Regioselective Palladium-Catalyzed Synthesis of β-Arylated Primary Allylamine Equivalents by an Efficient Pd−N Coordination

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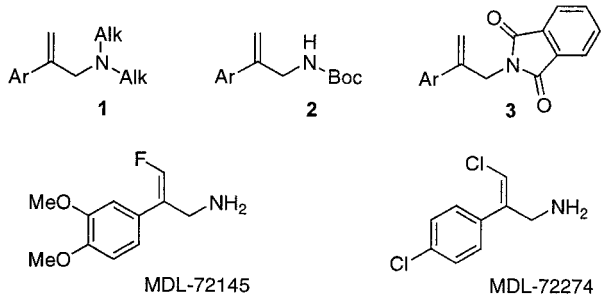
A highly regioselective Heck arylation, utilizing aryl triflates and a palladium/dppf catalytic system, can be performed at the internal, β-carbon of Boc- and phthalimido-protected allylamines, yielding arylated primary allylamine equivalents. The very high regioselectivity obtained with secondary Boc-protected allylamides is suggested to be caused by an efficient coordination between an anionic nitrogen and palladium. Single-mode microwave irradiation has been utilized to shorten the reaction times and, in the case of Boc-protected allylamides, to improve the yields of two electron-poor aryl triflates.

Introduction

The importance of finding new and attractive synthetic methods for compounds encompassing arylethylamine fragments is hardly overestimable as a result of the ubiquity of biologically active primary arylethylamines. We recently reported a regioselective Heck reaction[1−7] yielding tertiary *N*,*N*-dialkylallylamines **1**[8] (Chart 1) as branched arylallylamines were needed in our medicinal chemistry program.[9,10] Unfortunately, the corresponding primary allylamines were not accessible by this experimentally facile procedure.

Although several methods for the synthesis of primary allylamines exist,[11,12] few short and direct methods for the preparation of β-arylated allylamines are available.[13] A regioselective synthesis of the Boc-protected allylamine **2**, using palladium chemistry with (*E*)-*N*-(*tert*-butoxycarbonyl)-3-(trimethylsilyl)allylamine as olefin was published by Blart and Ricci,[14] where the vinylic trimethylsilyl group improved the regiocontrol. We argued that

Chart 1



primary, internally β-arylated arylallylamines might be accessible with high regioselectivities by a direct Heck reaction of aryl triflates with Boc-protected allylamines, provided that a favorable Pd−N coordination could be achieved.

The phthalimido (Pht)-protected compounds **3** (Chart 1) were of interest as they have been used in the synthesis of GABA receptor antagonists,[15,16] MAO-B inhibitors[17] (e.g., MDL-72145[18]) and SSAO inhibitors[19] (e.g., MDL-72274[20]), the last of which have recently emerged as drug candidates in many fields of medicinal chemistry, e.g., diabetes mellitus,[21,22] prevention of secondary effects of stroke[23,24] and atherosclerosis.[25] (*E*)-3-

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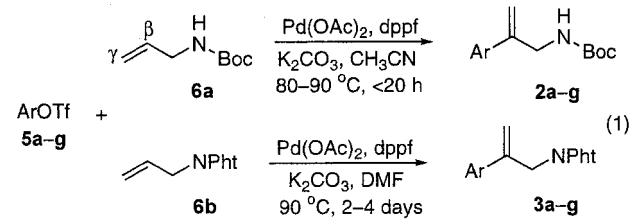
Halo-2-phenylallylamines in general, such as MDL-72145 and MDL-72274 (Chart 1), have received attention as irreversible enzyme inhibitors.[26−29]

We are now reporting the highly regioselective internal arylation of Boc-protected allylamines, yielding compounds **2** in high to moderate yields (eq 1). This method



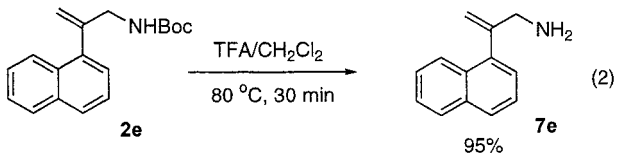
allows for the use of the easily available Boc-protected allylamine as olefin. 2-Aryl-3-phthalimido-1-propenes **3** were also synthesized in one step in good to poor yields, thus presenting a substantially shorter synthetic route than that previously published[17] (eq 1). Deprotection of the Boc and phthalimido groups can then provide primary and secondary amines.[17,30,31] In addition, microwave heating[32−38] has been applied to markedly accelerate the Heck reaction.

Results

Synthesis of Internally Arylated Boc-Protected Allylamines 2. In the standard, thermal experiments the aryl triflates **5a**−**g** were mixed with 3-(*N*-*tert*-butoxycarbonylamino)-1-propene **6a**, potassium carbonate and catalytic amounts of palladium acetate and dppf[39−42] in acetonitrile as solvent (eq 1). The preparative results are summarized in Table 1. The reactions were conducted at 80 °C (entries 3−6) or 90 °C (entries 1−2, 7) and completed within 20 h with full conversion of the triflate, yielding products **2a**−**g** with excellent regioselectivity and high to moderate isolated yields (with the exception of entry 6). Several bidentate ligands other than dppf were tested but failed to induce high regioselectivities. The use of monodentate ligands or the addition of LiCl to the reaction mixture, with dppf as ligand, both resulted in mixtures of β- and γ-arylated olefins.

Microwave heating with a single-mode reactor resulted in very short reaction times (3−6 min) with high regioselectivity, although the isolated yields deviated from the corresponding thermal reactions (Table 1). The solvent chosen for the microwave reactions was DMF, because of its higher boiling point and superior ability to absorb microwave irradiation as compared to acetonitrile[35,43] [tan δ (25 °C): 0.052 (CH_3CN), 0.142 (DMF)]. Notably, couplings with the electron-poor triflates in entries 6 and 7 resulted in higher, in the case of entry 6 even significantly higher, yields under microwave heating than under thermal heating, possibly as a result of a faster formation of product in competition with side reactions. Attempts to further accelerate these reactions by increasing the microwave power beyond 20 W (entries 1−5 and 7) or 35 W (entry 6) resulted in disappointing yields and formation of tar in the reaction mixture. The low yields and the somewhat lower regioselectivities in the microwave-heated entries 2 and 4 could be ascribed to catalyst breakdown to palladium black due to the higher temperatures reached in the sealed microwave vessels.[35]

Deprotection of the Boc-protected allylamine **2e** in TFA/CH_2Cl_2 was shown to yield the free amine **7e** in 95% isolated yield after 30 min at 80 °C, thermal heating (eq 2).



Synthesis of Internally Arylated Phthalimido-Protected Allylamines 3. Couplings with thermal heating at 90 °C using the phthalimido-protected allylamine **6b** in DMF as solvent (eq 1) were slower (2−4 days) than the corresponding couplings with **6a,** and aryl scrambling in the oxidative addition complex[44−46] reduced the yields and hampered the workup in entries 1 and 7, Table 1. The couplings were successful especially with *ortho*-substituted or sterically hindered aryl triflates (with the exception of entry 6, Table 1). The *ortho*-methoxyphenyl compound **3b** (entry 2) was isolated with a considerably higher regioselectivity and yield than the *para*-substituted **3a**. The higher yield for **3b** could partly be explained by the reduction of phenyl migration as no **3d** was detected by GC−MS. The *ortho*,*ortho*-disubstituted 2,3,6-trimethyl triflate was unreactive,[8] indicating that a high degree of steric hindrance impedes the reaction. The phenyl derivative **3d** (entry 4, Table 1) was formed with a slightly higher regioselectivity than that of **3b**, although it was difficult to maintain the high

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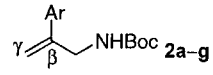
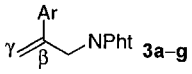
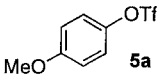
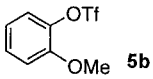
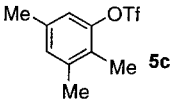
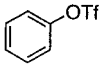
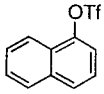
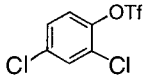
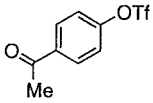
Table 1. Internal Arylation of Allylamines 6a and 6b with Aryl Triflates 5





		Thermal Heating[a]		Microwave Heating[b]			Thermal Heating[a]		Microwave Heating[b]		
Entry	Aryl Triflate	β/γ[c]	Isolated Yield **2** (%)[d]	Time (min)/ Effect (W)	β/γ[c]	Isolated Yield **2** (%)[d]	β/γ[c]	Isolated Yield **3** (%)[d]	Time (min)/ Effect (W)	β/γ[c]	Isolated Yield **3** (%)[d]
1	 **5a**	>99.5/0.5	41	6/20	>99.5/0.5	34	57/43	18[e]	5/20	67/33	21[e]
2	 **5b**	>99.5/0.5	74	6/20	95/5	64	86/14	57	6/20	86/14	24
3	 **5c**	>99.5/0.5	68	3/20	98/2	68	96/4	65	6/20	89/11	42
4	 **5d**	>99.5/0.5	70	4/20	93/7	40	88/12	34	5/20	45/55	18[e]
5	 **5e**	>99.5/0.5	70	5/20	>99.5/0.5	56	96/4	40	6/20	60/40	23
6	 **5f**	>99.5/0.5	7	6/35	>99.5/0.5	63	>99.5/0.5[f]	9	5/20	>99.5/0.5[f]	6
7	 **5g**	>99.5/0.5	45	5/20	>99.5/0.5	64	50/50	17[g]	5/20	50/50	13[g]

[a] The thermal reactions with **6a** were run in 2.5 mmol scale under nitrogen atmosphere at 80 °C (entries 3−6) or 90 °C (entries 1, 2, 7) with 1 equiv of **5a**−**g**, 0.03 equiv of $Pd(OAc)_2$, 0.132 equiv of dppf, 3 equiv of **6a** or **6b**, 1.2 equiv of K_2CO_3, and 10 mL of acetonitrile. All reactions with **6a** were completed within 20 h. The thermal reactions with **6b** were run at 90 °C with DMF as solvent and were completed after 2 days (entries 1, 2, 7), 3 days (entries 4−6), or 4 days (entry 3). Otherwise as with **6a**. [b] Continuous irradiation at 2450 MHz. The microwave heated reactions were run in 1.0 mmol scale in septum-sealed Pyrex tubes with 1 equiv of **5a**−**g**, 3 equiv of **6a** or **6b**, 0.03 equiv of $Pd(OAc)_2$, 0.132 equiv of dppf, and 1.2 equiv of K_2CO_3 in 1.0 mL of DMF. [c] Selectivity internal β-arylation/terminal γ-arylation. Determined by GC−MS and ^{1}H NMR. [d] Greater than 95% by GC−MS, except where otherwise indicated. [e] Purity 92−93%. Mixture of internally and terminally arylated products. [f] Ratio uncertain because of low yield. [g] Purity 91−93%. Mixture of internally and terminally arylated products. No elemental analysis made.

regioselectivity with other, less sterically hindered aryl triflates. It was also particularly important to have fresh dppf in couplings with **6b** as the regioselectivity was found to deteriorate otherwise. Single-mode microwave heated reactions succeeded in reducing the reaction times but were difficult to optimize, and the regioselectivities and isolated yields were not improved compared to the thermal reactions. The deprotection of phthalimido-protected internally arylated allylamines has been published previously.[17]

Discussion

The use of aryl triflates in combination with palladium/bidentate ligand catalysts in the Heck coupling with acyclic, electron-rich olefins was first reported by Cabri et al.[3,47] The cationic palladium complexes produced as intermediates after the dissociation of the weakly coordinated triflate anion[48] are thought to influence the insertion of the aryl fragment to the preferred internal position of the olefin.[3,7]

The regioselectivities in the palladium-catalyzed internal phenylation of *N*,*N*-dialkylallylamines[8] were found to be higher (β/γ = >99.5/0.5) than with alkenes (β/γ = 86/14) and allyltrimethylsilane (β/γ = 95/5),[3,49] and a coordination of the amine moiety to palladium was suggested to dictate the regiochemical outcome of the reaction.[8,50−55] A similar coordination can account for the powerful regiocontrol with secondary Boc-protected

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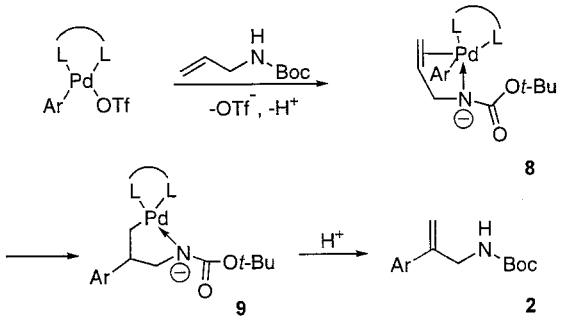
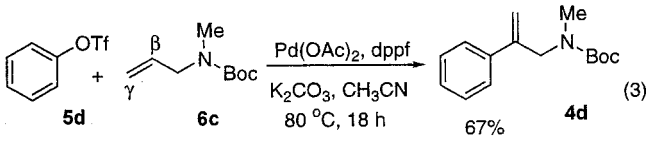
Scheme 1



allylamides, such as **6a**, as olefins[14] where chelation can lead to the pentacoordinated[6,56] π-complex **8** (Scheme 1). The electron density of the metal-coordinating nitrogen atom should be reduced in **8**, and the dissociation of the hydrogen located on the nitrogen should be facilitated,[57] yielding an anionic nitrogen.[58] The charge developed on the nitrogen after the dissociation of the amide hydrogen may further strengthen the Pd^{2+}−N coordination. The ease of deprotonation depends on the coordinating metal, and a representative pK_a value of 2 for Pd^{2+}-coordinated small peptides has been estimated.[58] Similar deprotonations have been proposed in association with allyl alcohols in heteroatom directed Heck couplings.[59] The insertion will then result in the energetically favored five-membered ring intermediate[56,60] **9**, and subsequent β-hydride elimination will yield the internally arylated product **2** (Scheme 1). It is in this context important to point out that the Pd^{2+}−N coordination cannot be so strong as to hinder the dissociation of palladium from the nitrogen, as no *cis*-hydrogens are available for β-elimination in the Pd^{2+}−N coordinated complex **9**.

To further investigate the regioselectivity of tertiary Boc-protected allylamines under our reaction conditions we investigated the arylation of the methyl-substituted, Boc-protected allylamine **6c** as olefin with **5d** as aryl triflate (eq 3). The coupling resulted in formation of **4d**



(3)

in 67% isolated yield (pure β-arylated product) but with only moderate regioselectivity (β/γ = 89/11) after 18 h at 80 °C thermal heating (eq 3). Even though the coupling between **6c** and **5d** was completed overnight, couplings with other aryl triflates were slower (2−3 days) indicating that the reactivity of **6c** is similar to that of **6b**.

One difference that should be noted between allylamines and allylamides in the discussion of chelation control is the additional possibility of palladium−carbonyl coordination[14,58,60−62] in the case of allylamides. It has been suggested that the anionic forms of amides in peptides coordinate to palladium through the deprotonated nitrogen and the neutral forms chiefly through the carbonyl.[58] If palladium−carbonyl coordination takes place with Boc- and phthalimido-protected allylamides and to what extent it influences the regioselectivity is at present uncertain.

Chart 2

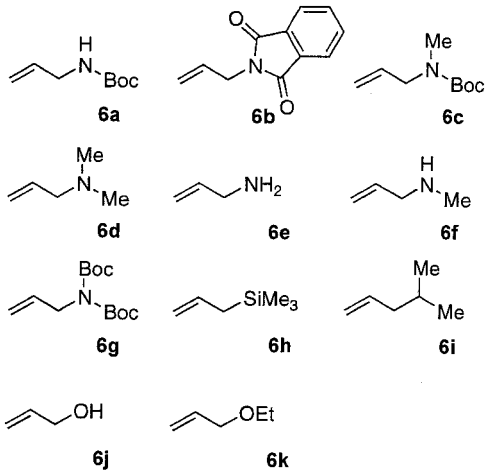


Table 2. Product Distribution in Competitive Arylations

olefin	distribution	olefin	distribution	olefin	distribution
6a/6b	60/40[a]	**6a/6h**	33/67	**6d/6i**	35/65
6a/6c	63/37	**6a/6i**	69/31	**6h/6k**	57/43
6a/6d	91/9	**6a/6j**	35/65	**6i/6k**	28/72
6a/6e−f	nr	**6a/6k**	38/62	**6j/6k**	51/49
6a/6g	>99.5/0.5	**6b/6c**	55/45[a]		

[a] Calculation based on a 1.9 times larger response factor for arylated **6b**.

A series of competitive Heck couplings with 11 olefins (Chart 2) was performed in order to study the influence of heteroatom-containing olefins on the reactivity and regioselectivity of the palladium−dppf system. Phenyl triflate **5d** was in each experiment coupled with two olefins (5 equiv of each) under the standard, thermal reaction conditions, and the ratios of the phenylated products were measured by GC−MS and ^{1}H NMR.[63] The product distributions are summarized in Table 2.

The secondary Boc-protected amine **6a** has in the competitive reactions a high reactivity compared to those of the tertiary amine **6d** and the heteroatom-lacking alkene **6i** and a somewhat lower preference over that of the tertiary Boc-protected methyl-substituted **6c**. The reactivity of the phthalimido compound **6b** was comparable with that of **6c**. The oxygen-containing olefins **6j**,**k** and the trimethylsilyl compound **6h**[49] are all slightly more reactive than **6a**.

The primary (**6e**) and secondary, methyl-substituted (**6f**) allylamines suppress the reaction in competition with **6a**, giving only traces of **2** and no trace of arylated **6e** or **6f** on GC−MS. Strong coordination can thus cause

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(63) Equimolar amounts of the internally arylated olefins were injected on the GC−MS, and their integrated areas were compared in order to ensure that the GC−MS response factors for the different arylated olefins were comparable. When pure samples of the internally arylated olefins were not at hand the ratios were analyzed by ^{1}H NMR of the reaction mixtures. Only the arylated **6b** had a different response factor; approximately 1.9 times higher than those of the other arylated olefins.

catalyst poisoning with a primary or a secondary allylamine lacking electron-withdrawing substituents on the nitrogen. The electron density on the amine moiety has previously been found to influence its coordinating ability.[64,65]

The long reaction times with phthalimido-protected allylamine **6b** (eq 1) (Table 1) might indicate a slower insertion process caused either by steric factors or the presence of an extra carbonyl group. The theory that a large steric bulk on the olefin hampers the reaction is supported by the loss of reactivity when an additional Boc group is added to **6a**, giving the di-Boc protected **6g**. Couplings with **6g** yield no product, and the presence of **6g** in a competitive coupling with **6a** does not disturb the product formation of **2d**, indicating that the reason for the lack of reactivity of **6g** is not deactivation of the catalyst (Table 2). The synthesis of the terminally arylated **6g**, which should not be as sensitive to steric hindrance, appears to run smoothly with vinyl triflates and monodentate ligands.[66]

The results show that the investigated allylic olefins can, in large, be divided into three groups on the basis of their reactivity under the present reaction conditions: group 1, olefins that coordinate via the nitrogen in five-membered rings and couple readily with high regioselectivity (i.e., **6a** and **6d**); group 2, olefins that cannot generate an anionic nitrogen and couple with good to low regioselectivity (**6b** and **6c**); and group 3, olefins with a strong Pd^{2+}-coordinating ability (**6e,f**) or a large steric bulk (**6h**) that impede either a rate-determining oxidative addition or insertion step in the catalytic cycle.

In summary, a one-step reaction procedure has been presented that gives access to protected, internally arylated allylamine compounds that upon deprotection can yield primary (through **2** and **3**) or secondary allylamines (through **4** or through methylation of **2** before deprotection), which are of interest for applications in medicinal chemistry. These results serve as a complement to our previously reported synthesis of internally arylated tertiary dialkylallylamines, and an easily performed Heck coupling procedure can now yield primary, secondary, and tertiary, internally arylated allylamine compounds. The reaction times for the internal arylation of the Boc-protected allylamine can be reduced to a couple of minutes with single-mode microwave heating.

Experimental Section

Procedures. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 270 and 67.8 MHz, respectively. Chemical shifts were reported as δ values (ppm) indirectly referenced to TMS by the solvent signal ($CHCl_3$) δ 7.26 and ($CDCl_3$) δ 77.0. Low resolution mass spectra were recorded on a GC−MS instrument equipped with a HP-1 capillary column (25 m × 0.22 mm) operating at an ionization potential of 70 eV. The oven temperatures were 70−305 °C (gradient 30 °C/min) for **2**, **4**, and **6** and 100−315 °C (gradient 20 °C/min) for **3**. The regioisomers (β- and γ-arylated products) had the same response factors, as determined by GC−MS and ^{1}H NMR. Microwave heating was carried out with a MicroWell 10 single-mode microwave cavity[67] producing continuous irradiation at 2450 MHz. All microwave reactions were performed under nitrogen in Pyrex tubes[43] with a perforated stopcock with septa. In the event of overpressurization, the septum should burst. The inner diameter of the lower part of the tubes (to the height of 3 cm) was 8 mm. The upper part was slightly wider (inner diameter 11 mm) to increase the expansion volume. Great care should be taken when performing pressurized reactions using microwave heating.[68] The microwave-heated reactions were performed without stirring. Temperature profiles were recorded using a NoEMI-TS Reflex (Nortech Fibronic, Inc. Québec, Canada), utilizing temperature-sensitive fluoroptic probes (TPP-01-M2.5-A; Nortech Fibronic). The probe was positioned approximately 1 cm from the bottom of the reaction tube. Sampling rate was 3 Hz. Elemental analyses were performed by Mikro Kemi AB, Uppsala, Sweden, and high-resolution MS was performed by Dr. Einar Nilsson, Lunds universitet, Sweden.

Materials. Aluminum oxide (150 mesh, 58 Å, Aldrich no. 19,997-4, deactivated with 6% water) was used for chromatography and Silica gel 60_{PF254} containing $CaSO_4$ (Merck no. 1.07749) was used for circular chromatography. All reagents except the aryl triflates and olefins **6a**−**c**,**h** were commercially available. The aryl triflates were prepared from the corresponding phenols.[69−71] The Boc-protected allylamines were made from the corresponding allylamines[72] and the phthalimido-protected allylamine from allylbromide.[73] Products **2a**[14] and **3d**[17] were previously characterized. All products are >95% pure except **3a** (thermal and microwave heating), **3d** (microwave heating), and **3g** (thermal and microwave heating) as indicated in Table 1.

General Procedure for the Thermal Internal Arylation of 3-*N*-*tert*-Butoxycarbonylamino-1-propene 6a (Table 1). A mixture of 2.50 mmol of aryl triflate **5a**−**g**, 0.075 mmol (16.8 mg) of $Pd(OAc)_2$, 0.330 mmol (183 mg) of dppf, 7.5 mmol (1.18 g) of 3-*N*-*tert*-butoxycarbonylamino-1-propene, 3.75 mmol (518 mg) of K_2CO_3, and 10 mL of acetonitrile was heated at 80−90 °C (entries 1, 2, 7, 90 °C; entries 3−6, 80 °C) on an oil bath under nitrogen in oven-dried, heavy-walled and thin-necked Pyrex tubes, sealed with a Teflon stopcock. Samples were periodically taken and partitioned between diethyl ether and 0.1 M NaOH. The organic layers were dried over potassium carbonate before analyses by GC−MS. All reactions were completed in 20 h with full conversion of the aryl triflate. All reactions were worked up by extraction between diethyl ether and 0.1 M NaOH. The eluents were removed under reduced pressure and filtered through aluminum oxide (eluent isohexanes−ethyl acetate 1:1) before removal of olefin by bulb-to-bulb distillation. If necessary further column chromatography with aluminum oxide was performed until the products **2a**−**g** were purified (>95% purity). Eluents: isohexanes−ethyl acetate 9:1 (**2a**,**b**), isohexanes−ethyl acetate 19:1 (**2c**−**g**).

Microwave-Heated Internal Arylation of 3-*N*-*tert*-Butoxycarbonylamino-1-propene 6a (Table 1). To a heavy-walled, oven-dried Pyrex tube were added 1.00 mmol of aryl triflate **3a**−**h**, 0.03 mmol (6.7 mg) of $Pd(OAc)_2$, 0.132 mmol (73 mg) of dppf, 3.0 mmol (0.26 g) of 3-*N*-*tert*-butoxycarbonylamino-1-propene (0.47 g), 1.2 mmol (173 mg) of K_2CO_3, and 1.0 mL of DMF bubbled with N_2 for 5 min. The height of the reaction mixture in the tube was 3 cm. The reaction mixture was flushed with nitrogen and the screw cap tightened thoroughly (finger-tight) before mixing with a Whirlimixer. Heating was then applied by means of microwave irradiation.

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The reaction tube was allowed to cool in the microwave cavity for a couple of minutes before any handling of the reaction mixture took place and was thereafter purified as described in the preceding paragraph.

Thermal Internal Arylation 3-Phthalimido-1-propene 6b (Table 1). A mixture of 1.00 mmol of aryl triflate **5a**−**g**, 0.03 mmol (6.7 mg) of $Pd(OAc)_2$, 0.132 mmol (73 mg) of dppf, 3.0 mmol (0.57 g) of 3-phthalimido-1-propene, 1.2 mmol (173 mg) of K_2CO_3, and 1.0 mL of DMF was heated at 90 °C on an oil bath under nitrogen in oven-dried, heavy-walled, and thin-necked Pyrex tubes, sealed with a Teflon stopcock. The reactions were completed after 2 days (entries 1, 2, 7), 3 days (entries 4−6), or 4 days (entry 3). The reactions were purified as described above. Eluents: isohexanes−ethyl acetate 4:1 (**3a**,**b**,**g**); isohexanes−ethyl acetate 10:1 (**3c**−**f**). Products **3b**,**d**,**e** were separated by circular chromatography after bulb-to-bulb distillation.

Deprotection of Boc-Protected Internally Arylated Allylamine 2e (eq 2). To a heavy-walled, oven-dried Pyrex tube were added 0.134 mmol (37.9 mg) of **2e** and 2 mL of a 1:1 solution of TFA and CH_2Cl_2. After 1 h at 80 °C on an oil bath the reaction mixture was allowed to cool, alkalized with 1 M NaOH, and extracted to CH_2Cl_2. After drying with K_2CO_3 and removal of solvent under reduced pressure **7e** was separated on silica ($CHCl_3$−MetOH 19:1 + 1% Et_3N) and isolated to yield 23.2 mg (95%) of pure **7e** as a slightly greenish oil.

Competitive Phenylations of Olefins 6 (Table 2). The competitive experiments were performed with 1.00 mmol (0.226 g) of **5d**, 5.0 mmol of each of the two olefins, 0.030 mmol (6.7 mg) of $Pd(OAc)_2$, 0.132 mmol (73.2 mg) of dppf, and 1.2 mmol (173 mg) of K_2CO_3 in 4 mL of acetonitrile. The reactions were performed at 80 °C, except experiments with **6b**, which were run at 90 °C. The product ratios were analyzed by GC−MS integration, as this method allows for the detection and characterization of even very small amounts of product isomers, and subsequently with ^{1}H NMR to confirm that the GC−MS response factors for the different products were comparable. The ^{1}H NMR samples of the reaction mixtures were extracted between diethyl ether and 0.1 M NaOH, and the eluents were removed under reduced pressure. The response factors for the different products were checked by weighing equimolar amounts of arylated olefin **6** and thereafter comparing the geminal, vinylic ^{1}H NMR peaks of the major product of each olefin with the corresponding integration on GC−MS. Arylated **6b** was found to have a response factor approximately 1.9 times larger than that of the other arylated olefins **6**.

3-*N*-*tert*-Butoxycarbonylamino-2-phenyl-1-propene (2d). Compound **2d** was obtained in 70% yield at 80 °C and 40% yield after microwave irradiation (4 min/20 W). The boiling point at bulb-to-bulb distillation was ∼100 °C at 4 mmHg. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.42−7.29 (m, 5H), 5.40 (s, 1H), 5.21 (s, 1H), 4.66 (br s, 1H), 4.17 (d, J = 5.6 Hz, 2H), 1.41 (s, 9H). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 155.7, 144.9, 138.6, 128.4, 127.9, 126.1, 113.1, 79.4, 44.3, 28.3. MS *m*/*z* (relative intensity 70 eV) 177 (100), 160 (6), 132 (29), 116 (18). Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.1; H, 8.21; N, 6.00. Found: C, 72.1; H, 7.9; N, 6.1.

2-(2-Methoxyphenyl)-3-phthalimido-1-propene (3b). Compound **3b** was obtained in 57% yield at 90 °C and 24% yield after microwave irradiation (6 min/20 W). Mp 102 °C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.88−7.66 (m, 4H), 7.27−7.21 (m, 1H), 7.17−7.13 (m, 1H), 6.91−6.83 (m, 2H), 5.25 (q, J = 1 Hz, 1H), 5.19 (d, J = 1 Hz, 1H), 4.71 (t, J = 1 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 167.9, 156.9, 143.0, 133.9, 132.0, 130.4, 129.2, 128.9, 123.2, 120.5, 115.7, 110.5, 55.4, 42.1. MS *m*/*z* (relative intensity 70 eV) 293 (M^+, 100), 262 (11), 160 (27), 133 (56), 105 (61). Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.7; H, 5.15; N, 4.78. Found: C, 73.7; H, 5.2; N, 4.7.

3-*N*-*tert*-Butoxycarbonylamino-*N*-methyl-2-phenyl-1-propene (4d). Compound **4d** was obtained in 67% yield at 80 °C. The boiling point at bulb-to-bulb distillation was ∼140 °C at 2 mmHg. ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.49−7.18 (m, 5H), 5.41 (d, J = 17 Hz, 1H), 5.11 (s, 1H), 4.29 (d, J = 22 Hz, 1H), 2.81 (m, 3H), 1.45 (m, 9H). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 155.7, 144.3, 128.2, 127.8, 126.3, 113.6, 113.3, 79.5, 51.6, 33.3., 28.3. MS *m*/*z* (relative intensity 70 eV) 247 (M^+, 0.1), 191 (100), 174 (15), 146 (18), 118 (35). Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.8; H, 8.56; N, 5.66. Found: C, 73.1; H, 8.7; N, 5.7.

2-(1-Naphthyl)-allylamine (7e). Compound **7e** was obtained in 95% yield at 80 °C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.03−7.98 (m, 1H), 7.90−7.84 (m, 1H), 7.82−7.77 (m, 1H), 7.52−7.42 (m, 3H), 7.32−7.28 (m, 1H), 5.59 (q, J = 1 Hz, 1H), 5.18 (q, J = 1 Hz, 1H), 3.67 (t, J = 1 Hz, 2H), 1.60 (bs, 2H). ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.0, 139.3, 133.6, 131.4, 128.3, 127.5, 125.9, 125.7, 125.4, 125.3, 125.2, 114.0, 48.8. MS *m*/*z* (relative intensity 70 eV) 183 (M^+, 96), 165 (41), 153 (100), 128 (12). High-resolution MS (EI) calcd for $C_{13}H_{13}N$ (M^+) 183.1045, found 183.1043. Anal. Calcd for $C_{13}H_{13}N$: C, 85.2; H, 7.15; N, 7.64. Found: C, 84.5; H, 7.1; N, 7.2.

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Supporting Information Available: ^{1}H and ^{13}C NMR and MS spectra for all new compounds. Temperature profile for the microwave heated synthesis of **2e**. General procedures for thermal internal phenylation of 3-*N*-*tert*-butoxycarbonylamino-*N*-methyl-1-propene **6c** and microwave heated arylation of 3-phthalimido-1-propene **6b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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