Terminal Heck Vinylations of Chelating Vinyl Ethers

Alexander Stadler, Henrik von Schenck, Karl S. A. Vallin, Mats Larhed,* Anders Hallberg

Organic Pharmaceutical Chemistry, Department of Medicinal Chemistry, Uppsala Biomedical Centre, Uppsala University, Box 574, SE-751 23 Uppsala, Sweden
Fax: (+46)-18-471-4474, e-mail: mats@orgfarm.uu.se

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Abstract: Terminal chelation-controlled Heck vinylations of electron-rich amino-functionalized vinyl ethers were performed with high regioselectivity furnishing moderate to good isolated yields of the corresponding 1-alkoxy-1,3-butadienes. DFT calculations support an amine-palladium(II) coordination strength reactivity/selectivity rationale, where the dimethylamino group was the preferred metal presenting functionality. Controlled microwave heating effectively accelerated these palladium-catalyzed reactions and full conversion could be achieved within 30 minutes. Subsequent Diels–Alder reactions with dimethyl acetylenedicarboxylate under microwave irradiation resulted exclusively in partly aromatized bi- and tricyclic compounds by elimination of the aminoalkoxy group. Thus, the selected dimethylamino auxiliary both controlled the regiochemistry in the palladium-catalyzed vinylation and was easily displaced in the aromatization process.

Keywords: cycloaddition; DFT; Heck reaction; microwaves; regioselectivity; vinyl ether

Introduction

A vast number of palladium-catalyzed Heck coupling reactions with vinyl halides or pseudohalides have been described during the last three decades.[1–4] The vinylation generally occurs in the terminal β-position of electron-deficient alkenes, as in the case of the closely related Heck arylation reactions. In contrast, the vinylation of electron-rich olefins can be performed under cationic conditions to afford the electronically favored internal α-product, a branched 1,3-butadiene in high selectivity.[5–7] No direct Heck method has so far been reported to furnish linear 1,3-butadienes from electron-rich olefins, e.g., enol ethers or enamides.

We have previously developed a set of different auxiliary-controlled Heck arylations.[8,9] In these reactions the specific introduction of an appropriately designed palladium(II)-coordinating tertiary amino group into the olefin allowed an efficient substrate presentation and a high terminal regiocontrol.[10] Employing a cyclic vinyl ether with a chiral *N*-methylpyrrolidine group, highly diastereoselective β-arylations were realized.[11] The presented knowledge suggested to us that chelation-controlled β-vinylation of vinyl ethers should provide a new gateway into valuable 1-alkoxy-1,3-butadienes. Since *trans*-alkoxydienes should be useful in the synthesis of cyclohexene derivatives by Diels–Alder reactions[12,13] and since classical preparative routes to this class of dienes appear rather toilsome,[14,15] more efficient procedures should be valuable.

We herein report that the reaction of vinyl triflates with selected amino-functionalized alkyl vinyl ethers in the presence of a palladium catalyst gives linear 1-alkoxy-1,3-butadienes of predominantly *trans*-configuration in high selectivity (Scheme 1). Complementary DFT calculations provide a rationale for the experimental results with regard to the reactivity and selectivity difference in the Heck coupling employing the investigated chelating olefins. Finally, microwave (MW) mediated Diels–Alder reactions were performed to verify the usefulness of the nitrogen-containing dienes as synthetic building blocks (Scheme 1).

Results

Chelation-Controlled Heck Vinylation Reactions

We decided to initiate the investigation with three available two-carbon tethered β-amino substituted vinyl ethers (**1a–c**, Scheme 2). The olefins were selected to permit evaluation of the capacity of the different metal-coordinating amino groups in controlling the vinylation process. The choice of the proline derivative **1c** was triggered by the potential to study the influence

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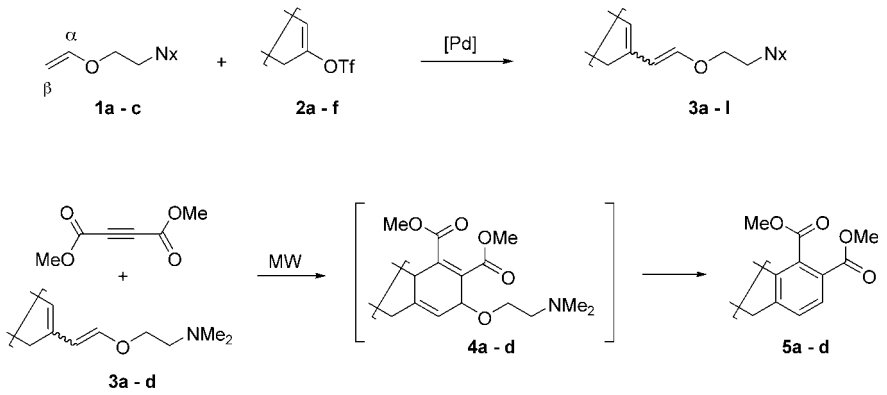
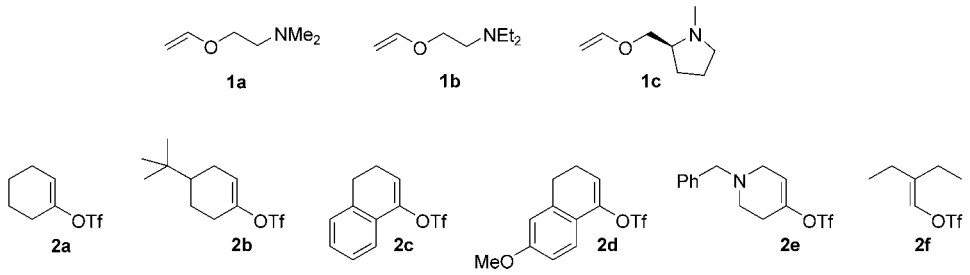


Scheme 1. Regioselective terminal vinylations and subsequent microwave-mediated Diels–Alder/amino alcohol elimination reactions.



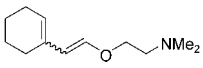
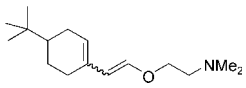
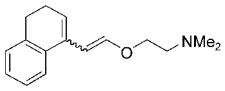
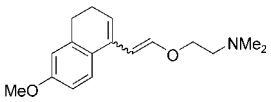
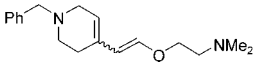
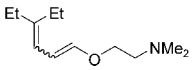
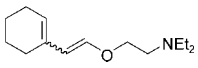
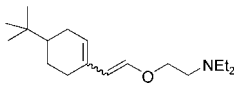
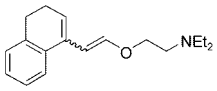
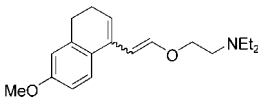
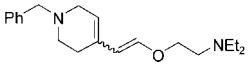
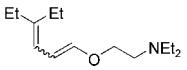
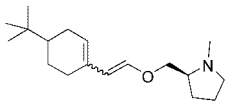
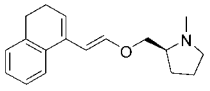
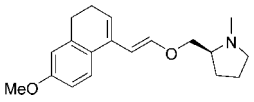
Scheme 2. Building blocks for terminal Heck vinylations.

of a chiral auxiliary in subsequent Diels–Alder reactions.

The reaction of vinyl triflates **2a**–**f** with the chelating enol ethers **1a**–**c** were performed on a 0.50-mmol scale under standard Heck reaction conditions (24 h oil-bath heating at 60 °C), using either a catalytic amount of the tris(dibenzylideneacetone)dipalladium(0)/tri-*t*-butylphosphonium tetrafluoroborate[16] system (Method A, see Table 1) or palladium acetate and triphenylphosphine as precatalytic combination (Method B, see Table 1). Since olefins **1a** and **1c** were not commercially available (or very expensive), the excess of **1a**–**c** was limited to 1.5 equivs. compared to the vinyl triflates. The addition of an external base (triethylamine) showed no positive effect on the reaction outcome but instead produced more by-products. Thus, since the olefins and the products (**3a**–**o**) are tertiary amines, the experiments were conducted with no external base. All but one vinylation of **1a** and **1b** furnished useful isolated yields with Method A (54–74% of **3**, except for product **3k**), although reactions employing the less reactive olefin **1c** did not proceed at all under these conditions (Table 1). Switching to the well-documented $Pd(OAc)_2/PPh_3$ combination[17] (Method B) generally afforded a slightly improved process with both **1a** and **1b** as coupling partners (56–92%). With Method B and an increased reaction temperature (80 °C), even sluggish **1c** produced dienes **3 m**–**o** in modest yields (22–36%). As evident from Table 1, the reaction underwent strict vinylic substitution at the β-carbon of the vinyl ethers resulting in clear terminal coupling products. Only the use of diethylamino vinyl ether **1b** produced small amounts of the internal coupling product with triflates **2c** and **2d** (β/α ≈ 96:4). Notably, the corresponding methyl ketone, that should have been formed after hydrolysis of the α-product, was never detected. Furthermore, the terminal vinylation turned out to be stereoselective with high *E/Z* ratios (Table 1). Importantly, and in contrast to the recent finding in Heck arylation chemistry by Chandrasekhar,[18] vinylation of non-chelating butyl vinyl ether using triethylamine as base was very sluggish and did not give terminal selectivity employing PEG as solvent. Similar to our previous investigation of palladium-catalyzed couplings of alkyl vinyl ethers with vinyl triflates,[5] high internal selectivity was achieved with butyl vinyl ether by using Method B after addition of 2 equivs. triethylamine. Butyl vinyl ether did not give any vinylation product in the absence of an external base.

In order to accelerate the reactions, the experiments have also been carried out in sealed vessels under controlled microwave irradiation[19–21] using the identical catalytic system as in Method B, but on a 0.20-mmol scale (Method C, see Table 2). Full conversion of **2** and similar yields as with classic heating could be obtained with all three olefins in only 30 minutes reaction time at 120 °C. However, with this method the stereoselectivity was reduced to an average of *E/Z* ≈ 70:30, whereas the regioselectivity remained unaffected, still resulting

Table 1. Chelation-controlled terminal vinylations of vinyl ethers with classic heating

Vinyl Ether	Triflate	Product		Method A[a] Isolated Yield	Method B[b] Isolated Yield
1a	**2a**		**3a**	54% $E/Z = 90:10$	65% $E/Z = 86:14$
	2b		**3b**	56% $E/Z = 94:6$	74% $E/Z = 89:11$
	2c		**3c**	62% $E/Z = 81:19$	64% $E/Z = 81:19$
	2d		**3d**	64% $E/Z = 86:14$	68% $E/Z = 87:13$
	2e		**3e**	61% $E/Z = 89:11$	56% $E/Z = 90:10$
	2f		**3f**	73% $E/Z = 40:60$	92% $E/Z = 52:48$
1b	**2a**		**3 g**	74% $E/Z = 83:17$	63% $E/Z = 92:8$
	2b		**3 h**	73% $E/Z = 86:14$	70% $E/Z = 89:11$
	2c		**3i**	57% $E/Z = 77:23$, $\beta/\alpha = 96:4$	50% $E/Z = 72:28$, $\beta/\alpha = 96:4$
	2d		**3j**	68% $E/Z = 93:7$, $\beta/\alpha = 97:3$	58% $E/Z = 76:24$, $\beta/\alpha = 94:6$
	2e		**3k**	$<5\%$	56% $E/Z = 57:43$
	2f		**3 l**	58% $E/Z = 40:60$	66% $E/Z = 50:50$
1c[c]	**2b**		**3 m**	$<5\%$	36% $E/Z = 88:12$
	2c		**3n**	$<5\%$	22% $E/Z = >99:1$
	2d		**3o**	$<5\%$	33% $E/Z = >99:1$

Reactions were conducted in sealed tubes with 0.50 mmol **2**, 0.75 mmol **1** and 1.5 mL DMSO at 60 °C for 24 h under N_2. More than > 95% conversion of **2** and more than > 95% purity of isolated products **3** (*E/Z*-mixture) by GC/MS and NMR.

[a] 3 mol % $Pd_2(dba)_3 \cdot CHCl_3$, 10 mol % *t*-Bu_3PHBF_4.

[b] 1 mol % $Pd(OAc)_2$, 3 mol % PPh_3.

[c] The reactions with **1c** were performed at 80 °C for 48 h.

Table 2. Results of microwave-accelerated Heck vinylations.

Entry	Product	Isolated Yield	*E/Z* ratio
1	**3a**	59%	80:20
2	**3b**	60%	81:19
3	**3c**	51%	60:40
4	**3d**	47%	77:23
5	**3e**	44%	68:32
6	**3f**	46%[a]	44:56
7	**3g**	65%	74:26
8	**3h**	64%	75:25
9	**3i**	51%	57:43
10	**3j**	45%	75:25
11	**3k**	50%[a]	93:7
12	**3l**	55%[a]	36:64
13	**3m**	30%	75:25
14	**3n**	28%	99:1
15	**3o**	30%	77:23

Reactions were conducted in sealed tubes with 0.20 mmol **2**, 0.30 mmol **1** and 0.6 mL DMSO at 120 °C for 30 min. More than > 95% conversion of **2** and more than > 95% purity of products **3** (*E/Z*-mixture) by GC/MS and NMR.
[a] Sluggish reaction with non-complete conversion of **2**, yield determined from GC/MS using 2,3-dimethylnaphthalene as internal standard.

in exclusively terminal vinylations to form the desired 1-alkoxy-1,3-butadienes **3** (Table 2). Contrary to the experiments with classic heating, compounds **3i** and **3j** showed no accompanying internal coupling product under microwave heating.

Photochemistry

In the presented Heck syntheses of 1-alkoxy-1,3-dienes chelation-control was successfully exploited to control the regioselectivity while the geometrical selectivity remained partly insufficient. Photoisomerization[22,23] of dihydronaphthalene derivative **3c** was therefore investigated as a model reaction with the aim to improve the *E/Z* ratio. The photoisomerization of the 1-alkoxy-1,3-diene **3c** was carried out in dry DMSO using a very dilute sample (1 μM) and focused 280 nm irradiation (λ_{max} for *cis*-**3c** = 281.5 nm). After 2 h, the selected regioisomeric mixture was converted from *E/Z* = 60:40 to *E/Z* = 90:10. Longer irradiation times did not improve the geometrical ratio, as a side reaction occurred, forming a non-identified by-product in amounts increasing with time. Changing the solvent did not improve the method, as both MeCN and MeOH promoted the unexpected side reaction directly from the beginning of the UV irradiation.

Diels–Alder Reactions

After purification, the *E/Z*-mixtures of **3a**–**d** were treated with the electron-poor dienophile dimethyl acetylenedicarboxylate (DMAD) in order to obtain the corresponding Diels–Alder adducts (Scheme 3). The thermal reactions (8 h at room temperature or 4 h at 60 °C, respectively) turned out to be rather sluggish, furnishing significant amounts of side products. However, the microwave protocol (60 min at 120 °C, Scheme 3) proceeded reasonably well with complete conversions of the *E/Z*-diene mixtures, but yielding the unexpected tetrahydronaphthalene and dihydrophenanthrene derivatives **5a**–**d**. The aromatic compounds **5a**–**d** were obtained in moderate to good yields after simple purification of the crude mixture by flash chromatography.

The formation of the resulting products **5** could be explained by immediate elimination of 2-dimethylaminoethanol from the primarily formed, intermediate Diels–Alder adducts **4** (Scheme 3).[12] In fact, performing the microwave-mediated Diels–Alder reaction with **3b** under reductive conditions (by addition of 3 equivs. hydroquinone) did not lead to the aromatic compound **5b** but rather to intermediate **4b**. In this reaction, non-conjugated **4b** was observed by GC/MS in an 82:18 ratio to the competing Diels–Alder adduct of alkoxybutadiene **3b** and hydroquinone.

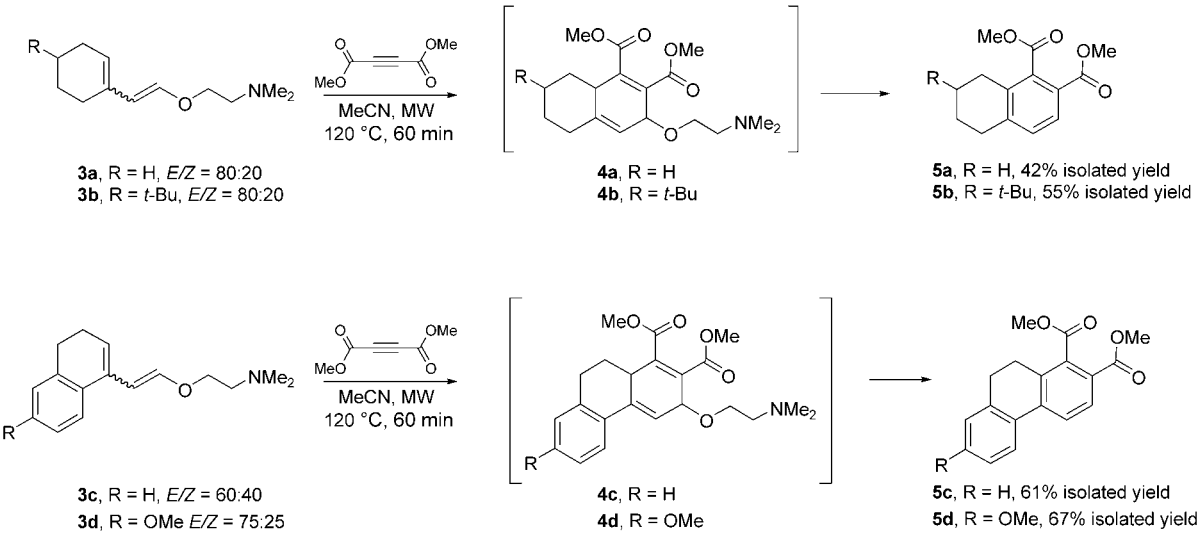
Full aromatization of the compounds **5c** and **5d** was realized under microwave conditions by treatment with 7 equivs. of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) for 60 minutes at 120 °C, furnishing the phenanthrene derivatives **6** (Scheme 4).[24]

Discussion

Mechanism

In a chelation-controlled terminal Heck vinylation process the reaction route exemplified in Scheme 5 appears reasonable.[8,25,26] Starting from vinyl triflates, cationic intermediates should prevail from the oxidative addition complex **A** and onwards.[6,27–29] The chelated ring size controls the direction of insertion into π-complex **B** and provides the σ-alkylpalladium complex **C** with high β-selectivity. This intermediate palladacycle collapses *via syn*-β-elimination to give the terminal product **3**.

In this scenario, the palladium-directing amino group must, a) function as a good ligand for the vinylpalladium(II) complex to enable an adequate presentation of the double bond and to control the regiochemistry in the insertion, and b) provide reversible coordination of the different palladium(II) species to allow catalytic turnover (Scheme 5). Thus, the nitrogen-palladium bond strength will be a compromise between these two contrasting demands. The results from the vinylation ex-



Scheme 3. Microwave-mediated synthesis of tetrahydronaphthalene and dihydrophenanthrene derivatives *via* Diels–Alder intermediates. The reactions were conducted in sealed vials with 0.20 mmol **3**, 0.40 mmol DMAD and 0.5 mL MeCN at 120 °C for 60 min. More than > 95% conversion of **3** (*E/Z*-mixture) and more than > 95% purity of isolated products **5** by GC/MS.

Scheme 4. Microwave-mediated aromatization to afford phenanthrene derivatives **6c** and **6d**. The reactions were conducted in sealed vials with 0.10 mmol **5**, 0.70 mmol DDQ and 1.5 mL MeCN at 120 °C for 60 min. More than > 95% conversion of **5** and more than > 95% purity of products **6** by GC/MS.

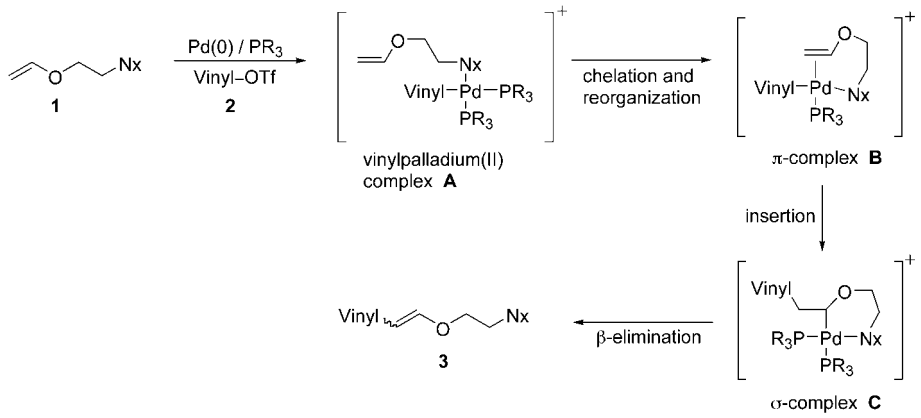
periments demonstrate that the dimethylamino- and the *N*-methylated pyrrolidine frameworks in **1a** and **1c** were comparable regarding regiocontrol, while the diethylamino auxiliary did not prove sufficiently effective (see Table 1, triflates **2c** and **2d**). When comparing the reactivity of olefins **1a–c**, the vinylation of the chiral **1c** was found to be very sluggish under all investigated reaction conditions. The reduced terminal selectivity with **1b** indicates a relatively weak metal-nitrogen binding and the low yields with pyrrolidine derivative **1c** suggest an enhanced stability of intermediates **A**, **B** or **C** (Scheme 5).

Competitive Experiments

Further evidence for the role of the *N*-methylpyrrolidine functionality as the most strongly palladium(II) binding auxiliary was provided in a series of competitive experiments with the model cyclohexenyl triflate **2b**. The reactions were performed with 1 equiv. **2b** and 1.5 equivs. each of two different vinyl ethers **1a–c** using Methods B and C.

*(i) Dimethylaminoethyl vinyl ether (**1a**)* vs. *diethylaminoethyl vinyl ether (**1b**):* GC/MS analysis of the product mixture showed clearly that the formation of dimethyl derivative **3b** was preferred to **3 h** in this experiment. On conducting the reaction with classic heating (60 °C, 24 h) **3b** was found to be predominant compared with **3 h** (**3b**/**3h** = 88:12). As **3b** was isolated in comparable yield to the single experiment in Table 1 (50%), no significant inhibition of the reaction could be assessed. Under microwave conditions (120 °C, 30 min) the reaction also showed high conversion, although **3b** was preferred only in a 75:25 ratio.

*(ii) Dimethylaminoethyl vinyl ether (**1a**)* vs. *(S)-N-methyl-2-vinyloxymethyl pyrrolidine (**1c**):* In the experiment at 80 °C according to Method B the pyrrolidine derivative **1c** inhibited the Heck process. Thus, only traces of **3m** could be detected and the yield of **3b** also drastically decreased (10%). Under high-density microwave irradiation, 30 min at 160 °C was needed to observe



Scheme 5. Reaction route for chelation-controlled Heck vinylations.

any dimethyl product (**3b**, $<10\%$). Still, only partial conversion was achieved as significant amounts of the starting triflate **2b** could be recovered. Increasing the temperature further led to considerable decomposition of both **1a** and **1c**.

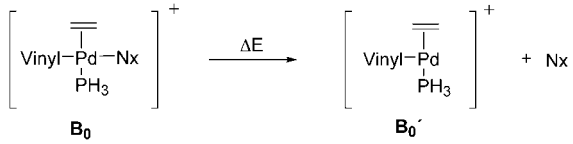
*(iii) Diethylaminoethyl vinyl ether (**1b**)* vs. *(*S*)-N-methyl-2-vinyloxymethylpyrrolidine (**1c**):* These final experiments furnished similar results as described under (ii). The pyrrolidine ether **1c** inhibited the reaction and only traces of the desired coupling products were detected, regardless of the condition used.

These experimental results indicate a rate-limiting effect of the pyrrolidine ether **1c** in the vinylation process. If no other vinyl ether is present in the catalytic cycle, **1c** acts as the olefinic reagent, sluggishly affording the corresponding diene in moderate yields. In competition with the other species, **1a** and **1b**, the pyrrolidine ether is responsible for the slow reaction and decreasing yields of the desired dimethyl and diethylamino products due to strong coordination/chelation of active palladium, rendering the regeneration of the active catalyst rate-determining. In the case where **1a** and **1b** are in competition, results suggest a relatively strong N-Pd(II) coordination for **1a**, however, without adverse effects on the overall reactivity.

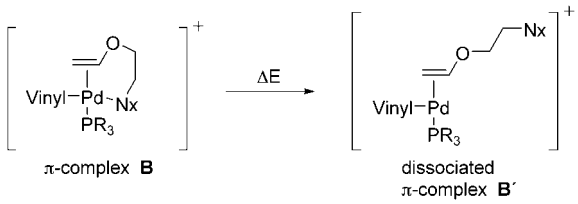
Computational Investigations

To provide further insight into the experimental difference of the studied enol ethers, we decided to investigate the palladium(II)-nitrogen coordination strength in the relevant chelated species using computational tools. Thus, the coordination strengths of a number of nitrogen containing auxiliaries were calculated using density functional theory at the B3LYP level. Computational details are provided below.

A set of square planar cationic vinylpalladium(II) complexes of increasing size were used to model the experimental systems. Initially, alkylated mimics of the utilized tertiary amine groups (N_x) were removed from the π-complex $\mathbf{B_0}$ (Scheme 6). The N-Pd(II) coordination strength, ΔE, was calculated as the energy difference between the dissociation products ($\mathbf{B_0}'$ and Nx) and starting $\mathbf{B_0}$. Results are reported in Table 3, Entries 1–3. The calculated order of increasing ΔE is in agreement with experimental results, where the coordination strength has been evaluated for a series of amines coordinating to the cationic complex Pd(dmpe)Me, where dmpe = 1,2-bis(dimethylphosphino)ethane.[30]



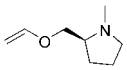
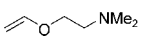
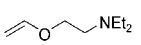
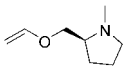
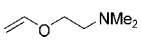
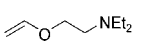
Scheme 6. General model system for investigating the N-Pd(II) coordination strength in vinylpalladium(II) complexes.



Scheme 7. Chelating and dissociated π-complexes of used nitrogen auxiliaries.

Increasingly detailed models more closely represented the π-complexes of the real experimental systems. In a second set of calculations, the coordination strength of the actual nitrogen auxiliary was determined in the chelated π-complex **B** (Scheme 7). While the amino-substituted vinyl ethers were fully represented, the phosphine ligand was first kept minimal with respect to size, as PH_3, (Table 3, Entries 4–6). Steric effects due to the phosphine ligand were later included by replacing PH_3 with PPh_3 (Entries 7–9).

Table 3. Calculated N-Pd(II) coordination strengths for utilized N-auxiliaries.

Entry	N_x		PR_3	ΔE [kcal/mol]	d_{Pd-N} [Å]
1			PH_3	28.6	2.29
2		NMe_3	PH_3	25.0	2.32
3		NEt_3	PH_3	23.2	2.32
4	**1c**		PH_3	22.7	2.29
5	**1a**		PH_3	18.9	2.32
6	**1b**		PH_3	17.1	2.33
7	**1c**		PPh_3	15.1	2.31
8	**1a**		PPh_3	10.7	2.35
9	**1b**		PPh_3	4.1	2.38

The successively more detailed models allowed for deconvolution of components affecting the N-Pd(II) coordination strength. In the first ligand set (Entries 1–3), ΔE was unaffected by palladacycle strain and by the significant steric effects introduced by PPh_3. A certain steric component of the total coordination energy is still expected, even for these reduced systems. An estimate of the steric component of ΔE was calculated by comparing the energy of free N_x in the geometry optimized for $\mathbf{B_0}$, with the energy of relaxed N_x. The energy loss due to geometrical rearrangement upon coordination of N_x to Pd $\mathbf{B_0}'$ was calculated to 1.6 kcal/mol for *N*-methylpyrrolidine, 1.9 kcal/mol for NMe_3 and 3.3 kcal/mol for NEt_3. These results imply that the proline moiety offered the most favorable electronic interactions with palladium while NEt_3 was the sterically most demanding, once again confirmed by experiments.[30] Introducing the effect of palladacycle ring strain in the second ligand set (Entries 4–6) revealed a systematic weakening of the N-Pd coordination strength. Comparing Entries 1 with 4, 2 with 5 and 3 with 6, gives differences in ΔE of 5.9, 6.1 and 6.1 kcal/mol, respectively. In the third ligand set (Entries 7–9), replacement of PH_3 with PPh_3 weakened the nitrogen coordination even further with the relatively bulky diethyl vinyl ether **1b** being most affected. Comparing Entries 4 with 7, 5 with 8 and 6 with 9, gives differences in ΔE of 7.6, 8.2 and 13.0 kcal/mol, respectively. This progressive influence due to phosphine size, in combination with the effects described above, leads to N-Pd(II) coordinations well separated in energy, influencing the respective ligands ability to function in the catalytic process.

In agreement with the competitive experiments, the pyrrolidine ether **1c** shows the highest ligand bond strength towards Pd(II), therefore withdrawing the catalyst from the reaction cycle and leading to significantly lowered yields. Comparing the dimethyl and the diethyl vinyl ethers, the dimethyl derivative **1a** has obviously the optimum ligand bond strength for proceeding the catalyst cycle, as observed in the competitive experiments. Energetics favor the coordination of **1a** to Pd, leading to a displacement of diethyl olefin **1b** from the metal and consequently to higher yields of the vinylated dimethyl product. Switching to the question of preparative usefulness in the investigated direct synthesis of 1-alkoxy-1,3-butadienes, **1a** is also the most attractive choice. Compared with **1b** both reactivity and regioselectivity are superior (Table 1). Due to the fairly weak N-Pd(II) coordination of **1b** ($\Delta E = 4.1$), it is quite reasonable that a fraction of the olefins could undergo reaction without the directing influence of the amine. The electronically favored α-product would then be formed, as was the case for **1b** reacting with triflates **2c** and **2d** (Table 1).

Conclusion

We have been able to perform highly selective terminal vinylations of vinyl ethers by utilizing palladium(II)-coordinating amino substituents. Furthermore, the scope of the method was extended by acceleration of the reactions with controlled high-density microwave irradiation. Theoretical DFT calculations assisted in explaining the experimental outcome for the different palladium(II)-coordinating nitrogen auxiliaries. Finally, the synthesized dimethylaminoethoxy-1,3-butadienes were investigated as substrates in microwave-mediated Diels–Alder reactions.

Experimental Section

General

Microwave heating was conducted in a single mode cavity (SmithSynthesizer), operating at 2.45 GHz, with a built-in magnetic stirrer, on-line IR and pressure sensors. Flash column chromatography (FCC) was generally carried out using commercially available silica gel 60, employing ethyl acetate/hexane 1:9 (+1% triethylamine) as eluent, except where otherwise indicated.

^{1}H NMR spectra were recorded in $CDCl_3$ at 270 and 400 MHz, respectively. Mass spectra were recorded on a GC/MS equipped with a CP-SIL 8 CB (30 m × 0.25 mm) capillary column, utilizing electron impact at an ionizing energy of 70 eV. Additionally LC/MS electrospray analyses were performed using a Chromolith Performance RP-18e column

(4.6 × 100 mm) and an MeCN/water gradient. Elemental analyses were performed by Analytische Laboratorien, Prof. Dr. H. Malissa and G. Reuter GmbH. The instability of the isolated compounds in some cases prevented accurate elemental analysis. The high resolution MS analyses were performed by Einar Nilsson, University of Lund.

Photochemical reactions were carried out on DMSO solutions under N_2 gas flow using an Oriel 1000 W Xe ARC light source and a 280 nm Oriel UV filter. The emitted light density was determined using a UV enhanced Si photodiode (5.8 mm^2) attached to a current meter.

Materials

(*t*-$Bu_3PH)BF_4$ was purchased from Strem Chemicals, DMSO (≥99.5%, over molecular sieves) was obtained from Fluka, all other chemicals, including **1b**, were purchased from Merck and used without further purification. Dimethylaminoethyl vinyl ether **1a** was prepared according the literature procedure.[8]

(S)-N-Methyl-2-vinyloxymethylpyrrolidine (1c)

A 50-mL thick-walled glass tube was equipped with a stirring bar and charged with *S*-(−)-*N*-methyl-2-hydroxymethylpyrrolidine (1.73 g, 15 mmol) dissolved in ethyl vinyl ether (28 mL). $Pd(OAc)_2$ (128 mg, 3.5 mol %) and 2,2′-bipyridyl (81 mg, 3.5 mol %) were added, the vessel was flushed with nitrogen, sealed and placed in an appropriate heating block. The mixture was refluxed ($T = 50\,^{\circ}C$) for at least 72 h, then diluted with pentane (40 mL) and washed with NaOH (0.1 M) and water (2 × 20 mL each). The organic layer was dried with K_2CO_3 and finally evaporated to obtain **1c** as an orange liquid; yield: 850 mg (6 mmol, 40%).

The corresponding triflates have been prepared according to literature protocols.[31,32]

N-Benzyl-1,2,3,6-tetrahydropyridine 4-triflate (2e); Representative Procedure

N-Benzylpiperidin-4-one (378 mg, 2.0 mmol) was dissolved in dry THF (10 mL) and cooled to −78 °C. A 1 M solution of LHMDS in THF (2.4 mL, 1.2 equivs.) was added dropwise under N_2 flush. After addition, the mixture was stirred at −78 °C for approx. 20 min, thereafter 1.2 equivs. of $PhN(Tf)_2$ (857 mg, 2.4 mmol) were added at once. The cooling bath was removed, allowing the mixture to warm up to room temperature under stirring for 1 h, then it was refluxed for additional 2 hours. Finally the reaction was quenched with water (10 mL), the mixture was extracted with EtOAc (3 × 10 mL), washed with NH_4Cl and brine (10 mL each) and dried with $MgSO_4$. Evaporation of the solvent afforded 827 mg dark orange highly viscous liquid. The crude product was purified by FCC, using hexane/EtOAc (9:1) as eluent, obtaining the desired triflate **2e** as colorless viscous liquid; yield: 460 mg (72%).

Heck Couplings, General Procedures

Method A: Vinyl triflate **2** (0.50 mmol) and 1.5 equivs. of vinyl ether **1** (0.75 mmol) were placed in a thick-walled glass vessel and dissolved in dry DMSO (1.5 mL). $Pd_2(dba)_3 \cdot CHCl_3$ (3 mol %) and (*t*-$Bu_3PH)BF_4$ (Fu salt, 10 mol %) were added, the vessel was flushed with nitrogen, sealed and inserted into a heating block. The mixture was kept at 60 °C for 24 h under slight stirring. Thereafter the reaction was quenched with 1 M NaOH (5 mL) and extracted with diethyl ether (2 × 10 mL). The combined organic layers were washed with brine (2 × 5 mL) and dried with $MgSO_4$ overnight. After filtration, evaporation of the solvent afforded the desired terminal coupling products as slightly yellow to orange oily liquids. Purification of the crude products was performed by FCC using ethyl acetate/hexane (1:9 + 1% triethylamine) as eluent.

Method B: The reactions were carried out as above, using $Pd(OAc)_2$ (1 mol %) and PPh_3 (3 mol %) as precatalytic system.

Method C: 0.20 mmol vinyl triflate **2** and 1.5 equivs. (0.30 mmol) of the corresponding vinyl ether **1** were placed in a 2-mL microwave reaction vessel and dissolved in 0.6 mL of dry DMSO. $Pd(OAc)_2$ (1 mol %) and PPh_3 (3 mol %) were added, the vessel was flushed with nitrogen, sealed and inserted into the microwave cavity and irradiated at 120 °C for 30 min, subsequently followed by air-jet cooling. Work-up was carried out as in Method A, yielding the products in comparable yields to the thermal runs. The β-vinylation products [as *(E)/(Z)* mixtures, unless separated] exhibited spectral and analytical properties as summarized in the Supplementary Information.

Photoisomerization

The dihydronaphthalene derivative **3c** (0.5 mg, 2.0 μmol, *E/Z* = 60:40) was dissolved in dry DMSO (2 mL) and placed in a conventional UV vessel ($d = 1$ cm). The vial was flushed with nitrogen and sealed with a septum. During irradiation N_2 was bubbled through the solution. Measuring a full UV spectrum of the sample, the absorption maxima were determined to 304.5 nm for the *trans*-compound and 281.5 nm for the *cis*-isomer. The sample was placed in the focus of a 280 nm optical lens and irradiated for several hours to transform the mixture into the *trans*-isomer (*E*) of **3c** (after 2 h *E/Z* = 90:10). Aliquot samples have been taken every hour and analyzed by GC/MS.

Diels–Alder Reactions, General Procedure

0.20 mmol of diene **3** (*E/Z* mixtures, see Table 1) was placed in a 2-mL microwave reaction vial and dissolved in MeCN (0.5 mL). 2 equivs. of dimethyl acetylenedicarboxylate (DMAD, 0.40 mmol) were added, the vial was flushed with nitrogen, sealed and inserted into the microwave cavity. The reaction mixture was irradiated at 120 °C for 60 min, subsequently followed by air-jet cooling. The solvent was removed under vacuum and the reminder purified by FCC, using ethyl acetate/hexane (9:1) + 1% triethylamine as eluent.

Aromatization Procedure of the Dihydrophenanthrene Derivatives

0.10 mmol dihydrophenanthrene **5** was placed in a 2-mL microwave reaction vial and dissolved in MeCN (1 mL). 7 equivs. of

2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 0.7 mmol) were added, the vial was flushed with nitrogen, sealed and inserted into the microwave cavity and irradiated at 120 °C for 60 min, subsequently followed by air-jet cooling. The solvent was removed under vacuum and the crude **6** purified by FCC, using ethylacetate/hexane (9:1) + 1% triethylamine as eluent.

Computational Details

Geometries and energies were fully optimized using the gradient-corrected hybrid density functional method B3LYP.[33] We used a basis set of double-ζ valence quality labeled lacvp in the Jaguar 4.0 program (Jaguar 4.0, Schrodinger, Inc., Portland, Oregon, 2000). For Pd, the core electrons were replaced by a relativistic electron core potential (ECP) developed by Hay and Wadt.[34] After geometry optimization, the energies were recalculated at the B3LYP level using a valence triple-ζ quality basis set labeled lacv3p** in the Jaguar 4.0 program.

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