Palladium-Catalyzed Sequential Alkylation−Alkenylation Reactions and Their Application to the Synthesis of Fused Aromatic Rings

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Received July 19, 2001

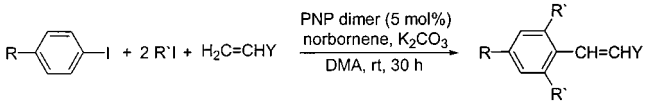
The synthesis of fused aromatic carbocycles from aryl iodides and difunctional acceptors is outlined. This methodology is based on a palladium-catalyzed aromatic substitution followed by an intramolecular Heck sequence. Under the optimized conditions ($Pd(OAc)_2$ (10 mol %), tri-2-furylphosphine (20−30 mol %), norbornene (2 equiv), Cs_2CO_3 (2 equiv), CH_3CN, reflux), bromoenoates react with aryl iodides bearing numerous substituents (F, Cl, CF_3, Me, etc.). The expanded description of our initial work as well as the use of polysubstituted aryl iodides is described.

Introduction

The ability to catalyze multistep processes is one of the most useful and interesting features of transition metal reactivity,[1]and by fine-tuning the ligands around the metal, reactivity can be controlled and even directed in a logical manner.[2,3] A particularly interesting system that combines multistep processes with selective aromatic substitution[4,5] was described by Catellani.[6] In this case, a palladium-catalyzed cascade allows the creation of three new carbon−carbon bonds in a one-pot process (Scheme 1). This methodology is based on a sequential double aromatic substitution and an intermolecular Heck reaction leading to *ortho,ortho′*-disubstituted vinylarenes **1**.

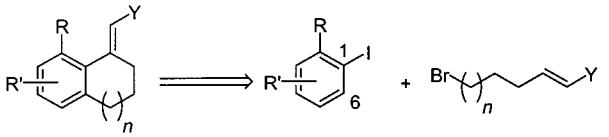
We sought to modify this sequence by using a difunctional acceptor **3** so that an intramolecular Heck reaction can follow the *ortho*-alkylation leading to fused aromatic compounds **2** (Scheme 2). This route is interesting since many bioactive molecules contain a substituted tetrahydronaphthalene core.[7−9] We have recently described

Scheme 1



PNP dimer = *cis,exo*-2-phenylnorbornyl palladium chloride

Scheme 2



our preliminary results in this area[10]and now report an expanded description of our studies including the use of functionalized aryl iodides for the synthesis of fused aromatic six- and seven-membered carbocycles.

Results and Discussion

Optimization. Our initial studies were carried out with iodobenzene (**4**) and ethyl (*E*)-6-bromohex-2-enoate (**5**) using the conditions described by Catellani[6] (i.e., the PNP dimer as catalyst[11] in DMA). The desired six-membered ring compound **6** was obtained in up to 33% yield as a single stereoisomer (Scheme 3). The most serious problem was the variability of the yield, which could be as low as 7% depending on the batch of catalyst. It was necessary to find improved conditions, and toward this end ligand effects as well as different palladium sources and solvents were examined.

(1) (a) Wender, P. A. *Chem. Rev.* **1996**, *96*, 1−2. (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49−92. (c) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115−136. (d) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223−270. (e) Harvey, D. F.; Sigano, D. M. *Chem. Rev.* **1996**, *96*, 271−288. (f) Malacria, M. *Chem. Rev.* **1996**, *96*, 289−306. (g) Negishi, E.-i.; Copéret, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365−394.

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(5) Catellani, M. *Transition Metal Catalysed Reaction*; Murahashi, S.-I.; Davies, S. G., Eds.; Blackwell Science: Oxford, 1999; pp 168−193.

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(10) Lautens, M.; Piguel, S. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 1045−1046.

(11) Horino, H.; Arai, M.; Inoue, N. *Tetrahedron Lett.* **1974**, 674−650.

10.1021/jo0107296 CCC: $20.00
Published on Web 10/27/2001

Scheme 3

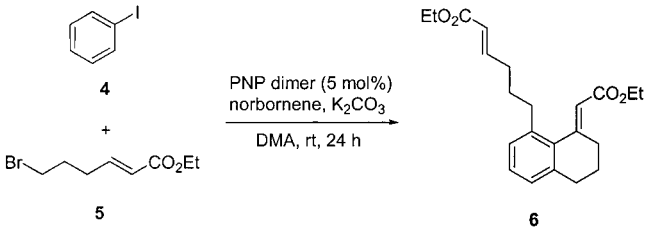
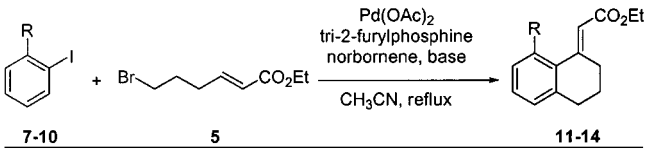


Table 1. Effects of *Ortho*-Substitution and Base



7-10 5 11-14

				yield[a] (%)	
entry	R	aryl iodide	product	K_2CO_3	Cs_2CO_3
1	CH_3	**7**	**11**	85	92
2	CH_2OMe	**8**	**12**	20	35
3	CH_2OTBS	**9**	**13**	41	60
4	OMe	**10**	**14**	29	26

[a] Isolated yield.

Among the combination of palladium sources and ligands examined, $Pd(OAc)_2$/tri-2-furylphosphine[12] proved to be the most encouraging catalytic system since the desired compound **6** was obtained in 24% yield as a single stereoisomer and in reproducible albeit, very low yield. Other systems such as $Pd(PPh_3)_4$, $Pd(dppf)Cl_2$/HgCl, $Pd_2(dba)_3$, $Pd(OAc)_2/PPh_3$, $Pd(OAc)_2/n$-Bu_3P, $Pd(OAc)_2$/tri-*o*-tolylphosphine, and $Pd(OAc)_2/P(OMe)_3$ gave little or none of the expected product.

Using the $Pd(OAc)_2$/tri-2-furylphosphine combination of catalyst/ligand, we then changed other variables (solvent, base) in order to improve the yield. An investigation of the solvent revealed that acetonitrile was the solvent of choice with the yield increasing from 24% in DMA to 43% in MeCN. Other solvents (CH_2Cl_2, benzene, THF) gave only traces of the desired product.

A variety of *ortho*-substituted aryl iodides were reacted under the optimized conditions to determine the scope of the reaction (Table 1). Using $Pd(OAc)_2$ (10 mol %), tri-2-furylphosphine (20 mol %), norbornene (2 equiv), K_2CO_3 (2 equiv), MeCN, reflux, we were able to obtain the desired six-membered carbocycle in moderate to good yield with a variety of *ortho*-substituted aryl iodides. Two new carbon−carbon bonds were formed in a one-pot reaction, and the bicyclic compounds were isolated as exclusively *E*-configured stereoisomers as determined by NOE experiments.

With R = Me (entry 1), the desired product **11** was isolated in 85% yield, whereas R = OMe (entry 4) gave a moderate yield of **14**. Interestingly, going from a methyl ether (entry 2) to a TBS ether protected benzyl alcohol (entry 3) improved the yield from 20 to 41%. This lack of reactivity might be explained by a complexation between the oxygen atom and the palladium center, which inhibits the subsequent steps in the catalytic cycle. We suppose that this phenomenon is minimized in the case of R = CH_2OTBS (entry 3) because of the steric bulk of the silyl group.

(12) Anderson, N. G.; Keay, B. A. *Chem. Rev.* **2001**, *101*, 997−1030.

Other parameters including base or additives[13,14] were then surveyed to further optimize the reaction. We found that using Cs_2CO_3 instead of K_2CO_3 provided the desired product in higher yield. For R = Me (entry 1), the yield increased to 92%. With the protected benzylic alcohol (entries 2 and 3), the yields improved but were still moderate, giving the carbocycles in 35% and 60% for the methyl ether and the TBS ether, respectively. The difference of the reactivity between Cs_2CO_3 and K_2CO_3 might be explained by the better solubility of Cs_2CO_3.[15] Other bases (Et_3N, K_3PO_4) were tried under the same conditions but were found to be less effective.

To complete our optimization studies, the effect of the nature of the Heck acceptor and the halogen on the difunctional acceptor was examined using **7** as the aryl iodide (Table 2). Comparison of the α,β-unsaturated esters **5** (Table 1, entry 1) and **15** (Table 2, entry 1) showed that the bromide gave better yields than the iodide probably because the iodide undergoes a variety of other side reactions.[6c] The geometry of the double bond does not seem to influence the yield since going from the *trans* (Table 1, entry 1) to *cis* enoate (Table 2, entry 2) gave the product in similar yield. The use of menthyl ester **17** or amide **18** gave the desired products **23** and **24** in 81 and 90%, respectively. The use of a Weinreb amide **19** or an acceptor bearing the Evans auxiliary **20** also gave the carbocycle in good yield. By using a cyano group (entry 7) as the acceptor, the bicyclic compound was obtained as a mixture of *cis* and *trans* isomers (2:1 in favor of the *cis* isomer) but in moderate yield. Utilizing a phenyl sulfone or a trimethylsilyl as acceptor group led to unreacted starting material and decomposition, respectively.

A possible mechanism for the formation of fused aromatic carbocycle **11** is shown in Scheme 4 and follows a similar pathway to that proposed by Catellani.[6] The complex **28**, obtained after oxidative addition of **7**, undergoes carbopalladation with norbornene exclusively from the *exo* face[6a,11,16−20] to give complex **29**. Formation of palladacycle **30** occurs[6a,16,21−26] via C−H activation, and subsequent oxidative addition of **5** gives the palladium(IV) complex[6a] **31**, which undergoes a reductive elimination to afford **32**. Expulsion of norbornene[6b] occurs presumably due to steric effects leading to **33** which undergoes an intramolecular Heck reaction to give the desired carbocycle.

Effects of *Ortho*-Substitution and Ring Size. We have extended the reaction to include the formation of seven-membered carbocycles as well as determining the reactivity of other *ortho*-substituted aryl iodides in order to demonstrate the functional group tolerance at this position. The result shown in Table 3 indicates that the scope of the reaction is quite broad since even halogens and heteroatoms are well tolerated.

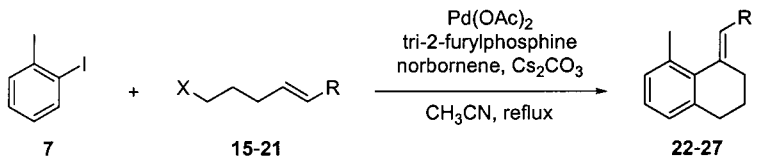
The production of a seven-membered ring using the same aryl iodides presented in Table 1 gave comparable results for all the substituents except with R = OMe

(13) For a recent example of the importance of the choice of base in palladium catalysis, see Viciu, M. S.; Grasa, G. A.; Nolan, S. P. *Organometallics* **2001**, *20*, 3607−3612.

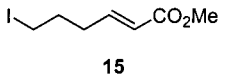
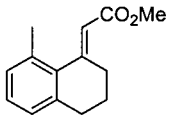
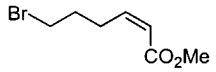
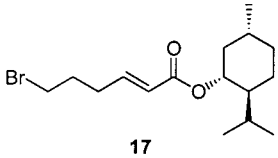
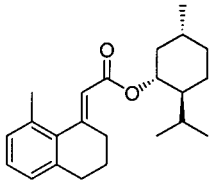
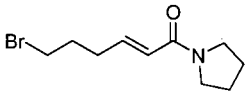
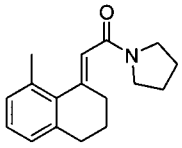
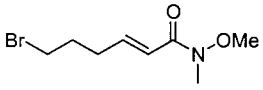
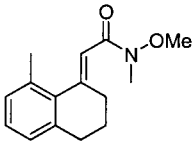
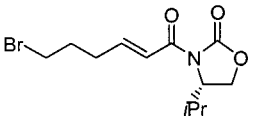
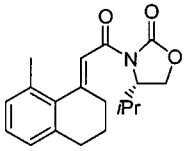
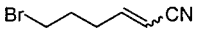
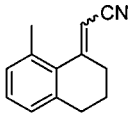
(14) Jeffery, T. *Tetrahedron* **1996**, *52*, 10113−10130, and references therein.

(15) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1144−1157, and references therein.

Table 2. Effect of the Heck Acceptor



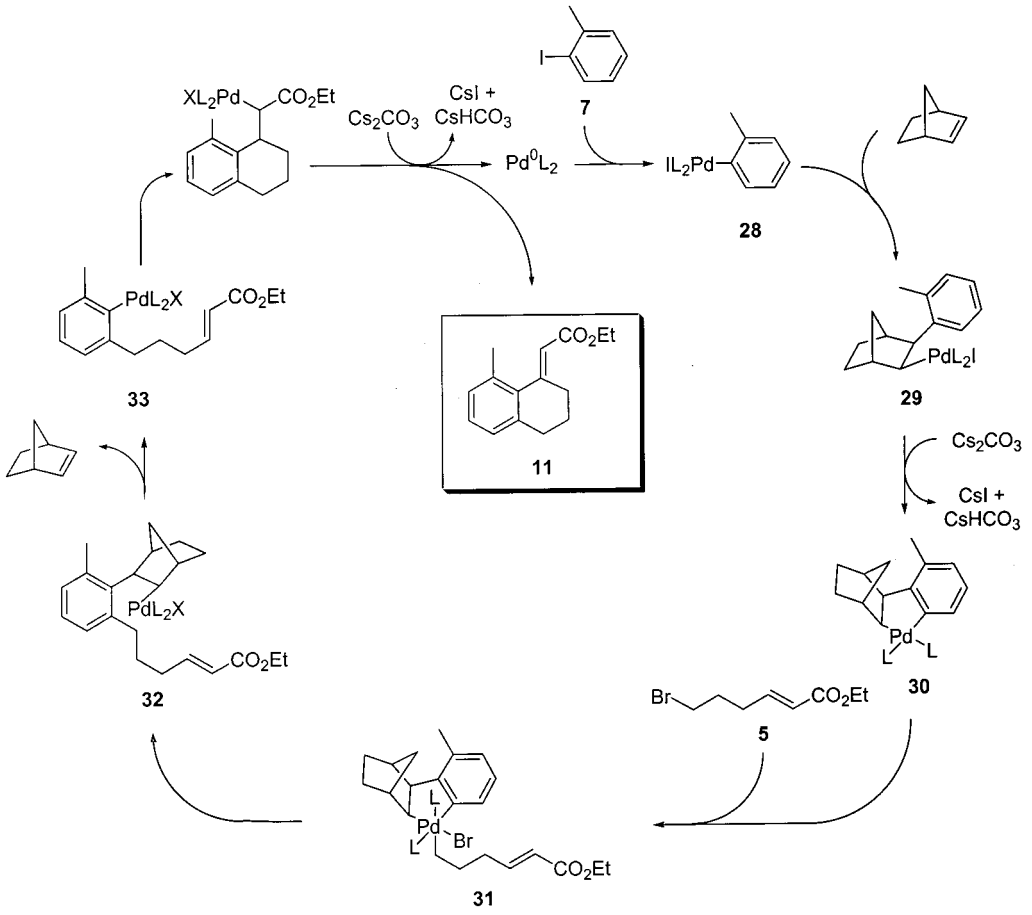
7 15-21 22-27

Entry	Acceptor	Product	Yield[a] (%)
1	 **15**	 **22**	62
2	 **16**		> 80[b]
3	 **17**	 **23**	81
4	 **18**	 **24**	90
5	 **19**	 **25**	84
6	 **20**	 **26**	95
7	 **21**	 **27**	63[c]

[a] Isolated yield. [b] Estimated by NMR spectroscopy. [c] **21** is a mixture of *cis*/*trans* isomer (3.5:1) and **27** is a mixture of *E*/*Z* isomer (2:1).

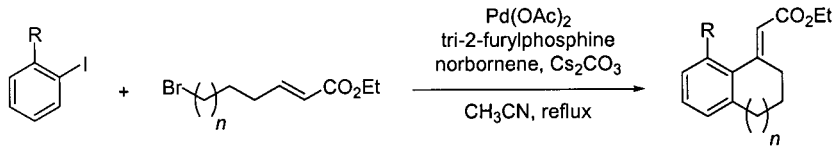
where the desired carbocycle **41** was isolated in much better yield (entry 4). The same trends observed previously for the protected benzylic alcohol also applied here where the TBS ether protected alcohol gave a better yield than the methyl ether (entries 2 and 3). Methyl 2-iodobenzoate gave no desired product whereas 2-iodobenzyl chloride gave only decomposition of the starting material in the six- and seven-membered ring series. The cyclic acetal of 2-iodobenzaldehyde [2-(2-iodophenyl)-5,5-dimethyl-1,3-dioxane] yielded only traces of the desired product. 2-Iodobenzotrifluoride (**34**) reacts to form the six-membered ring **42** in 76% yield but failed to give the desired seven-membered ring. 2-Chloroiodobenzene (**35**) gave the carbocycle **43** in 80% yield, which is of great interest, since it opens the way to the introduction of otherwise incompatible substituents on the aromatic ring. The presence of bromine was not tolerated on the ring since 2-bromoiodobenzene and 1,2-dibromobenzene gave mainly decomposition of the starting material. The presence of a pyrrolidine ring at the *ortho* position (entry 7) had some effect, but **44** was still isolated in 55% yield. Changing the iodide to bromide [2-bromotoluene] or triflate [2-(trifluoromethylsulfonyl)toluene] led to degradation and unreacted starting material, respectively.

Scheme 4



L = olefin, phosphine, CH_3CN

Table 3. Effect of *Ortho* Substitution of the Aryl Iodides



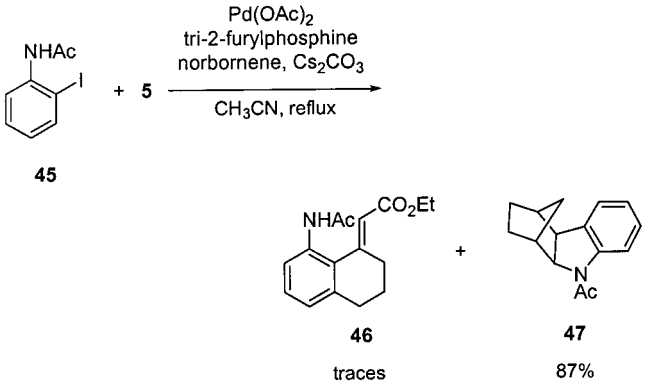
7-10, 34-36 **5**, n = 1; **37**, n = 2 **38-44**

Entry	R	Aryl iodide	n	Product	Yield[a] (%)
1	Me	**7**	2	**38**	83
2	CH_2OMe	**8**	2	**39**	25
3	CH_2OTBS	**9**	2	**40**	47
4	OMe	**10**	2	**41**	93
5	CF_3	**34**	1	**42**	76
6	Cl	**35**	1	**43**	80
7		**36**	1	**44**	55

[a] Isolated yield.

When iodoamide **45** was reacted under the standard conditions, disappearance of the starting material occurred within 10−12 h (eq 1).

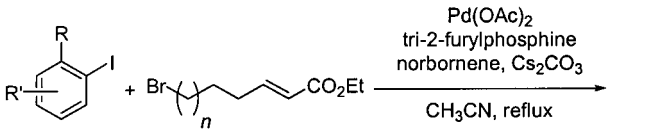
However, only traces of the desired product **46** were observed along with formation of **47** in 87% yield. This compound can be formed if, after carbopalladation of the aryl palladium species onto norbornene, an intramolecular amination occurred instead of the standard palladacycle formation. This reactivity has been observed before and used for the synthesis of fused dihydrofurans and



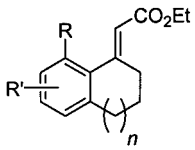
-pyrroles.[27] The use of the tertiary amide [*N*-acetyl-*N*-methyl-2-iodoaniline] also failed to undergo cyclization to form the six or the seven-membered ring and only consumption of the starting material was observed along with traces of the desired product.

Polysubstituted Aryl Iodides. We next investigated the reactivity of polysubstituted aryl iodides (Table 4) and found that many functional groups are tolerated on the aromatic ring including an amide (entry 3), phenyl (entries 4 and 5), methyl (entries 1−3, 6−8, 10), methoxy (entry 10), chlorine (entries 1 and 2, 8−9), and fluorine (entries 6 and 7) with yields ranging from 52 to 90%. Although the presence of an ester at position 2 [methyl 2-iodobenzoate] or 5 [methyl 3-iodo-4-methylbenzoate] is not tolerated, Catellani showed[6a] that its presence did not affect the reaction when it was present at position 4, extending the possibility for further manipulation. It is interesting to note that the type of substituent at position 5 seemed relevant to the success of the reaction. Aryl iodides having a methyl [2-iodo-*p*-xylene], an ester [methyl 3-iodo-4-methylbenzoate], an aldehyde [3-iodo-4,5-dimethoxybenzaldehyde], or a protected aldehyde [2-(3-iodo-4,5-dimethoxyphenyl)-5,5-dimethyl-1,3-dioxane] at this position completely inhibited the annulation although all the starting aryl iodides were consumed. The formation of the palladacycle (e.g., **30**) was postulated[26] to occur via an electrophilic attack of the palladium on the *ortho*-position of the phenyl ring to give a Wheland-type intermediate, which then formed the palladacycle. Therefore, any substituents that destabilize this intermediate may be not tolerated. Although this may explain the lack of reactivity for the ester and the aldehyde, our results cannot exclude steric effects or side reactions for the methyl and the protected aldehyde.[28] Further experiments in order to better understand the reactivity are underway.

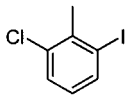
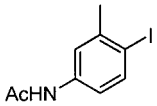
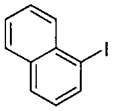
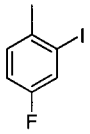
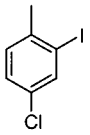
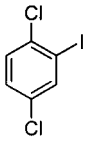
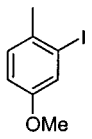
Table 4. Effect of Polysubstituted Aryl Iodides



48-54 **5**, *n* = 1; **37**, *n* = 2



55-64

Entry	Aryl iodide	*n*	Product	Yield[a] (%)
1		1	**55**	86
2	**48**	2	**56**	65
3	 **49**	1	**57**	82
4		1	**58**	90
5	**50**	2	**59**	82
6		1	**60**	72
7	**51**	2	**61**	61
8	 **52**	1	**62**	86
9	 **53**	1	**63**	52
10	 **54**	1	**64**	70

[a] Isolated yield.

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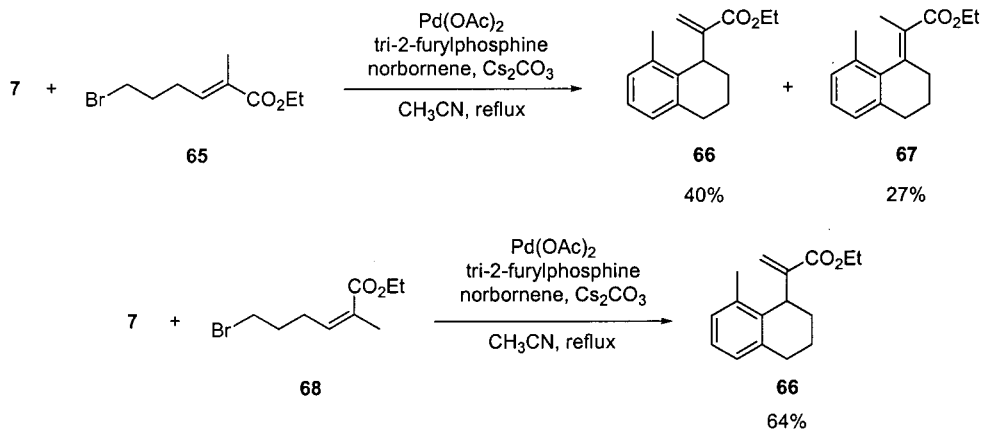
Scheme 5



We also investigated the effect of having a trisubstituted Heck acceptor (Scheme 5). Under the standard conditions, the *E*-isomer **65** reacted with **7** to give a mixture of the external olefin **66** and the internal olefin **67** in 40 and 27% yield, respectively. More interestingly, using the *Z*-isomer **68** under the same conditions led only to the formation of the external olefin **66** in 64% yield. The reasons for this behavior are not fully understood but it appears that diastereomeric palladium complexes undergo β-elimination with different propensities. Further investigation is underway and will be reported in due course.

Conclusion

We have developed a new approach for the synthesis of fused carbocycles, which proceeds by a palladium-catalyzed process based on a sequential aromatic substitution and an intramolecular Heck reaction of substituted aryl iodides. Two new carbon−carbon bonds are formed in one pot. Numerous functional groups are tolerated including amide, amine, protected alcohol, halogen, trifluoromethyl, alkyl, and aryl groups. Substituent at position 5 of the aryl iodide seems to be important for the success of the reaction. Under optimized conditions, we were able to obtain polyfunctionalized six- and seven-membered carbocycles as single stereoisomers. Application of these methods to the synthesis of more complex carbocycles as well as heterocyclic compounds is currently in progress in our laboratory.

Experimental Section

The following includes general experimental procedures, specific details for representative reactions, and isolation and spectroscopic information for illustrative compounds. Specific information for all other new compounds can be found in the Supporting Information. All ^{1}H and ^{13}C NMR spectra were recorded in deuterated chloroform using tetramethylsilane or residual chloroform as internal standard. High-resolution mass spectra were obtained at 70 eV. Aryl iodides were purchased from commercial sources (**4**, **7**, **10**, **34**, **35**, **48**, **50**, **51**, **53**, 2-bromotoluene, 1,2-dibromobenzene, 2-bromoiodobenzene, 2-iodobenzyl chloride, 2-iodo-*p*-xylene, 3-iodo-4,5-dimethoxybenzaldehyde), synthesized using literature procedures (**8**,[29] **45**,[30] 2-(trifluoromethylsulfonyl)toluene,[36] methyl 2-iodobenzoate,[29] *N*-acetyl-*N*-methyl-2-iodoaniline[30]), or prepared as described in the Supporting Information section (**9**, **36**, **49**, **52**, **54**, 2-(2-iodophenyl)-5,5-dimethyl-1,3-dioxane, 2-(3-iodo-4,5-dimethoxyphenyl)-5,5-dimethyl-1,3-dioxane, methyl 3-iodo-4-methylbenzoate). The difunctional acceptors were synthesized using literature procedures (**5**,[31] **37**[31]), or prepared as described in the Supporting Information section (**15**, **16**, **17**, **18**, **19**, **20**, **21**, **65**, **68**).

Cyclization Using Iodobenzene. General Procedure. Ethyl (*E*)-6-[(8*E*)-8-(2-Ethoxy-2-oxoethylidene)-5,6,7,8-tetrahydronaphthalen-1-yl]hex-2-enoate (6). Under inert atmosphere, a flame-dried round-bottom flask equipped with a condenser was charged with iodobenzene (20 μL, 0.179 mmol), **5** (174.6 mg, 0.79 mmol), Cs_2CO_3 (116.7 mg, 0.358 mmol), norbornene (36.2 mg, 0.384 mmol), tri-2-furylphosphine (8.3 mg, 0.035 mmol), $Pd(OAc)_2$ (4.7 mg, 0.021 mmol), and CH_3CN (5 mL). The resulting mixture was heated at 85 °C for 19 h and then quenched by addition of satd NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3×). The organic layers were combined, washed with brine, and dried over $MgSO_4$. The crude product was purified by flash chromatography on silica gel with 1−3% ether in hexane to afford **6** (30 mg, 47%) as a yellow pale oil. IR (neat) ν = 1619, 1654, 1713, 2936 cm^{-1}; ^{1}H NMR δ 1.28 (t, 3H, J = 7.2 Hz), 1.31 (t, 3H, J = 7.2 Hz), 1.76 (m, 4H), 2.21 (q, 2H, J = 7.2 Hz), 2.58 (t, 2H, J = 6.0 Hz), 2.83 (t, 2H, J = 6.0 Hz), 3.13 (dt, 2H, J = 7.2, 2.0 Hz), 4.17 (q, 2H, J = 7.2 Hz), 4.19 (q, 2H, J = 7.2 Hz), 5.80 (dt, 1H, J = 16.0, 1.6 Hz), 5.86 (t, 1H, J = 1.6 Hz), 6.91−7.18 (m, 4H); ^{13}C NMR δ 14.2, 14.3, 21.3, 27.8, 30.0, 30.1, 31.9, 32.3, 59.7, 60.1, 118.0, 121.6, 125.1, 127.9, 128.1, 136.8, 138.5, 141.9, 148.5, 154.8, 166.5, 166.6; HRMS calcd for $C_{22}H_{29}O_4$ 357.2070, found 357.2065.

Cyclization Using *Ortho*-Substituted and Polysubstituted Aryl Iodides. General Procedure. Ethyl (*E*)-(8-Methyl-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethanoate (11). A round-bottom flask equipped with a condenser was charged with Cs_2CO_3 (130 mg, 0.400 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), tri-2-furylphosphine (9.2 mg, 0.040 mmol), and norbornene (37.7 mg, 0.400 mmol). A solution of **5** (88.4 mg, 0.400 mmol) and iodotoluene (25.5 μL, 0.200 mmol) in CH_3CN (2 mL) was added. The resulting mixture was heated at 85 °C for 19 h and then quenched by addition of satd NH_4Cl. The organic layer was separated, and the aqueous layer was

(28) No side products were isolated since only unreacted **5** or **37** along with baseline material was detectable by TLC after workup.

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extracted with Et_2O (3×). The organic layers were combined, washed with brine, and dried over $MgSO_4$. Removal of the solvent gave a crude oil that was purified by flash chromatography using EtOAC/hexane (1:19) as the eluant to yield **11** (42.2 mg, 92%) as a colorless oil. IR (neat) ν = 1615, 1708, 2951 cm^{-1};^{1}H NMR δ = 1.31 (t, 3H, J = 7.2 Hz), 1.70 (m, 2H), 2.47 (s, 3H), 2.60 (t, 2H, J = 6.1 Hz), 3.10 (td, 2H, J = 7.0, 2.0 Hz), 4.20 (q, 2H, J = 7.2 Hz), 5.90 (t, 1H, J = 2.0 Hz), 6.90 (m, 1H), 7.10 (m, 2H); ^{13}C NMR δ 14.3, 21.6, 21.7, 28.2, 30.2, 59.7, 118.2, 125.2, 127.8, 129.5, 134.9, 136.3, 141.8, 154.7, 166.9; HRMS calcd for $C_{15}H_{18}O_2$ 230.1311, found 230.1306.

1′-(1′*R*,2′*S*,5′*R*)-Menthyl-(*E*)-(8-methyl-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethanoate (23). Following the general procedure (using 30 mol % of tri-2-furylphosphine instead of 20 mol %) on a 0.157 mmol scale using **17** and **7**, **23** was isolated as a colorless oil (43.4 mg, 81%) by flash chromatography using Et_2O/hexane (1:15) as eluant. IR (neat) ν = 1162, 1261, 1364, 1703, 2863, 2947 cm^{-1}; ^{1}H NMR δ 0.80 (d, 3H, J = 7.2 Hz), 0.84−2.13 (m, 17H), 2.47 (s, 3H), 2.63 (t, 2H, J = 6.0 Hz), 3.15 (m, 2H), 4.76 (dt, 1H, J = 10.8, 4.5 Hz), 5.91 (t, 1H, J = 1.8 Hz), 6.98 (m, 1H), 7.11 (m, 2H); ^{13}C NMR δ 16.6, 20.7, 21.6, 21.8, 22.1, 23.7, 26.4, 28.3, 30.3, 31.4, 34.3, 41.1, 47.0, 73.4, 118.7, 125.3, 127.8, 129.6, 134.9, 136.4, 141.8, 154.4, 166.5; HRMS calcd for $C_{23}H_{32}O_2$ 340.2402, found 340.2413.

1-[(*E*)-2-(8-Methyl-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethanoyl]pyrrolidine (24). Following the general procedure (using 30 mol % of tri-2-furylphosphine instead of 20 mol %) on a 0.157 mmol scale using **18** and **7**, **24** was isolated as a colorless oil (36.0 mg, 90%) by flash chromatography using toluene/EtOAc (1:2) as eluant. IR (neat) ν = 1135, 1189, 1349, 1550, 1634, 2863, 2939 cm^{-1}; ^{1}H NMR δ 1.79 (m, 2H), 1.92 (m, 4H), 2.48 (s, 3H), 2.64 (t, 2H, J = 6.3 Hz), 3.05 (dt, 2H, J = 6.9, 1.5 Hz), 3.45 (t, 2H, J = 6.6 Hz), 3.56 (t, 2H, J = 6.6 Hz), 6.09 (t, 1H, J = 1.5 Hz), 6.98 (m, 1H), 7.10 (m, 2H); ^{13}C NMR δ 21.6, 22.1, 24.3, 26.2, 27.8, 30.1, 45.5, 46.9, 120.7, 125.3, 127.2, 129.3, 134.3, 137.2, 141.4, 148.2, 166.1; HRMS calcd for $C_{17}H_{21}NO$ 255.1623, found 255.1623.

(*E*)-*N*-Methoxy-*N*-methyl-2-(8-methyl-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethanamide (25). Following the general procedure (using 30 mol % of tri-2-furylphosphine instead of 20 mol %) on a 0.157 mmol scale using **19** and **7**, **25** was isolated as a colorless oil (32.5 mg, 84%) by flash chromatography using EtOAc/hexane (1:1) as eluant. IR (neat) ν = 1178, 1377, 1435, 1642, 2862, 2935 cm^{-1}; ^{1}H NMR δ 1.79 (m, 2H), 2.49 (s, 3H), 2.64 (t, 2H, J = 6.4 Hz), 3.12 (t, 2H, J = 6.8 Hz), 3.26 (s, 3H), 3.67 (s, 3H), 6.39 (br s, 1H), 6.99 (m, 1H), 7.13 (m, 2H); ^{13}C NMR δ 21.6, 22.0, 28.0, 30.2, 61.6, 117.0, 125.3, 127.5, 129.5, 134.6, 137.2, 141.7, 151.7, 153.4, 159.7; HRMS calcd for $C_{15}H_{19}NO_2$ 245.1416, found 245.1411.

(4*S*)-4-Isopropyl-3-[(*E*)-2-(8-methyl-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethanoyl]-1,3-oxazolidin-2-one (26). Following the general procedure (using 30 mol % of tri-2-furylphosphine instead of 20 mol %) on a 0.157 mmol scale using **20** and **7**, **26** was isolated as a colorless oil (46.6 mg, 95%) by flash chromatography using Et_2O/hexane (1:2) as eluant. IR (neat) ν = 1139, 1269, 1383, 1463, 1592, 1672, 1771, 2870, 2954 cm^{-1}; ^{1}H NMR δ 0.93 (m, 4H), 1.78 (m, 2H), 2.45 (m, 1H), 2.54 (s, 3H), 2.63 (m, 2H), 3.16 (m, 2H), 4.25 (m, 2H), 4.54 (m, 1H), 6.98 (m, 1H), 7.13 (m, 2H), 7.35 (t, 1H, J = 2.1 Hz); ^{13}C NMR δ 14.7, 18.0, 21.7, 21.9, 28.5, 29.8, 30.4, 58.5, 63.0, 117.1, 125.2, 128.2, 129.8, 135.7, 136.4, 142.1, 153.9, 157.3, 164.9; HRMS calcd for $C_{19}H_{23}NO_3$ 313.1678, found 313.1672.

(8-Methyl-3,4-dihydronaphthalen-1(2*H*)-ylidene)-ethanenitrile (27). Following the general procedure on a 0.157 mmol scale using **21** and **7**, **27** was isolated as a mixture of isomers that were separable by flash chromatography using Et_2O/hexane (1:2) as eluant. The *E*-isomer was isolated as a colorless oil (6.2 mg, 22%) and the *Z*-isomer as a colorless oil (12.1 mg, 42%). *E*-isomer; IR (neat) ν = 1465, 1602, 2211, 2932 cm^{-1};^{1}H NMR δ 1.90 (m, 2H), 2.45 (s, 3H), 2.74 (t, 2H, J = 6.4 Hz), 2.89 (dt, 2H, J = 7.2, 1.6 Hz), 5.43 (s br, 1H), 7.02 (d, 1H, J = 7.6 Hz), 7.11 (d, 1H, J = 7.6 Hz), 7.18 (d, 1H, J = 7.6 Hz); ^{13}C NMR δ 21.8, 22.0, 30.1, 31.4, 96.6, 117.4, 126.1, 129.0, 129.8, 133.6, 135.1, 140.7, 159.7; HRMS calcd for $C_{15}H_{13}N$ 183.1048, found 183.1044. *Z*-isomer; IR (neat) ν = 1468, 1611, 2214, 2866, 2949, 3056 cm^{-1}. ^{1}H NMR δ 1.85 (m, 2H), 2.49 (s, 3H), 2.61 (m, 4H), 5.45 (t, 1H, J = 1.2 Hz), 7.00 (d, 1H, J = 7.2 Hz), 7.14−7.26 (m, 2H); ^{13}C NMR δ 20.1, 20.6, 29.1, 33.0, 96.0, 117.6, 124.5, 128.8, 128.9, 134.1, 135.0, 140.6, 161.0; HRMS calcd for $C_{15}H_{13}N$ 183.1048, found 183.1047.

Ethyl (*E*)-(4-Methyl-6,7,8,9-tetrahydro-5*H*-benzo[*a*][7]-annulen-5-ylidene)ethanoate (38). Following the general procedure on a 0.157 mmol scale using **37** and **7**, **38** was isolated as a colorless oil (31.7 mg, 83%) by preparative TLC using Et_2O/hexane (1:9) as eluant. IR (neat) ν = 1637, 1715, 2854, 2927, 3063 cm^{-1};^{1}H NMR δ 1.31 (t, 3H, J = 7.2 Hz), 1.56 (m, 1H), 1.89 (m, 3H), 2.03 (m, 1H), 2.25 (s, 3H), 2.61 (m, 1H), 2.74−3.68 (m, 2H), 4.21 (q, 2H, J = 7.2 Hz), 5.69 (s, 1H), 6.94−7.07 (m, 3H); ^{13}C NMR δ 14.2, 20.1, 27.9, 29.5, 31.8, 34.9, 59.7, 118.4, 126.1, 127.1, 128.2, 133.0, 139.5, 143.2, 162.7, 166.4; HRMS calcd for $C_{16}H_{20}O_2$ 244.1470, found 244.1463.

***N*-Acetyl-1,4-methano-1,2,3,4,4a,9b-hexahydrocarbazole (47).** Following the general procedure on a 0.200 mmol scale using **5** and **45**, **47** was isolated as a yellow solid (39.7 mg, 87%) by flash chromatography using EtOAc/hexane (1:4) as eluant. IR (neat) ν = 1392, 1482, 1660, 2961 cm^{-1}; ^{1}H NMR δ 0.82−2.52 (m, 8H), 2.29 (s, 3H), 3.39 (d, 1H, J = 7.5 Hz), 4.11 (d, 1H, J = 7.8 Hz), 7.00 (t, 1H, J = 7.2 Hz), 7.15 (m, 2H), 8.19 (d, 1H, J = 8.4 Hz); ^{13}C NMR δ 23.8, 25.7, 28.0, 32.1, 42.8, 43.2, 50.7, 68.0, 116.6, 123.8, 124.0, 127.6, 133.7, 144.6, 169.2; HRMS calcd for $C_{15}H_{17}O_4$ 227.1310, found 227.1313.

Ethyl (*E*)-(7-Chloro-8-methyl-3,4-dihydronaphthalen-1(2*H*)-ylidene)ethanoate (55). Following the general procedure on a 0.200 mmol scale using **5** and **48**, **55** was isolated as a colorless oil (45.4 mg, 86%) by flash chromatography using EtOAc/hexane (1:19) as eluant. IR (neat) ν = 1163, 1622, 1713, 2942 cm^{-1}; ^{1}H NMR δ 1.31 (t, 3H, J = 7.2 Hz), 1.76 (m, 2H), 2.48 (s, 3H), 2.56 (t, 2H, J = 6.0 Hz), 3.14 (dt, 2H, J = 7.2, 1.8 Hz), 4.21 (q, 2H, J = 7.2 Hz), 5.85 (t, 1H, J = 2.4 Hz), 6.93 (d, 1H, J = 8.4 Hz), 7.24 (d, 1H, J = 8.1 Hz); ^{13}C NMR δ 14.3, 18.8, 21.4, 27.8, 29.8, 59.9, 119.6, 125.8, 128.6, 132.7, 133.8, 138.6, 140.3, 154.1, 166.5; HRMS calcd for $C_{15}H_{17}O_2Cl$ 264.0917, found 264.0929.

Cyclization Using Trisubstituted Difunctional Acceptors. General Procedure. Ethyl (*E*)-2-(8-Methyl-3,4-dihydronaphthalen-1(2*H*)-ylidene)propanoate (66) and Ethyl 2-(8-Methyl-1,2,3,4-tetrahydronaphthalen-1-yl)acrylate (67). To a mixture of $Pd(OAc)_2$ (8.1 mg, 0.036 mmol) and tri-2-furylphosphine (15.6 mg, 0.066 mmol) was added CH_3CN (2 mL), and the resulting mixture was stirred 30 min at room temperature. Cs_2CO_3 (205.8 mg, 0.632 mmol), 2-iodotoluene (40 μL, 0.314 mmol), norbornene (0.207M/CH_3CN, 3.48 mL, 0.720 mmol), and a solution of **65** (149.5 mg, 0.636 mmol) in CH_3CN (2 mL) were added successively. The resulting mixture was heated at 85 °C for 16 h and then quenched by addition of satd NH_4Cl (6 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (3×). The organic layers were combined, washed with brine, and dried over $MgSO_4$. The solvent was evaporated to give a yellow oil that was purified by flash chromatography using hexane/toluene (1:1) as eluant to yield **66** (30.3 mg, 40%) and **67** (20.7 mg, 27%). **66**: IR (film) ν = 1127, 1255, 1465, 1708, 2859, 2945, 2978, 3056 cm^{-1}; ^{1}H NMR δ 1.34 (t, 3H, J = 7.2 Hz), 1.50 (m, 1H), 1.80 (s, 3H), 1.98 (m, 1H), 2.18−2.26 (m, 4H), 2.40 (m, 1H), 2.59 (ddd, 1H, J = 14.0, 5.2, 2.4 Hz), 3.29 (m, 1H), 4.25 (m, 2H), 6.98 (d, 1H, J = 7.2 Hz), 7.08 (d, 1H, J = 6.8 Hz), 7.14 (t, 1H, J = 8.0 Hz); ^{13}C NMR δ 14.3, 17.7, 19.4, 21.0, 28.4, 29.1, 60.3, 124.0, 124.8, 127.2, 127.8, 134.4, 137.6, 141.3, 143.9, 169.8; HRMS calcd for $C_{16}H_{20}O_2$ 244.1463, found 244.1466. **67**: IR (film) ν = 1129, 1255, 1460, 1624, 1718, 2859, 2934, 2978, 3056 cm^{-1}; ^{1}H NMR δ 1.34 (t, 3H, J = 7.2 Hz), 1.68 (m, 2H), 1.84 (m, 2H), 2.10 (s, 3H), 2.78 (m, 2H), 4.20 (t, 1H, J = 4.0 Hz), 4.27 (q, 2H, J = 7.2 Hz), 4.84 (t, 1H, J = 1.2 Hz), 6.21 (d, 1H, J = 1.6 Hz), 6.96 (d, 2H, J = 7.6 Hz), 7.06 (t, 1H, J = 7.6 Hz); ^{13}C NMR δ 14.2, 17.1, 19.0, 27.3, 29.5, 36.7, 60.7, 126.0, 126.3, 126.9, 127.7, 135.9, 136.8, 137.7, 144.0, 167.0; HRMS calcd for $C_{16}H_{20}O_2$ 244.1463, found 244.1460.

Ethyl (*E*)-2-(8-Methyl-3,4-dihydronaphthalen-1(2*H*)-ylidene)propanoate (66). Following the same procedure on

a 0.157 mmol scale using **68** and **7**, **66** was isolated as the only product as a colorless liquid (24.6 mg, 64%) by flash chromatography using hexane/toluene (1:1) as eluant.

Acknowledgment. We gratefully acknowledge the financial support of the Natural Sciences and Engineering Research Council (NSERC) of Canada, the Ontario Research and Development Challenge Fund (ORDCF), and the University of Toronto. J.-F.P. acknowledges NSERC for a PGS scholarship. S.P. thanks the Fondation Bettencourt-Schueller, and M.D. the Deutsche Forschungsgemeinschaft for postdoctoral fellowships.

Supporting Information Available: Experimental details for selected aryl iodides and difunctional acceptors as well as characterization information for new compounds prepared. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0107296