12), 105 (20), 92 (100).

3-[2-(1-Naphthyl)ethenyloxymethyl]pyridine (**5j**) *and 3-[1-(1-napthyl)ethenyloxymethyl]pyridine* (**6j**). Isolated yield 92%. Anal. $C_{18}H_{15}NO$: C, H. The ^1H NMR spectrum was recorded on the isomeric mixture of the α- and β-arylated products (270 MHz, $CDCl_3$): δ 8.70–7.20 (m, aryl), 7.01 (d, $J = 13$ Hz) **5j***E*, 6.63 (d, $J = 13$ Hz) **5j***E*, 6.48 (d, $J = 7$ Hz) **5j***Z*, 6.00 (d, $J = 7$ Hz) **5j***Z*, 5.04 (s) **6j**, 5.00 (s) **5j***E* and *Z*, 4.67 (d, $J = 2$ Hz) **6j**, 4.55 (d, $J = 2$ Hz) **6j**. MS [IP 70 eV; *m/z* (% rel. int.)]: **5j**; 261 (75, *M*), 232 (46), 169 (97), 141 (100), 115 (35). **6j**; 261 (20, *M*), 232 (8), 218 (17), 141 (74), 92 (100).

4-(2-Phenylethenyloxymethyl)pyridine (**5k**) *and 4-(1-phenylethenyloxymethyl)pyridine* (**6k**). Isolated yield 88%. Anal. $C_{14}H_{13}NO$: C, H. The ^1H NMR spectrum was recorded on the isomeric mixture of the α- and β-arylated products (270 MHz, $CDCl_3$): δ 8.64–8.58 (m, aryl), 7.70–7.10 (m, aryl), 7.06 (d, $J = 13$ Hz) **5k***E*, 6.22 (d, $J = 7$ Hz) **5k***Z*, 5.96 (d, $J = 13$ Hz) **5k***E*, 5.34 (d, $J = 7$ Hz) **5k***Z*, 5.01 (s) **5k***Z*, 5.00 (s) **6k**, 4.92 (s) **5k***E*, 4.79 (d, $J = 3$ Hz) **6k**, 4.28 (d, $J = 3$ Hz) **6k**. MS [IP 70 eV; *m/z* (% rel. int.)]: **5k**; 211 (61, *M*), 182 (81), 119 (14), 91 (100). **6k**; 211 (5, *M*), 168 (3), 105 (100), 92 (23), 65 (20).

4-[2-(1-Naphthyl)ethenyloxymethyl]pyridine (**5l**) *and 4-[1-(1-napthyl)ethenyloxymethyl]pyridine* (**6l**). Isolated yield 84%. Anal. $C_{18}H_{15}NO$: C, H. The ^1H NMR spectrum was recorded on the isomeric mixture of the α- and β-arylated products (90 MHz, $CDCl_3$): δ 8.70–7.20 (m, aryl), 6.99 (d, $J = 13$ Hz) **5l***E*, 6.60 (d, $J = 13$ Hz) **5l***E*, 6.40 (d, $J = 7$ Hz) **5l***Z*, 6.0 (d, $J = 7$ Hz) **5l***Z*, 4.99 (s) **6l**, 4.94 (s) **5l***E* and **5l***Z*. MS [IP 70 eV; *m/z* (% rel. int.)]: **5l**; 261 (78, *M*), 232 (18), 169 (90), 141 (100), 115 (33). **6l**; 261 (10, *M*), 218 (6), 169 (9), 155 (100), 141 (69).

2-[2-(2-Phenylethenyloxy)ethyl]pyridine (**5m**). Isolated yield 68%. Anal. $C_{15}H_{15}NO$: C, H. ^1H NMR (90 MHz, $CDCl_3$): δ 8.65–8.45 (m, aryl), 7.70–7.00 (m, aryl), 6.97 (d, $J = 13$ Hz) *E*, 6.18 (d, $J = 7$ Hz) *Z*, 5.85 (d, $J = 13$ Hz) *E*, 5.19 (d, $J = 7$ Hz) *Z*, 4.26 (dt, $J = 6$ Hz), 3.18 (t, $J = 7$ Hz). MS [IP 70 eV; *m/z* (% rel. int.)]: 225 (10, *M*), 106 (100), 93 (9), 78 (20).

2-{2-[2-(1-Naphthyl)ethenyloxy]ethyl}pyridine (**5n**). Isolated yield 76%. Anal. $C_{19}H_{17}NO$: C, H. ^1H NMR (90 MHz, $CDCl_3$): δ 8.65–8.50 (m, aryl), 8.15–7.00 (m, aryl), 6.92 (d, $J = 13$ Hz) *E*, 6.50 (d, $J = 13$ Hz) *E*, 6.43 (d, $J = 7$ Hz) *Z*, 5.87 (d, $J = 7$ Hz) *Z*, 4.34 (t, $J = 6$ Hz), 3.21 (dt, $J = 7$ Hz). MS [IP 70 eV; *m/z* (% rel. int.)]: 275 (13, *M*), 170 (4), 152 (6), 141 (12), 106 (100).

1-[2-(3-Methylbutoxy)ethenyl]naphthalene (**5p**) *and 1-[1-(3-methylbutoxy)ethenyl]naphthalene* (**6p**). Isolated yield 76%. Anal. $C_{17}H_{20}O$: C, H. The ^1H NMR spectrum was recorded on the isomeric mixture of the α- and β-arylated products (90 MHz, $CDCl_3$): δ 8.20–7.30 (m, aryl), 6.94 (d, $J = 13$ Hz) **5p***E*, 6.48 (d, $J = 13$ Hz) **5p***E*, 6.40 (d, $J = 7$ Hz) **5p***Z*, 5.9 (d, $J = 7$ Hz) **5p***Z*, 4.49 (d, $J = 2$ Hz) **6p**, 4.37 (d, $J = 2$ Hz) **6p**, 3.96 (t, $J = 6$ Hz), 1.80–1.50 (m), 1.10–0.90 (m). MS [IP 70 eV; *m/z* (% rel. int.)]: **5p**; 240 (66, *M*), 170 (100), 152 (13), 141 (47), 115 (15). **6p**; 240 (9, *M*), 170 (100), 155 (64), 141 (33), 115 (7).

1-(2-Benzyloxyethenyl)naphthalene (**5t**) *and 1-(1-benzyloxyethenyl)naphthalene* (**6t**). Isolated yield 80%. Anal. $C_{19}H_{16}O$: C, H. The ^1H NMR spectrum was recorded on the isomeric mixture of the α- and β-arylated products (90 MHz, $CDCl_3$): δ 8.30–7.20 (m, aryl), 7.02 (d, $J = 13$ Hz), **5t***E*, 6.59 (d, $J = 13$ Hz) **5t***E*, 6.50 (d, $J = 7$ Hz) **5t***Z*, 5.90 (d, $J = 7$ Hz) **5t***Z*, 5.10 (s) **5t***Z*, 5.05 (s) **6t**, 5.00 (s) **5t***E*, 4.64 (d, $J = 2$ Hz) **6t**, 4.49 (d, $J = 2$ Hz) **6t**. MS [IP 70 eV; *m/z* (% rel. int.)]: **5t**; 260 (40, *M*), 231 (10), 169 (35), 153 (21), 141 (45), 91 (100). **6t**; 260 (1, *M*), 168 (14), 155 (64), 141 (23), 91 (100).

2-(2-Phenylethoxy)ethenylbenzene (**5u**) *and 1-(2-phenylethoxy)ethenylbenzene* (**6u**). Isolated yield 64%. Anal. $C_{16}H_{16}O$: C, H. The ^1H NMR spectrum was recorded on the isomeric mixture of the α- and β-arylated products (270 MHz, $CDCl_3$): δ 7.60–7.10 (m, aryl), 6.99 (d, $J = 13$ Hz) **5u***E*, 6.19 (d, $J = 7$ Hz) **5u***Z*, 5.84 (d, $J = 13$ Hz) **5u***E*, 5.22 (d, $J = 7$ Hz) **5u***Z*, 4.64 (d, $J = 3$ Hz) **6u**, 4.20 (d, $J = 3$ Hz) **6u**, 4.15–4.00 (tt, $J = 7$ Hz), 3.12 (t, $J = 7$ Hz) 3.06–2.99 (dt, $J = 7$ Hz). MS [IP 70 eV; *m/z* (% rel. int.)]: **5u**; 224 (20, *M*), 105 (100), 91 (9), 79 (13). **6u**; 224 (<1, *M*), 105 (64), 104 (100), 91 (5), 79 (12), 77 (8).

1-[2-(2-Phenylethoxy)ethenyl]naphthalene (**5v**) *and 1-[1-(2-phenylethoxy)ethenyl]naphthalene* (**6v**). Isolated yield 84%. Anal. $C_{20}H_{18}O$: C, H. The ^1H NMR spectrum was recorded on the isomeric mixture of the α- and β-arylated products (90 MHz, $CDCl_3$): δ 8.1–7.2 (m, aryl), 6.93 (d, $J = 13$ Hz) **5v***E*, 6.50 (d, $J = 13$ Hz) **5v***E*, 6.40 (d, $J = 7$ Hz) **5v***Z*, 5.90 (d, $J = 7$ Hz) **5v***Z*, 4.49 (d, $J = 2$ Hz) **6v**, 4.39 (d, $J = 2$ Hz) **6v**, 4.14 (dt), 3.89 (t), 3.20–2.80 (m). MS [IP 70 eV; *m/z* (% rel. int.)]: **5v**; 274 (45, *M*), 169 (6),

152 (5), 141 (12), 105 (100). **6v**; 274 (19, *M*), 170 (57), 155 (49), 141 (22), 105 (100).

Reaction of **1a** *or* **3c** *with iodobenzene in the presence of pyridine, and reaction of* **2a** *or* **3c** *with iodobenzene in the presence of triethylamine.* Palladium acetate (0.06 mmol), potassium carbonate (4 mmol) and tetrabutylammonium chloride (2 mmol) were stirred in 3 ml of DMF for 5 min. Iodobenzene (2 mmol), vinyl ether (2.4 mmol) and pyridine or triethylamine (2.4 mmol), dissolved in 3 ml of DMF, were added to the mixture. After thorough mixing of the components, the tube was closed and heated at 80°C in an oil bath for 18–48 h. After cooling, samples of ca. 0.3 ml were collected, partitioned between diethyl ether and water, and analyzed by GLC and GC–MS.

Competitive experiment with **1a** *and* **2a**. Palladium acetate (0.06 mmol), potassium carbonate (4 mmol) and tetrabutylammonium chloride (2 mmol) were stirred in 3 ml of DMF for 5 min. To the suspension were added iodobenzene (2 mmol), **1a** (2.4 mmol) and **2a** (2.4 mmol). The tube was closed and heated to 80°C in an oil bath. Samples were periodically removed and subjected to GC–MS analysis. The iodobenzene was consumed after 20 h.

Preparation of 2-phenylethanal from **5g**. A solution of **5g** (3.4 mmol) in 40 ml of THF was stirred with concentrated hydrochloric acid (4 ml) for 16 h at 20°C. Water was added (40 ml) and the solution was extracted with diethyl ether (2×40 ml). The combined organic phase was washed with brine, dried ($MgSO_4$) and concentrated. The crude product was subjected to GC–MS analysis for determination of the yield of 2-phenylethanal (69%). Flash chromatography (silica gel; diethyl ether–pentane 1:6) followed by Kugelrohr distillation at aspirator pressure afforded the title compound (0.19 g, 46%) as a colorless oil. GLC indicated a purity of 92%.

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References

1. Heck, R. F. *Org. React. 27* (1982) 345.
2. Heck, R. F. *Palladium Reagents in Organic Synthesis*, Academic Press, London 1985.
3. Trost, B. M. and Verhoeven, T. R. In: Wilkinson, G., Stone, F. G. A. and Abel, E. W., Eds., *Comprehensive Organometallic Chemistry*, Pergamon Press, Oxford 1982, Vol. 8, p. 855.
4. Heck, R. F. In: Trost, B. M. and Fleming, I., Eds., *Comprehensive Organic Synthesis*, Pergamon Press, Oxford 1991, Vol. 4, p. 833.
5. Daves, G. D., Jr. and Hallberg, A. *Chem. Rev. 89* (1989) 1433.
6. Kasahara, A., Izumi, T. and Fukuda, N. *Bull. Chem. Soc. Jpn. 50* (1977) 551.
7. Arai, I. and Daves, G. D., Jr. *J. Org. Chem. 44* (1979) 21.
8. Hallberg, A., Westfelt, L. and Holm, B. *J. Org. Chem. 46* (1981) 5414.
9. Hegedus, L. S., Toro, J. L., Miles, W. H. and Harrington, P. J. *J. Org. Chem. 52* (1987) 3319.
10. Andersson, C.-M., Hallberg, A. and Daves, G. D., Jr. *J. Org. Chem. 52* (1987) 3529.
11. Cabri, W., Candiani, I., Bedeschi, A. and Santi, R. *J. Org. Chem. 55* (1990) 3654.
12. Cabri, W., Candiani, I., Bedeschi, A., Penco, S. and Santi, R. *J. Org. Chem. 57* (1992) 1481, and references therein.
13. Andersson, C.-M. and Hallberg, A. *J. Org. Chem. 54* (1989) 1502.
14. Andersson, C.-M. and Hallberg, A. *J. Org. Chem. 53* (1988) 235.
15. Andersson, C.-M. and Hallberg, A. *J. Org. Chem. 53* (1988) 2112.
16. Andersson, C.-M., Larsson, J. and Hallberg, A. *J. Org. Chem. 55* (1990) 5757.
17. Jeffery, T. J. *J. Chem. Soc., Chem. Commun.* (1984) 1287.
18. Heck, R. F. and Nolley, J. P. *J. Org. Chem. 37* (1972) 2320.
19. McCrindle, R., Ferguson, G., Arsenault, G. J. and McAlees, A. J. *J. Chem. Soc., Chem. Commun.* (1983) 571.
20. Newkome, G. R., Puckett, W. E., Gupta, V. K. and Kiefer, G. E. *Chem. Rev. 6* (1986) 451, and references therein.
21. McCrindle, R., Ferguson, G., Khan, M. A., McAlees, A. J. and Ruhl, B. L. *J. Chem. Soc., Dalton Trans.* (1981) 986.
22. McCrindle, R., Stephenson, D. K., McAlees, A. J. and Wilson, J. M. *J. Chem. Soc., Dalton Trans.* (1986) 641.
23. McCrindle, R., Ferguson, G., Arsenault, G. J., McAlees, A. J. and Stephensson, D. K. *J. Chem. Res. (S)* (1984) 360.
24. McCrindle, R. and McAlees, A. J. *J. Chem. Soc., Dalton Trans.* (1983) 127.
25. McCrindle, R., Ferguson, G., McAlees, A. J. and Ruhl, B. L. *J. Organomet. Chem. 204* (1981) 273.
26. McCrindle, R., Alyea, E. C., Dias, S. A. and McAlees, A. J. *J. Chem. Soc., Dalton Trans.* (1979) 640.
27. McCrindle, R., Alyea, E. C., Ferguson, G., Dias, S. A., McAlees, A. J. and Parvez, M. *J. Chem. Soc., Dalton Trans.* (1980) 137.
28. Kasahara, A., Izumi, T., Takeda, T. and Imamura, H. *Bull. Chem. Soc. Jpn. 47* (1974) 183.
29. USP 3,227,672, *Chem. Abstr. 64* (1966) 8436b.
30. Voronov, V. K., Andriyankov, M. A. and Skvortsova, G. G. *Khim. Geterotsikl. Soedin. (5) 666*; *Chem. Abstr. 83* (1975) 77939j.
31. Watanabe, W. H. and Conlon, L. E. *J. Am. Chem. Soc.* (1957) 2828.
32. Morlyan, N. M., Muradyan, A. G. and Kirakosyan, D. E. *Metody Poluch. Khim. Reaktiv. Prep.* (1971) 38; *Chem. Abstr. 78* (1973) 15426c.
33. Reppe, W. *Liebigs Ann. Chem. 601* (1956) 81.
34. Posner, G. H. and Wettlaufer, D. G. *J. Am. Chem. Soc.* (1986) 7373.
35. JP 59,167,531; *Chem. Abstr. 102* (1985) 45607u.
36. Langhals, H., Julia, M. and Uguen, D. *Liebigs Ann. Chem.* (1982) 2216.

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