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Fast and Regioselective Heck Couplings with *N*-Acyl-*N*-vinylamine Derivatives

Anders Lindhardt Hansen and Troels Skrydstrup*

Department of Chemistry and the Interdisciplinary Nanoscience Center, University of Aarhus, Langelandsgade 140, 8000 Aarhus C, Denmark

ts@chem.au.dk

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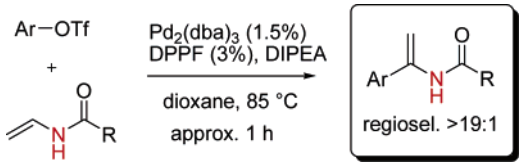

Highly regioselective Heck couplings of aryl triflates with *N*-acyl-*N*-vinylamines lacking an *N*-alkyl substituent were achieved with reaction times of approximately 1 h in yields ranging from 62 to 98% using 1.5 mol % of $Pd_2(dba)_3$, 3 mol % of DPPF, and diethylisopropylamine in dioxane. The efficiency of these cross-couplings were studied with several *N*-vinylamides and an example each of an *N*-vinylcarbamate and an *N*-vinylurea. The Heck coupling products easily underwent acidic hydrolysis to the corresponding aryl methyl ketone or in situ hydrogenation in the presence of $(Ph_3P)_3RhCl$ under a hydrogen atmosphere to provide the *N*-acyl derivatives of pharmaceutically relevant benzylic amines. The coupling of a vinyl triflate and more interestingly a vinyl tosylate to *N*-vinyl acetamide was also studied affording a 2-acylamino-1,3-butadiene with the same high regioselectivity in preference for the α-isomer. This result suggests that Heck couplings of electron-rich alkenes with vinyl tosylates also follow a cationic pathway.

Introduction

The palladium(0)-catalyzed coupling between aryl halides/triflates and olefins, referred to as the Heck reaction, represents a viable method for carbon−carbon bond construction.[1] The degree of the regioselective outcome for this important arylation reaction is influenced by a number of factors including the substitution pattern of the olefin, where alkenes bearing electron-withdrawing groups (e.g., acrylates, acrolein) selectively provide products of β-substitution, while with electron-rich substituents (vinyl ethers and amides), arylation generally occurs at the α-position.[2] In the latter class, successful regioselective couplings also necessitate the use of aryl triflates and a palladium catalyst with bidentate ligands, ideal conditions for an ionic pathway.[3−5]

Only a few cyclic and acyclic enamides have hitherto been examined in this Pd-catalyzed reaction, where all examples tested represent cases with an alkyl substituent on the nitrogen.[2b,3,4,6] Yet, the products obtained from the coupling with *N*-acyl-*N*-vinylamines lacking an *N*-alkyl

(1) For some relevant reviews, see: (a) Heck, R. F. *Palladium Reagents in Organic Syntheses*; Academic Press: Orlando, 1985. (b) Tsuji, J. *Palladium Reagents and Catalysts: Innovation is Organic Synthesis*; Wiley: Chichester, U.K., 1995. (c) Brase, S.; de Meijere, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; Chapter 3. (c) Link, J. T.; Overman, L. E. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; Chapter 6. (d) *Transition Metal Catalyzed Reactions*; Davis S. G., Murahashi, S.-I., Eds.; Blackwell Science, Oxford, 1999. (e) Beletskaya, I.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (f) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2002. (f) Whitcombe, N. J.; Hii, K. K.; Gibson, S. E. *Tetrahedron* **2001**, *57*, 7449. (g) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*, 2nd ed.; University Science Books: Sausalito, CA, 1999; Chapter 4.6. (h) Beller, M.; Riermeier, T. H.; Stark, G. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, Germany, 1998; Vol. 1, p 208. (i) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427.

(2) For a few papers on the topic of insertion and regioselectivity, see: (a) Ozawa, F.; Kubo, A.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 1417. (b) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2. (c) Ludwig, M.; Stromberg, S.; Svensson, M.; Akermark, B. *Organometallics* **1999**, *18*, 970. (d) Larhed, M.; Hallberg, A. *In Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; John Wiley & Sons: New York, 2002.

(3) Cabri, W.; Candiani, I.; Bedeschi, A.; Santi, R. *J. Org. Chem.* **1992**, *57*, 3558.

(4) For an excellent and historical account on factors controlling regioselectivity in the Heck reaction with electron-rich alkenes, see: Mo, J.; Xu, L.; Xiao, J. *J. Am. Chem. Soc.* **2005**, *127*, 751.

(5) For an exception to this rule using ionic solvents, see ref 4.

(6) (a) Andappan, M. M. S.; Nilsson, P.; von Schenck, H.; Larhed, M. *J. Org. Chem.* **2004**, *69*, 5212. (b) Vallin, K. S. A.; Zhang, Q.; Larhed, M.; Curran, D. P.; Hallberg, A. *J. Org. Chem.* **2003**, *68*, 6639. (c) Harrison, P.; Meek, G. *Tetrahedron Lett.* **2004**, *45*, 9277.

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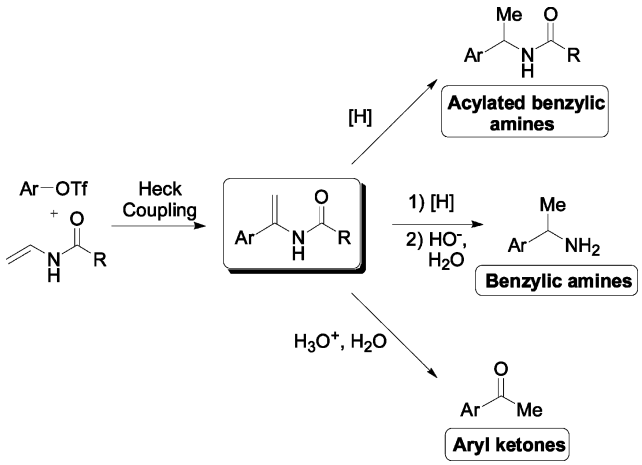
SCHEME 1



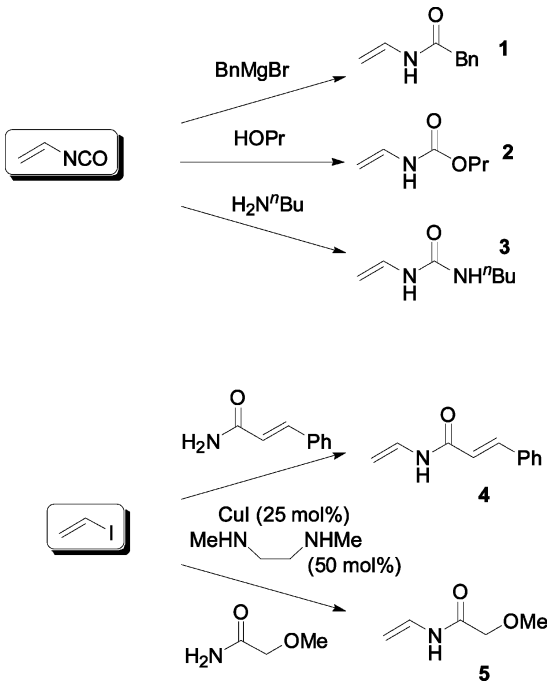
substituent would provide compounds of potentially higher synthetic versatility and value. As displayed in Scheme 1, the Heck coupling between such substrates not only allows access to α-aryl enamides and aryl ketones, but the hydrogenation of the alkene product would lead to an alternative and facile entry to benzylic amines and *N*-acyl derivatives thereof, which represent important constituents of numerous compounds of potential medicinal applications.[7,8] In contrast, almost identical substrates have been demonstrated to undergo successful intermolecular C−N bond-forming reactions which represents potentially a major competing reaction to the desired Heck coupling.[9]

Herein we describe general reaction conditions for the preparation of *N*-acyl-α-arylvinylamines[10] in good yields and short reaction times (≤1 h) via the Pd(0)-catalyzed coupling of *N*-acyl-*N*-vinylamines with aryl triflates without competing amidations. In addition, a protocol for Heck coupling and in situ hydrogenation is reported for a facile access to chiral benzylic amides and carbamates.

Results and Discussion

Two approaches were adapted for the preparation of the noncommercially available starting *N*-acyl *N*-vinylamines required for this study.[11] In the first and nonoptimized approach, nucleophiles were simply added to freshly prepared vinyl isocyanate[12] providing access to the corresponding enamides **1**−**3**, including one example each of a vinyl carbamate and vinyl urea. In an alternative method, Buchwald's protocol for the amidation of vinyl iodides employing a combination of copper iodide, *N*,*N*′-dimethyl ethylenediamine, and vinyl iodide was adapted (Scheme 2).[13,14] Although vinyl iodide was not examined in this reported work, its coupling with *trans*-cinnamide and 2-methoxyacetamide provided the corresponding vinylamides **4** and **5** in 50 and 56% yield, respectively (see the Supporting Information). Nevertheless, higher catalyst loading was required in order for this coupling reaction to proceed compared to the originally reported protocol, which may be linked to the low purity of the commerically obtained vinyl iodide.

SCHEME 2



Initial efforts were focused on identifying suitable reaction conditions for promoting the Heck coupling between 2-naphthyl triflate and *N*-vinyl acetamide, as displayed in Table 1. Particular attention was paid to the reaction times later, and hence all reactions were first run over a period of approximately 17 h in accordance with earlier reports.[3,6] Four bidentate ligands (3 mol %) were tested using $Pd_2(dba)_3$ (1.5 mol %) as the palladium(0) source and 3 equiv of the popular base dicyclohexylmethylamine[15] in dioxane (entries 1−4). DPPP, DPPF, and Dmphen[6a,16,17] provided the best yields, which were

(7) During the course of these investigations, Harrison and Meek (ref 6c) published a short and nonoptimized Heck coupling study with *N*-vinylacetamide, with coupling yields ranging from 24 to 69%.

(8) For some recent examples, see: (a) Kessler, A.; Faure, H.; Petrel, C.; Ruat, M.; Dauban, P.; Dodd, R. H. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3345. (b) Milkiewiez, K. L.; Marsilje, T. H.; Woodworth, R. P., Jr.; Bifulco, N., Jr.; Hangauer, M. J.; Hangauer, D. G. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 483. (c) Venkatachalam, T. K.; Sudbeck, E. A.; Mao, C.; Uckun, F. M. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2071. (d) Dankwardt, S. M.; Martin, R. L.; Chan, C. S.; Van Wart, H. E.; Walker, K. A. M.; Delaet, N. G.; Robinson, L. A. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2085. (e) Venkatachalam, T. K.; Qazi, S.; Samuel, P.; Uckun, F. M. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 485. (f) Auberson, Y. P.; Allegeier, H.; Bischoff, S.; Lingenhoehl, K.; Moretti, R.; Schmutz, M. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1099. (g) Ashwood, V. A.; Field, M. J.; Horwell, D. C.; Julien-Larose, C.; Lewthwaite, R. A.; McCleary, S.; Pritchard, M. C.; Raphy, J.; Singh, L. *J. Med. Chem.* **2001**, *44*, 2276. (h) Hanano, T.; Adachi, K.; Aoki, H.; Morimoto, H.; Naka, Y.; Hisadome, M.; Fukuda, T.; Sumichika, H. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 881.

(9) Yin, J.; Buchwald, S. L. *Org. Lett.* **2000**, *2*, 1101.

(10) For other approaches to the synthesis of *N*-acyl α-arylvinylamines, see: (a) Padwa, A.; Akiba, M.; Cohen, L. A.; MacDonald, G. J. *Tetrahedron Lett.* **1981**, *22*, 2435. (b) Padwa, A.; Akiba, M.; Cohen, L. A.; MacDonald, G. J. *J. Org. Chem.* **1983**, *48*, 695. (c) Burk, M. J.; Casy, G.; Johnson, N. B. *J. Org. Chem.* **1998**, *63*, 6084. (d) van den Berg, M.; Haak, R. M.; Minnaard, A. J.; De Vries, A. H. M.; Feringa, B. L. *Adv. Synth. Catal.* **2002**, *344*, 1003. (e) Wallace, D. J.; Klauber, D. J.; Chen, C.-Y.; Volante, R. P. *Org. Lett.* **2003**, *5*, 4749.

(11) *N*-Vinylacetamide is commerically available.

(12) (a) Hart, R. *Bull. Soc. Chim. Belg.* **1956**, *65*, 291. (b) Kirby, C.; Kroto, H. W. *J. Mol. Spectrosc.* **1978**, *70*, 216.

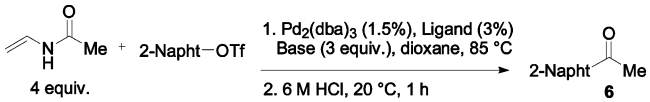
(13) Jiang, L.; Job, G. E.; Klapars, A.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 3667.

(14) See the Supporting Information.

(15) For some examples, see: (a) Gürtler, C.; Buchwald, S. L. *Chem. Eur. J.* **1999**, *5*, 3107. (b) Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989. (c) Hills, I. D.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 13178.

(16) Andappan, M. M. S.; Nilsson, P.; Larhed, M. *Chem. Commun.* **2004**, 218.

TABLE 1. Optimization of Heck Coupling between 2-Naphthyl Triflate and *N*-Vinylacetamide Followed by Acid-Catalyzed Hydrolysis



entry	ligand	base	time (h)	yield[a] (%) (α/β ratio)
1	(*R*)-BINAP	Cy_2NMe	19	75 (>19:1)
2	DPPP	Cy_2NMe	15	83 (>19:1)
3	Dmphen	Cy_2NMe	17	83 (77:23)
4	DPPF	Cy_2NMe	15	84 (>19:1)
5	DPPF	Cs_2CO_3	17	23 (>19:1)
6	DPPF	TEA	17	76 (>19:1)
7	DPPF	DIPEA	17	90 (>19:1)

[a] Isolated yields.

obtained after acid hydrolysis of the acid-labile arylvinyl product to the corresponding methyl ketone, although in the latter case the regioselectivity proved poor. Reducing the number of equivalents of the enamide or base, or using other polar solvents (DMF, DMA), was less effective in terms of either the yields or regioselectivity. Further optimization of the base with DPPF as the ligand showed that the use of diethylisopropylamine provided the highest coupling yield (90%, entry 7).

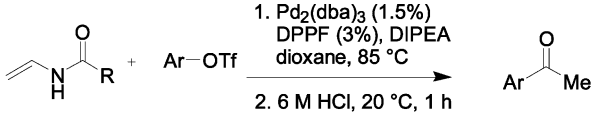
This two-step coupling protocol was then tested with a few other aryl triflates and *N*-acyl-*N*-vinylamines, including a vinylurea and vinyl carbamate (Table 2). The aryl ketones **6**−**9** were obtained in yields reaching 90% and greater (entries 1−3 and 5−7) in all but one example. Only in the case with the vinyl urea (entry 4) was the reaction mixture complex after the Heck coupling according to the ^{1}H NMR spectrum of the crude reaction mixture. Nevertheless, a 64% yield of the 2-naphthyl methyl ketone **6** could be obtained after subjection to aqueous HCl. Many of these ketones are trivial and comercially available, but this study does serve to prove the high efficiency of the Heck coupling step.

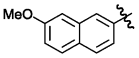
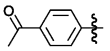
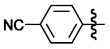
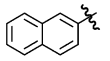
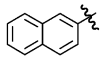
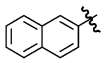
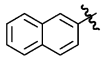
Although long reaction times were expected for these Heck couplings as previously reported for other *N*-vinylamides (≥15 h), analysis of some of these reactions revealed that completion of the coupling step was reached within approximately 1 h (Table 2, entries 2, 3, 6, and 7). This is also illustrated in Table 3, where the *N*-acyl-α-arylvinylamines are isolated via column chromatography. In all cases, only short reaction periods were required for obtaining the Heck product, *even as brief as 15 min* as observed for the 3-*N*,*N*-dimethylaminophenyl triflate in entry 9. In general, the yields are good, but somewhat lower than in the two-step protocol to the aryl ketones. This discrepancy is most likely due to the coupling product's slight acid instability. Nevertheless, the *N*-acyl-α-arylvinylamines survived quick column isolation, and their spectral analyses by ^{1}H and ^{13}C NMR were run in other solvents than $CDCl_3$. It should also be noted that in none of these cases did we identify products from a potentially competing amidation reaction.[9]

Alternatively, we examined the possibility of subjecting the Heck coupling product to hydrogenation conditions with Wilkinson's catalyst without an intermediate purification step (Table 4). Hence, after completion of the cross-coupling step, 5 mol % of $(PPh_3)_3RhCl$ was added directly to the reaction mixture followed by stirring overnight under a hydrogen atmosphere. Under these conditions, the *N*-acyl benzylic amines were isolated in yields ranging from 53% to 92% after isolation.[18] Harrison and Meek have already revealed the possibility of performing asymmetric hydrogenations with an *N*-acyl α-arylvinylamine implying the adaptability of this approach to enantiomerically enriched *N*-acyl benzylic amines.[6c]. Whereas the *trans*-isomer **25** of the vinyl triflate was prepared using *N*-phenyltriflimide according to a known procedure,[19] the tosylate furnished a 2.5:1 *trans*/*cis* (**26**/**27**) isomeric mixture in a yield of 69% upon treatment of the ketoester with potassium *tert*-butoxide and tosyl anydride in acetonitrile. Attempts to prepare solely the *trans*-isomer **26** according to the same procedure described for the synthesis of the triflate were not successful and only led to an approximately 1:1 mixture of the two double-bond isomers in low yield. Fortunately, the vinyl tosylates could be separated by column chromatography.

Subjection of the vinyl triflate **25** and *N*-vinylacetamide to the same Heck coupling conditions as described above provided the 2-acetamido-1,3-butadiene **28** in a coupling yield of 62% with the expected control of regiochemistry

TABLE 2. Heck Coupling of *N*-Acyl-*N*-vinylamines and Aryl Triflates Followed by Acid-Catalyzed Hydrolysis[a]



Entry	R	Ar	Time	Yield[b]	Compound nr.
1	Me		4.5 h	86%	**7**
2	Me		1 h	92%	**8**
3	Me		1.5 h	94%	**9**
4	NH^{n}Bu		4.5 h	64%	**6**
5	OPr		4 h	94%	**6**
6	CH_2OMe		1.5 h	95%	**6**
7	Bn		1.5 h	98%	**6**

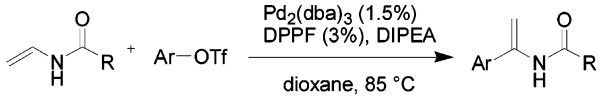
[a] All reactions was carried out using 4 equiv of olefin, 1 equiv of triflate, and 3 equiv of base. [b] Isolated yields, all selectivities >19:1 (branched/linear).

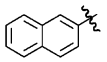
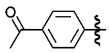
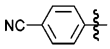
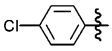
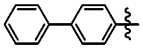
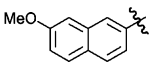
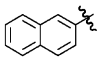
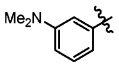
(17) dppp = 1,3-bis(diphenylphosphino)propane, dppf = 1,1′-bis-(diphenylphosphino)ferrocene, (*R*)-BINAP = (*R*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, dmphen = 2,9-dimethyl-1,10-phenanthroline.

(18) For an example of an asymmetric version of this hydrogenation step, see ref 6c.

(19) Ohba, M.; Kawase, N.; Fujii, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 8250.

TABLE 3. Heck Coupling of Enamides and Aryl Triflates[a]

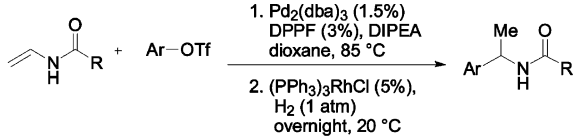


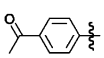
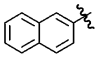
Entry	R	Ar	Time	Yield[b]	Compound nr.
1	Me		60 min	77%	**10**
2	Me		105 min	89%	**11**
3	Me		60 min	81%	**12**
4	Me		60 min	79%	**13**
5	Me		60 min	72%	**14**
6	Me		75 min	75%	**15**
7	Me		60 min	70%	**16**
8	Bn		75 min	62%	**17**
9	Me		15 min	65%	**18**

[a] All reactions was carried out using 4 equiv of olefin, 1 equiv of triflate, and 3 equiv of base. [b] Isolated yields, all selectivities >19:1 (branched/linear).

in favor of the α-vinylation product (Scheme 2). More interesting though was the performance of the *trans*-vinyl tosylate **26** which upon treatment under identical coupling conditions generated the same butadiene product with both a comparable reactivity (55% yield) and high regioselectivity.[20] This result not only suggests that vinyl tosylates are suitable for Heck coupling reactions with electron-rich alkenes but that a cationic mechanism may potentially be operating for the tosylates as well. Whether this successful C−C bond formation can be expanded to the use of aryl tosylates will certainly be an interesting route to pursue considering that tosylating reagents are generally less expensive and more readily accessible than triflating agents. Nevertheless, more suitable ligands for the palladium center would undoubtedly be required to perform the more difficult oxidative addition step.[21] Finally, it should be noted that the corresponding *cis*-vinyl tosylate **27** displayed no reactivity under the conditions studied reflecting possible detrimental sterical interactions under the oxidative addition step.

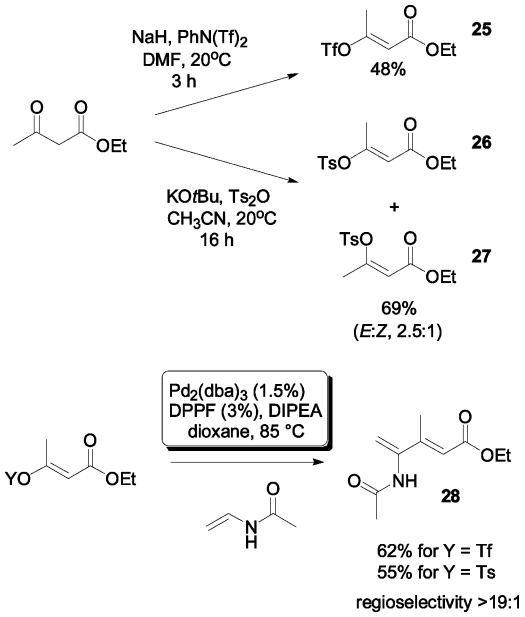
TABLE 4. Heck Coupling *N*-Acyl-*N*-vinylamines and Aryl Triflates[a]



Entry	R	Ar	Time	Yield[b]	Compound nr.
1	Me		45 min	92%	**19**
2	Me		60 min	90%	**20**
3	Me		60 min	77%	**21**
4	CH_2OMe		75 min	53%	**22**
5	OPr		60 min	86%	**23**
6			60 min	68%[c]	**24**

[a] All reactions was carried out using 4 equiv of olefin, 1 equiv of triflate, and 3 equiv of base. [b] Isolated yields, all selectivities >19:1 (branched/linear). [c] Both double bonds hydrogenated.

SCHEME 3



Conclusion

We have successfully developed standard reaction conditions for the Heck coupling of non-*N*-alkylated *N*-acyl-*N*-vinylamines with aryl triflates providing access to *N*-acyl-α-arylvinylamines in good yields and with regioselectivities attaining >19:1. Subsequent acidic hydrolysis or in situ hydrogenation with Wilkinson's catalyst allowed for the preparation of the corresponding

(20) For examples on the use of vinyl and aryl tosylates in palladium(0)-catalyzed coupling reactions, as well as oxidative addition studies, see: (a) Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1998**, *120*, 7369. (b) Fu, X.; Zhang, S.; Yin, J.; McAllister, T. L.; Jiang, S. A.; Tann, C.-H.; Thiruvengadam, T. K.; Zhang, F. *Tetrahedron Lett.* **2002**, *43*, 573. (c) Roy, A. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 8704. (d) Roy, A. H.; Hartwig, J. F. *Organometallics* **2004**, *23*, 194. (e) Klapars, A.; Campos, K. R.; Chen, C.-y.; Volante, R. P. *Org. Lett.* **2005**, *7*, 1185.

(21) Not unexpectedly, aryl tosylates were not reactive to the coupling conditions developed.

methyl ketones and the *N*-acyl derivative of benzylic amines. Extrapolation of these Heck reactions to a vinyl triflate and tosylate proved successful in both cases in terms of coupling yields and regiocontrol. The latter case suggests that vinyl tosylates also couple via a cationic mechanism as demonstrated for aryl and vinyl triflates. Further work is now ongoing to apply this Heck coupling reaction with aryl tosylates, in addition to its exploitation as a key step for the synthesis of natural products with pharmaceutically interesting activities.

Experimental Section

General Procedure for Heck Coupling. The olefin (4 equiv), aryl triflate (1 equiv), DIPEA (3 equiv), and DPPF (0.03 equiv) were dissolved in dioxane (3 mL). $Pd_2(dba)_3$ (0.015 equiv) was then added, and the sample vial was fitted with a Teflon-sealed screwcap and removed from the glovebox. The reaction mixture was heated for the time stated for each product at 85 °C. The reaction was monitored by TLC. Saturated aqueous $NaHCO_3$ was added, and the aqueous phase was extracted with ethyl acetate (3 times). The combined organic phases were dried over $MgSO_4$. After concentration in vacuo, the crude product were purified by column chromatography.

***N*-(1-Naphth-2-ylvinyl)acetamide (10).**[22] 2-Naphthyl triflate (92.4 mg, 0.335 mmol), *N*-vinylacetamide (123 mg, 1.45 mmol), DIPEA (0.190 mL, 1.09 mmol), DPPF (6.0 mg, 0.011 mmol), and $Pd_2(dba)_3$ (4.9 mg, 0.0054 mmol) were reacted for 1 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:9) as eluent. This yielded a brown solid which was recrystallized in ethyl acetate/pentane. This afforded 54 mg of the title compound (77% yield) as off-white crystals: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 8.07 (bs, 1H), 7.96 (s, 1H), 7.92−7.86 (m, 3H), 7.61 (dd, 1H, J = 8.8, 2 Hz), 7.55−7.50 (m, 2H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 170.7, 142.6, 136.4, 134.2, 134.1, 129.1, 129.0, 128.5, 127.5, 127.4, 126.0, 125.4, 103.7, 24.2; HRMS $C_{14}H_{13}ON$ [M + Na^+] calcd 234.0895, found 234.0884.

***N*-[1-(4-Acetylphenyl)vinyl]acetamide (11).**[23] *N*-Vinylacetamide (30 mg, 0.36 mmol), 4-acetylphenyl triflate (194 mg, 0.742 mmol), DIPEA (0.094 mL, 0.54 mmol), DPPF (6.0 mg, 0.011 mmol), and $Pd_2(dba)_3$ (5.0 mg, 0.0054 mmol) were reacted for 105 min. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:4) as eluent. This afforded 65 mg of the title compound (89% yield) as an orange solid: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 8.03 (bs, 1H), 7.92 (d, 2H, J = 8.8 Hz), 7.55 (d, 2H, J = 8.8 Hz), 5.64 (s, 1H), 5.15 (s, 1H), 2.56 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 198.4, 170.4, 143.2, 142.0, 137.8, 129.2(2C), 127.2(2C), 105.1, 27.0, 24.0; HRMS $C_{12}H_{14}O_2N$ [M + Na^+] calcd 226.0844, found 226.0848.

***N*-[1-(4-Cyanophenyl)vinyl]acetamide (12).**[23] *N*-Vinylacetamide (50 mg, 0.56 mmol), 4-cyanophenyl triflate (221 mg, 0.881 mmol), DIPEA (0.154 mL, 0.881 mmol), DPPF (9.8 mg, 0.018 mmol), and $Pd_2(dba)_3$ (8.0 mg, 0.0088 mmol) were reacted for 1 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (3:2) as eluent. This afforded 88 mg of the title compound (81% yield) as bright yellow crystals: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 7.91 (bs, 1H), 7.66−7.63 (m, 2H), 7.54−7.52 (m, 2H), 5.55 (bs, 1H), 5.10 (bs, 1H), 1.96 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 170.4, 143.4, 141.7, 133.2(2C), 127.9(2C), 119.6, 112.4, 106.2, 23.9; HRMS $C_{11}H_{10}ON_2$ [M + Na^+] calcd 209.0691, found 209.0694.

***N*-[1-(4-Chlorophenyl)vinyl]acetamide (13).**[24] *N*-Vinylacetamide (50 mg, 0.59 mmol), 4-chlorophenyl triflate (230 mg, 0.881 mmol), DIPEA (0.154 mL, 0.881 mmol), DPPF (9.8 mg, 0.018 mmol), and $Pd_2(dba)_3$ (8.0 mg, 0.0088 mmol) were reacted for 1 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:9) as eluent. This afforded 90 mg of the title compound (79% yield) as a colorless solid: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 7.92 (bs, 1H), 7.44−7.41 (m, 2H), 7.37−7.34 (m, 2H), 5.59 (bs, 1H), 5.03 (bs, 1H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 170.4, 141.8, 137.8, 134.6, 129.3(2C), 128.8(2C), 103.7, 24.1; HRMS $C_{10}H_{10}ONCl$ [M + Na^+] calcd 218.0349, found 218.0355.

***N*-(1-Biphenyl-4-ylvinyl)acetamide (14).**[22] *N*-Vinylacetamide (50 mg, 0.59 mmol), biphenyl-4-yl triflate (226 mg, 0.881 mmol), DIPEA (0.154 mL, 0.881 mmol), DPPF (9.8 mg, 0.018 mmol), and $Pd_2(dba)_3$ (8.0 mg, 0.0088 mmol) were reacted for 1 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:9) as eluent. This afforded 101 mg of the title compound (72% yield) as colorless crystals: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 7.81 (bs, 1H), 7.71−7.66 (m, 4H), 7.59−7.56 (m, 2H), 7.52−7.47 (m, 2H), 7.43−7.38 (m, 1H), 5.63 (bs, 1H), 5.13 (bs, 1H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN + 5% DMSO-d_6) δ (ppm) 170.4, 142.5, 141.5, 141.0, 138.3, 129.9(2C), 128.5, 127.8(2C), 127.72-(2C), 127.54(2C), 103.0, 24.2; HRMS $C_{16}H_{15}ON$ [M + Na^+] calcd 260.1051, found 260.1056.

***N*-[1-(7-Methoxynaphthalen-2-yl)vinyl]acetamide (15).** *N*-Vinylacetamide (50 mg, 0.59 mmol), 7-methoxy-2-naphthyl triflate (270 mg, 0.881 mmol), DIPEA (0.154 mL, 0.881 mmol), DPPF (9.8 mg, 0.018 mmol), and $Pd_2(dba)_3$ (8.0 mg, 0.0088 mmol) were reacted for 1 h 15 min. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2/pentane (1:8:1) as eluent. This afforded 106 mg of the title compound (75% yield) as off-white crystals: mp 139.2−141.0 °C; ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 7.90 (bs, 1H), 7.85 (bs, 1H), 7.79−7.76 (m, 2H), 7.44 (dd, 1H, J = 8.8, 2.0 Hz), 7.27 (d, 1H, J = 2.8 Hz), 7.15 (dd, 1H, J = 8.8, 2.4 HZ), 5.72 (bs, 1H), 5.16 (bs, 1H), 3.90 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 170.3, 159.2, 142.8, 137.1, 135.5, 130.0, 129.7, 128.7, 125.0 123.1, 120.0, 107.2, 103.2, 56.0, 24.3; HRMS $C_{15}H_{15}O_2N$ [M + Na^+] calcd 264.1000, found 264.1000.

***N*-(1-Phenylvinyl)acetamide (16).**[22] *N*-Vinylacetamide (85 mg, 1.0 mmol), phenyl triflate (339 mg, 1.50 mmol), DIPEA (0.261 mL, 1.50 mmol), DPPF (17 mg, 0.031 mmol), and $Pd_2(dba)_3$ (14 mg, 0.015 mmol) were reacted for 1 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2/pentane (1:6:3) as eluent. This afforded 113 mg of the title compound (70% yield) as a brown solid: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 7.805 (bs, 1H), 7.48−7.45 (m, 2H), 7.40−7.35 (m, 3H), 5.65 (bs, 1H), 5.02 (bs, 1H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 170.3, 142.8, 139.2, 129.5, 129.4 (2C), 127.2(2C), 102.6, 24.2; HRMS $C_{10}H_{11}ON$ [M + Na^+] calcd 184.0738, found 184.0732.

***N*-(1-Naphthalen-2-yl-vinyl)-2-phenylacetamide (17).** *N*-Vinyl-2-phenylacetamide (30 mg, 0.19 mmol), 2-naphthyl triflate (77 mg, 0.28 mmol), DIPEA (0.049 mL, 0.28 mmol), DPPF (3.1 mg, 0.0056 mmol), and $Pd_2(dba)_3$ (2.5 mg, 0.0028 mmol) were reacted for 75 min. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2/pentane (1:2:7) as eluent. This afforded 33 mg of the title compound (62% yield) as off-white crystals: mp 114.2−115.8 °C; ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 7.97 (bs, 1H), 7.89−7.83 (m, 4H), 7.56 (dd, 1H, J = 8.8, 1.6 Hz), 7.53−7.50 (m, 2H), 7.34−7.28 (m, 5H), 5.73 (s, 1H), 5.23 (s, 1H), 3.68 (s, 2H); ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 171.1, 142.4, 136.9, 136.3, 134.2, 134,1, 130.4, 129.6, 129.1, 129.0, 128.5, 127.9, 127.6, 127.5, 125.8, 125.3, 104.0, 44.6; HRMS $C_{20}H_{17}ON$ [M + Na^+] calcd 310.1208, found 310.1210.

***N*-(1-(3-Dimethylaminophenyl)vinyl)acetamide (18).** *N*-Vinylacetamide (50 mg, 0.59 mmol), (3-dimethylamino)-phenyl triflate (237 mg, 0.881 mmol), DIPEA (0.154 mL, 0.881 mmol), DPPF (9.8 mg, 0.018 mmol), and $Pd_2(dba)_3$ (8.1 mg, 0.0089 mmol) were reacted for 15 min. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:4) as eluent. This afforded 78 mg of the title compound (65% yield) as a colorless solid: mp 133.0−135.4 °C;^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 7.69 (bs, 1H), 7.19 (t, 1H, J = 8.0 Hz), 6.80−6.72 (m, 3H), 5.68 (bs, 1H), 4.98 (bs,

1H), 2.94 (s, 6H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 170.3, 151.9, 143.5, 140.2, 130.0, 115.4, 113.7, 111.2, 101.3, 40.8, 24.4; HRMS $C_{10}H_{11}ON$ [M + H^+] calcd 205.1341, found 205.1344.

General Procedure for Heck Coupling Followed by Hydrogenation. The olefin (4 equiv), aryl triflate (1 equiv), DIPEA (3 equiv), and DPPF (0.03 equiv) were dissolved in dioxane (3 mL). $Pd_2(dba)_3$ (0.015 equiv) was then added, and the sample vial was fitted with a Teflon-sealed screwcap and removed from the glovebox. The reaction mixture was heated for the time stated for each product (see the Supporting Information) at 85 °C. The reaction was monitored by TLC. After completion of the Heck coupling, the reaction mixture were transferred to a round-bottomed flask, and 3 mL of dry ethanol was added. $Rh(PPh_3)_3Cl$ (0.05 equiv) was added, and the flask was sealed with a rubber septum. A balloon filled with H_2(g) was connected to the system, and the reaction was left at 20 °C for the time stated for the individual products. Saturated aqueous NH_4Cl was added, and the aqueous phase was extracted with ethyl acetate (3 times). The combined organic phases were dried over $MgSO_4$. After concentration in vacuo, the crude products were purified by column chromatography.

***N*-(1-Naphthalen-2-ylethyl)acetamide (19).**[25] 2-Naphthyl triflate (100 mg, 0.362 mmol), *N*-vinylacetamide (123 mg, 1.45 mmol), DIPEA (0.190 mL, 1.09 mmol), DPPF (6.0 mg, 0.011 mmol), and $Pd_2(dba)_3$ (4.9 mg, 0.0054 mmol) were reacted for 45 min. After transfer of the reaction mixture, $Rh(PPh_3)_3Cl$ (16.7 mg, 0.0181 mmol) was added. The reaction time was 3 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:1) as eluent. This afforded 71 mg of the title compound (92% yield) as a colorless oil. Yield corrected for contamination with minor amounts of triphenylphosphine oxide: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72−7.69 (m, 3H), 7.64 (bs, 1H), 7.38−7.32 (m, 3H), 5.93 (bd, 1H, J = 5.6 Hz), 5.23−5.15 (m, 1H) 1.89 (s, 3H), 1.47 (d, 3H, J = 6.8); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 169.3, 140.7, 133.4, 132.8, 128.6, 128.0, 127.7, 126.3, 126.0, 124.9, 124.7, 49.0, 23.6, 21.8; HRMS $C_{14}H_{15}ON$ [M + Na^+] calcd 236.1051, found 236.1079.

***N*-[1-(4-Acetylphenyl)ethyl]acetamide (20).**[26] 4-Acetylphenyl triflate (102 mg, 0.381 mmol), *N*-vinylacetamide (123 mg, 1.45 mmol), DIPEA (0.190 mL, 1.09 mmol), DPPF (6.0 mg, 0.011 mmol), and $Pd_2(dba)_3$ (4.9 mg, 0.0054 mmol) were reacted for 60 min. After transfer of the reaction mixture, $Rh(PPh_3)_3$-Cl (16.7 mg, 0.0181 mmol) was added. The reaction time was 6 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:1) as eluent. This afforded 67 mg of the title compound (90% yield) as an off-white solid. Yield corrected for contamination with minor amounts of triphenylphosphine oxide: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.92 (d, 2H, J = 8.4 Hz), 7.39 (d, 2H, J = 8.4 Hz), 5.84 (bd, 1H, J = 6 Hz), 5.19−5.12 (m, 1H), 2.58 (s, 3H), 2.00 (s, 3H), 1.49 (d, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 197.8, 169.4, 148.8, 136.3, 128.9(2C), 126.4-(2C), 48.8, 26.8, 23.5, 21.9; HRMS $C_{12}H_{15}O_2N$ [M + Na^+] calcd 228.1000, found 228.0994.

***N*-(1-Phenylethyl)acetamide (21).**[27] *N*-Vinylacetamide (85 mg, 1.0 mmol), phenyl triflate (339 mg, 1.50 mmol), DIPEA (0.261 mL, 1.50 mmol), DPPF (17 mg, 0.031 mmol), and Pd_2-$(dba)_3$ (14 mg, 0.015 mmol) were reacted for 1 h. After transfer of the reaction mixture, $Rh(PPh_3)_3Cl$ (23.0 mg, 0.05 mmol) was added. The reaction was left overnight. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:1) as eluent. This afforded 149 mg of the title compound (77% yield) as a light brown solid. Yield corrected for contamination with minor amounts of triphenylphosphine oxide: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 7.35−7.30 (m, 3H), 7.25−7.21 (m, 2H), 6.81 (bs, 1H), 4.98−4.90 (m, 1H), 1.87 (s, 3H), 1.38 (d, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 169.8, 145.9, 129.4, 127.8, 126.9, 49.6, 23.1, 22.8; HRMS $C_{10}H_{13}ON$ [M + Na^+] calcd 186.0895, found 186.0888.

***N*-(1-Naphthalen-2-ylethyl)-2-methoxyacetamide (22).**[28] 2-Naphthyl triflate (100 mg, 0.362 mmol), *N*-vinyl-2-methoxyacetamide (144 mg, 1.45 mmol), DIPEA (0.190 mL, 1.09 mmol), DPPF (6.0 mg, 0.011 mmol), and $Pd_2(dba)_3$ (4.9 mg, 0.0054 mmol) were reacted for 75 min. After transfer of the reaction mixture, $Rh(PPh_3)_3Cl$ (16.7 mg, 0.0181 mmol) was added. The reaction was left overnight. The reaction was not finished, and the mixture was filtered through a silica plug with ethyl acetate. After concentration in vacuo, 3 mL of absolute ethanol and $Rh(PPh_3)_3Cl$ (16.7 mg, 0.0181 mmol) was added. The reaction was left overnight under an atmosphere of hydrogen. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:4) as eluent. This afforded 47 mg of the title compound (53% yield) as an off-white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.84−7.81 (m, 3H), 7.77 (s, 1H), 7.50−7.44 (m, 3H), 6.82 (bd, 1H, J = 6 Hz), 5.39−5.32 (m, 1H), 3.95 (d, 1H, J = 16.0 Hz), 3.89 (d, 1H, J = 16.0 Hz), 3.41 (s, 2H), 1.62 (d, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 168.7, 140.4, 133.5, 132.9, 128.7, 128.0, 127.7, 126.4, 126.0, 124.8, 124.7, 72.1, 59.3, 48.2, 21.9; HRMS $C_{15}H_{17}O_2N$ [M + Na^+] calcd 266.1157, found 266.1163.

(1-Naphthalen-2-ylethyl)carbamic Acid Propyl Ester (23). 2-Naphthyl triflate (100 mg, 0.362 mmol), vinylcarbamic acid propyl ester (94 mg, 0.72 mmol), DIPEA (0.095 mL, 0.54 mmol), DPPF (6.0 mg, 0.011 mmol), and $Pd_2(dba)_3$ (4.9 mg, 0.0054 mmol) were reacted for 1 h. After transfer of the reaction mixture, $Rh(PPh_3)_3Cl$ (16.7 mg, 0.0181 mmol) was added. The reaction was left overnight. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2/pentane (1:6:13) as eluent. This afforded 80 mg of the title compound (86% yield) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.83−7.80 (m, 3H), 7.75 (s, 1H), 7.48−7.43 (m, 3H), 5.05−4.94 (m, 2H), 4.92−3−90 (m, 2H), 1.68−1.55 (m, 5H), 0.921 (t, 3H, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 156.2, 141.4, 133.7, 133.0, 128.6, 128.0, 127.8, 126.3, 125.9, 124.6, 124.5, 66.73, 51.0, 22.6, 22.5, 10.3; HRMS $C_{16}H_{19}O_2N$ [M + Na^+] calcd 280.1313, found 280.1314.

***N*-(1-Naphthalen-2-ylethyl)-3-phenylpropionamide (24).** 2-Naphthyl triflate (50 mg, 0.18 mmol), *N*-vinyl-*trans*-cinnamide (63 mg, 0.36 mmol), DIPEA (0.047 mL, 0.27 mmol), DPPF (3.0 mg, 0.054 mmol), and $Pd_2(dba)_3$ (2.5 mg, 0.0027 mmol) were reacted for 1 h. After transfer of the reaction mixture, $Rh(PPh_3)_3Cl$ (8.3 mg, 0.0090 mmol) was added. The reaction was left overnight. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2/pentane (1:6:3) as eluent. This afforded 37 mg of the title compound (68% yield) as a colorless solid: mp 109.9−112.0 °C; ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 7.86−7.81 (m, 3H), 7.71 (s, 1H) 7.51−7.45 (m, 2H), 7.39 (dd, 1H, J = 8.4, 1.6 Hz), 7.27−7.16 (m, 5H), 6.84 (bd, 1H, J = 5.6 Hz), 5.15−5.08 (m, 1H), 2.89 (t, 2H, J = 7.2 Hz), 2.48 (t, 2H, J = 7.6 Hz), 1.43 (d, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 172.0, 143.2, 142.5, 134.3, 133.5, 129.4, 129.3, 129.0, 128.7, 128.5, 127.1, 127.0, 126.7, 125.9, 125.0, 49.6, 38.4, 32.3, 22.5; HRMS $C_{21}H_{21}ON$ [M + Na^+] calcd 326.1521, found 326.1521.

(*E*)-3-[[(Trifluoromethyl)sulfonyl]oxy]-2-butenoic Acid Ethyl Ester (25).[19] Ethyl acetoacetate (0.253 mL, 3 mmol) in DMF (2 mL) was added dropwise to a mixture of sodium hydride (72 mg, 3.0 mmol) in DMF (2 mL). The reaction mixture was stirred for 10 min at 20 °C. *N*-Phenyltrifluoromethanesulfonimide (1.07 g, 3.00 mmol) was added, and the reaction was allowed to stir for an additional 3 h. The crude mixture was diluted with 60 mL of ether, and the organic phase was washed with saturated aqueous NH_4Cl, H_2O, and brine. The organic phase was dried over $MgSO_4$. After concentration in vacuo, the crude product was purified by flash chromatography on silica gel using CH_2Cl_2/pentane (1:4) as eluent. This afforded 252 mg of the title compound (48% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.94 (s,

1H), 4.21 (q, 2H, $J = 7.2$ Hz), 2.50 (s, 3H), 1.29 (t, 3H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 164.3, 162.1, 118.9 (q, 1C, $J = 318.3$ Hz), 113.5, 61.3, 18.5, 14.2.

Ethyl (*E*)-3-(*p*-Toluenesulfonoxy)-2-butenoate (26).[29] Ethyl acetoacetate (0.324 mL, 2.56 mmol) in acetonitrile (5 mL) was added dropwise to a mixture of potassium *tert*-butoxide (0.315 g, 2.81 mmol) in acetonitrile (15 mL) at 20 °C. The reaction mixture was stirred for 30 min. Tosyl anhydride (1.00 g, 3.07 mmol) was added, and the reaction mixture was stirred for an additional 16 h. The reaction mixture was concentrated in vacuo, and 20 mL of water was added, after which the aqueous phase was extracted with ether (3 times). The combined organic phases were dried over $MgSO_4$. After concentration in vacuo, the crude product was purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2/pentane (1:4:15) as eluent. The *E*- and *Z*-isomers was separated on the column. This afforded 358 mg of the title compound (49% yield) and 144 mg (20% yield) of the *Z*-isomer as colorless oils: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.81 (d, 2H, $J = 8.4$ Hz), 7.36 (d, 2H, $J = 8.4$ Hz), 5.70 (s, 1H), 4.13 (q, 2H, $J = 7.2$ Hz), 2.46 (s, 3H), 2.26 (s, 3H), 1.25 (t, 3H, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 165.5, 162.4, 145.9, 133.1, 130.1(2C), 128.3(2C), 111.1, 60.6, 21.8, 18.7, 14.2; HRMS $C_{13}H_{16}O_5S$ [M + Na^+] calcd 307.0616, found 307.0616.

***Z*-Isomer (27):**[30] ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.89 (d, 2H, $J = 8.4$ Hz), 7.35 (d, 2H, $J = 8.4$ Hz), 5.48 (s, 1H), 4.04 (q, 2H, $J = 7.1$ Hz), 2.44 (s, 3H), 2.10 (s, 3H), 1.19 (t, 3H, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 163.0, 156.3, 145.5, 133.6, 129.8(2C), 128.5(2C), 110.9, 60.4, 21.8, 21.7, 14.2; HRMS $C_{13}H_{16}O_5S$ [M + Na^+] calcd 307.0616, found 307.0626.

(*E*)-Ethyl-4-acetamido-3-methyl-2,4-pentadienoate (28) from Tosylate Coupling. Ethyl (*E*)-3-(*p*-toluenesulfonoxy)-2-butenoate (150 mg, 0.53 mmol), *N*-vinylacetamide (0.040 mL, 0.35 mmol), DIPEA (69 mg, 0.53 mmol), DPPF (5.8 mg, 0.011 mmol), and $Pd_2(dba)_3$ (4.8 mg, 0.0053 mmol) were heated to 85 °C for 5 h. The crude reaction mixture was concentrated directly onto silica gel and purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:4) as eluent. This afforded 38 mg of the title compound (55% yield) as an off-white amorphous solid: ^{1}H NMR (400 MHz, CD_3CN) δ (ppm) 7.63 (bs, 1H), 5.93 (bs, 1H), 5.42 (bs, 1H), 5.17 (bs, 1H), 4.11 (q, 2H, $J = 7.2$ Hz), 2.21 (s, 3H), 1.95 (s, 3H), 1.22 (t, 3H, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CD_3CN) 170.0, 167.5, 152.2, 144.0, 117.4, 108.5, 60.8, 23.8, 16.1, 14.6; HRMS $C_{10}H_{15}O_3N$ [M + Na^+] calcd 220.0950, found 220.0956.

(*E*)-Ethyl-4-acetamido-3-methyl-2,4-pentadienoate (28) from Triflate Coupling. (*E*)-3-[[(Trifluoromethyl)sulfonyl]-oxy]-2-butenoic acid ethyl ester (150 mg, 0.57 mmol), *N*-vinylacetamide (41 mg, 0.48 mmol), DIPEA (124, 0.72 mmol), DPPF (7.9 mg, 0.014 mmol), and $Pd_2(dba)_3$ (6.5 mg, 0.0072 mmol) were heated to 85 °C for 3 h. The crude reaction mixture was concentrated directly onto silica gel and purified by flash chromatography on silica gel using ethyl acetate/CH_2Cl_2 (1:4) as eluent. This afforded 59 mg of the title compound (62% yield) as a off-white solid.

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Supporting Information Available: Experimental procedures for (a) the synthesis of the *N*-acyl-*N*-vinylamines and (b) the Heck coupling reactions followed by acidic hydrolysis. ^{1}H NMR and ^{13}C NMR spectra for the *N*-acyl-*N*-vinylamines and coupling products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) Zhu, G.; Zhang, X. *J. Org. Chem.* **1998,** *63, 25*, 9590.
(23) Harrison, P.; Meek, G. *Tetrahedron Lett.* **2004**, *45*, *50*, 9277.
(24) Berg, M.; Haak, R. M.; Minnaard, A. J.; Vries, A. H. M. de; Vries, J. G. de; Feringa, B. L. *Adv. Synth. Catal. 344*, *9*, **2002**, 1003.
(25) Reetz, M. T.; Mehler, G.; Meiswinkel, A. *Tetrahedron: Asymmetry* **2004**, *15*, *14*, 2165.
(26) Hanano, Y.; Adachi, K.; Aoki, Y.; Morimoto, H.; Naka, Y.; Hisadome, M.; Fukuda, T.; Sumichika, H. *Bioorg. Med. Chem. Lett.* **2000**, *10*, *9*, 881.
(27) Lopez-Serrano, P.; Jongejan, J. A.; Rantwijk, F. van.; Sheldon, R. A. *Tetrahedron: Asymmetry.* **2001**, *12*, *2*, 219.
(28) Youshko, M. I.; Rantwijk, van F.; Sheldon, R. A. *Tetrahedron: Asymmetry* **2001**, *12*, *23*, 3267.
(29) Nakaminami, G. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1629.
(30) Jalander, L.; Mattinen, J.; Oksanene, L.; Rosling, A. *Synth. Commun.* **1990**, *20*, *6*, 881.