Palladium-Catalyzed Annulation of Allenes Using Functionally Substituted Vinylic Halides

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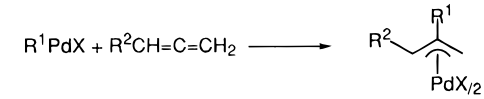
Palladium catalyzes the regio- and stereoselective annulation of allenes by vinylic halides bearing alcohol-, amine-, sulfonamide-, carboxylic acid-, carboxamide- and carbanion-stabilizing groups to produce a variety of five- and six-membered-ring unsaturated heterocycles and carbocycles. The reaction appears to proceed by vinylic palladium formation and addition to the allene, followed by intramolecular nucleophilic displacement of the palladium. Six-membered rings are formed more readily than five-membered rings. The regioselectivity is generally high, with vinylic halides bearing alcohol, carboxylic acid, or carboxamide groups affording predominantly the product of intramolecular attack on the more substituted end of the π-allylpalladium intermediate, while amines and carbanions attack quite selectively at the less substituted end of the π-allylpalladium intermediate. Vinylic halides bearing tosylamides afford mixtures of regioisomers, where the predominant six-membered ring product arises by attack on the less substituted end of the allene, while the major five-membered ring products involve addition to the more substituted end of the allene.

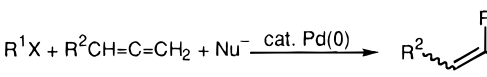
Introduction

π-Allylpalladium intermediates have proven extraordinarily useful in organic synthesis.[1] One important route to such compounds involves the addition of organopalladium compounds to allenes (eq 1).[2] This approach to π-allylpalladium compounds has recently found increasing utility in organic synthesis. Thus, aryl and vinylic halides or triflates have been allowed to react with allenes and nucleophiles to afford products containing all three moieties (eq 2).[3] In an analogous manner, allenes bearing internal carbon nucleophiles react with aryl or vinylic halides to form carbocyclic products.[4] The intermolecular and intramolecular alkoxy-, amido-, and aminopalladation of allenes and subsequent carbon monoxide or alkene insertion has also provided a useful route to a variety of allene addition products.[5]

The palladium-catalyzed hetero- and carboannulation of unsaturated cyclopropanes and cyclobutanes,[6] 1,2-dienes,[7] 1,3-dienes,[8] and alkynes[9] by functionally substituted *aromatic* halides provides a valuable route to a wide variety of arene-containing heterocycles and carbocycles (Scheme 1). Preliminary studies have indicated that *vinylic* halides bearing functionality might be utilized in analogous annulation reactions of allenes.[7b] We now wish to report that indeed vinylic halides bearing



(1)



(2)

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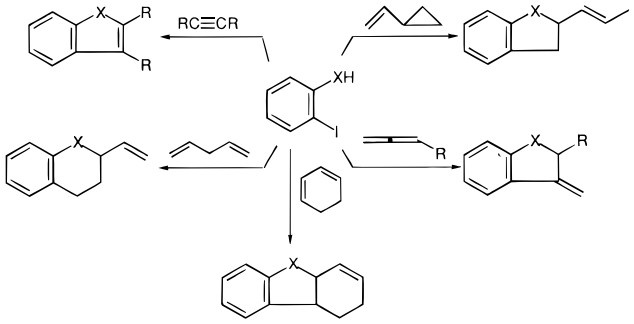
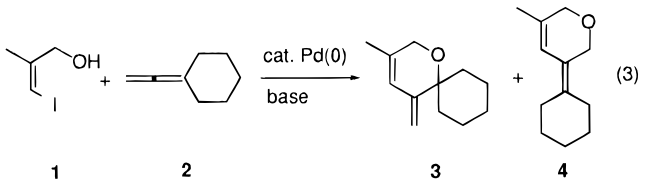
Scheme 1



alcohol, amine, carboxylic acid, amide, and sulfonamide groups, as well as carbanion-stabilizing groups, also react regio- and stereoselectively with allenes to produce five- and six-membered-ring heterocycles and carbocycles in good yields.

Results and Discussion

Heteroannulation. The reaction of (*Z*)-3-iodo-2-methyl-2-propenol (**1**) and vinylidenecyclohexane (**2**) was chosen as a model reaction to explore the best reaction conditions for the palladium-catalyzed heteroannulation reaction (eq 3). Since two regioisomers (**3** and **4**) were observed in the reaction, our studies concentrated on improving the total yield and the regioselectivity.



(3)

1 **2** **3** **4**

The best reaction conditions used previously for the annulation of allenes by functionally substituted *aromatic* halides[7a] were employed initially as our standard reaction conditions [1 equiv of vinylic halide, 5 equiv of allene, 5 mol % $Pd(OAc)_2$, 5 mol % PPh_3, 1 equiv of n-Bu_4NCl (TBAC, Aldrich Chemical Co., monohydrate), 5 equiv of Na_2CO_3, DMF (1 mL per 0.25 mmol of vinylic halide)] and the effect of varying the catalyst, base, amount of TBAC, the presence of additives, solvent and temperature on the product distribution was examined. The results are summarized in Table 1.

The conclusions from that study follow. The solvent makes a big difference in the distribution of the products but does not have too much effect on the total yield of the products (Table 1, compare entries 1 and 2). Excess PPh_3 has little effect on the reaction (entry 3). When the catalytic amount of PPh_3 was removed from the reaction system, the reaction was much slower and also exhibited very poor regioselectivity (Table 1, entry 4). When sodium carbonate was replaced by sodium acetate, the reaction was very slow, and the regioselectivity was also very poor (Table 1, entry 5). When sodium carbonate was replaced by potassium acetate, the reaction rate showed little change; however, the regioselectivity was reduced (Table 1, entry 6). When potassium acetate was used instead of sodium carbonate, and no PPh_3 was used, the ratio of the products was reversed, but the regioselectivity was poorer (entry 7). Sodium bicarbonate was better than either sodium acetate or potassium acetate as a base but poorer than sodium carbonate (Table 1, entry 8). When lithium carbonate was used instead of sodium carbonate, the reaction was very, very slow, and almost all the starting material was recovered after the fixed reaction time (Table 1, entry 9). Potassium carbonate was similar to sodium carbonate with regard to the reaction rate, but exhibits poorer regioselectivity (entry 10). When cesium carbonate was used instead of sodium carbonate, the reaction was much faster, but the regioselectivity was poorer (Table 1, entry 11). The use of LiCl, instead of TBAC, gave substantially lower yields and little regioselectivity (Table 1, entry 12), while the absence of a chloride salt gave a still slower reaction and much lower yield (Table 1, entry 13). In fact, when all these studies were done, the original procedure still gave the best overall yield and regioselectivity. In later work, it was observed that one can sometimes employ only 2 equiv of allene and get results comparable to those reactions using 5 equiv. Using these reaction conditions, the reactions of a variety of vinylic halides and allenes were studied and the results are summarized in Table 2.

Table 1. Optimization of Reaction Conditions (eq 3)

		% isolated yield		
entry	conditions changed	**3**	**4**	comment[a]
1	standard condtions	69	14	finished in 2 d
2	DMSO (1 mL)	41	29	
3	PPh_3 (4 equiv)	59	19	a little **1** left
4	No PPh_3	18	30	37% **1** recovered
5	NaOAc (5 equiv)	21	8	55% **1** recovered
6	KOAc (5 equiv)	55	29	
7	KOAc (5 equiv), no PPh_3	22	58	
8	$NaHCO_3$ (5 equiv)	69	19	
9	Li_2CO_3 (5 equiv)	trace	trace	only **1** left after 4 d
10	K_2CO_3 (5 equiv)	51	30	
11	Cs_2CO_3 (5 equiv)	37	25	finished in 20 h
12	LiCl (1 equiv)	21	18	47% **1** recovered
13	no TBAC or LiCl	16	6	68% **1** recovered

[a] No **1** left unless specified.

A wide variety of functionally substituted vinylic halides have been successfully employed in the annulation of allenes. Vinylic halides bearing functional groups as diverse as alcohols, amines, sulfonamides, and even carboxylic acids and amides undergo annulation. This is the first time that the latter functional group has been employed in this type of annulation process. Introduction of carbonyl functionality directly on the carbon−carbon double bond of the vinylic halide (Table 2, entries 19−30) allows one to employ for the first time in these annulation processes vinylic bromides, as well as iodides. These reactions can also be run at room temperature as opposed to the elevated temperatures generally required for other functionally substituted vinylic halides or aryl halides.

The ability to employ vinylic halides that produce heterocycles bearing either endocyclic or exocyclic double

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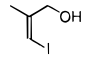
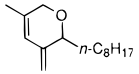
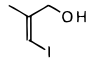
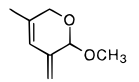
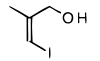
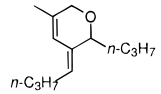
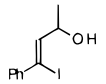
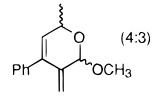
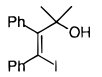
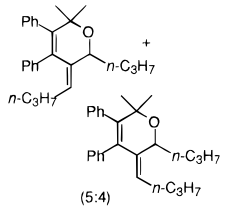
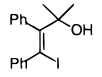
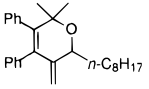
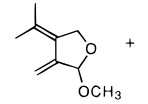
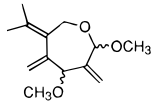
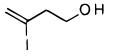
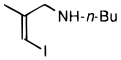
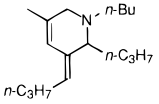
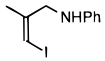
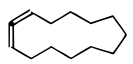
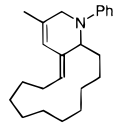
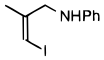
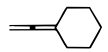
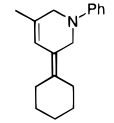
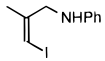
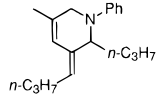
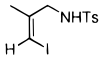
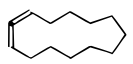
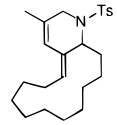
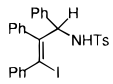
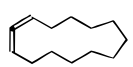
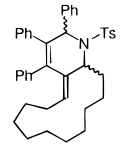
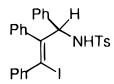
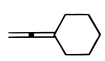
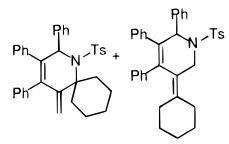
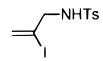
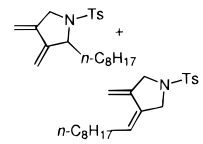
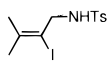
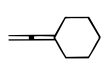
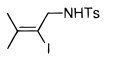
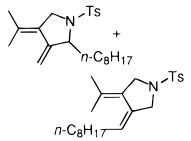
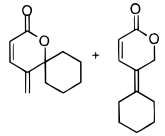
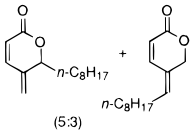
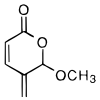
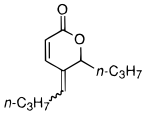
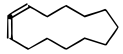
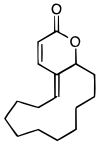
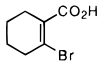
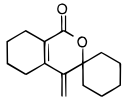
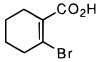
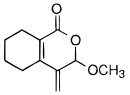
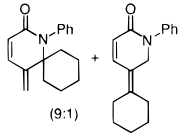
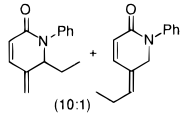
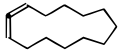
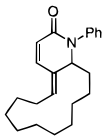
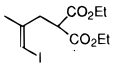
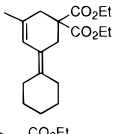
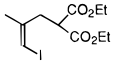
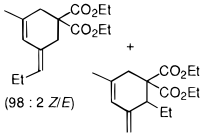
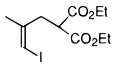
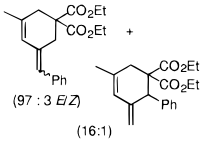
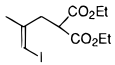
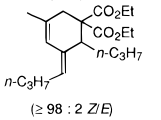
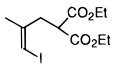
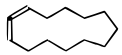
Table 2. Palladium-Catalyzed Annulation of Allenes by Vinylic Halides

entry	vinylic halide	allene	temp (°C), time (h)	product(s)[a] (ratio)	% isolated yield
1		*n*-C_8H_{17}CH=C=CH_2	80, 72		88
2		CH_3OCH=C=CH_2	80, 48		95
3		*n*-C_3H_7CH=C=CH-*n*-C_3H_7	80, 48		95
4		CH_3OCH=C=CH_2	80, 48	 (4:3)	71
5		*n*-C_3H_7CH=C=CH-*n*-C_3H_7	80, 24	 (5:4)	53
6		*n*-C_8H_{17}CH=C=CH_2	80, 41		67
7		CH_3OCH=C=CH_2	40, 72	 	34 (39)[b] 52
8		CH_3OCH=C=CH_2	40, 20		56
9		*n*-C_3H_7CH=C=CH-*n*-C_3H_7	80, 10		65
10			80, 14		67
11			80, 72		72
12		*n*-C_3H_7CH=C=CH-*n*-C_3H_7	80, 24		89
13			80, 20		65
14			80, 22	 (6:21:59:14)	80
15			80, 27		35 + 50
16		*n*-C_8H_{17}CH=C=CH_2	80, 31	 (7:1)	34
17			80, 31		51 + 15

[a] Isolated yield. [b] Combined yield.

18		n-$C_8H_{17}CH{=}C{=}CH_2$	80, 22	 (6:1)	84
19			25, 72		69 + 20
20		$CH_3OCH{=}C{=}CH_2$	25, 14		67
21		n-$C_8H_{17}CH{=}C{=}CH_2$	80, 48	 (5:3)	51
22		$CH_3OCH{=}C{=}CH_2$	25, 22		72
		n-$C_3H_7CH{=}C{=}CH$-n-C_3H_7			
23			80, 24	(3 : 1 *E*/*Z*)	58
24			40, 72	(7 : 1 *E*/*Z*)	50
25			25, 72		53
26			25, 72		53 [c]
27		$CH_3OCH{=}C{=}CH_2$	25, 72		60 [d]

28			25, 8	 (9:1)	93
29		$CH_3CH_2CH{=}C{=}CH_2$	25, 10	 (10:1)	77 [c]
30			25, 72		47
31			80, 48		75
32		$CH_3CH_2CH{=}C{=}CH_2$	80,48	 (98 : 2 *Z*/*E*) (9:1)	93
33		$PhCH{=}C{=}CH_2$	80, 48	 (97 : 3 *E*/*Z*) (16:1)	76
34		n-$C_3H_7CH{=}C{=}CH$-n-C_3H_7	80, 48	 (≥ 98 : 2 *Z*/*E*)	70
35			80, 48		64 [e]
36		n-$C_8H_{17}CH{=}C{=}CH_2$	80, 48	(85 : 15 *Z*/*E*)	69 [f]

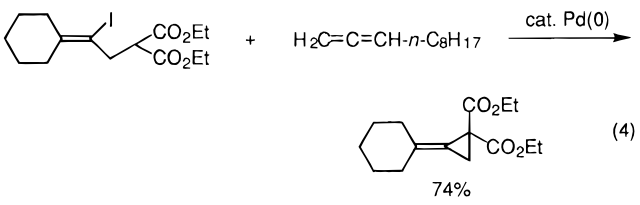
[a] All products gave appropriate ^1H and ^{13}C NMR, IR, and mass spectral data. [b] A 39% yield was obtained upon reaction for 20 h at 80 °C. [c] Only 2 equiv of allene was employed. [d] 10 mL of DMF was used instead of 1 mL. [e] KOAc was used as the base and DMSO as the solvent. [f] Contains 3% of the other regioisomer by GC analysis.

bonds demonstrates the versatility of this process. The majority of the five-membered ring heterocycles were obtained in relatively low yields, with entries 17 and 18 (Table 2) providing noteworthy exceptions. Conversely, six-membered ring heterocycles were readily formed in moderate to high yields. The regioselectivity of annulation, to be discussed later, is highly dependent on the size of the ring being formed and the nature of the functional group.

Allenes bearing a wide variety of substituents and substitution patterns undergo heteroannulation, including acyclic, cyclic, mono- and disubstituted allenes, as well as methoxyallene.

Carboannulation. We have previously reported the facile carboannulation of allenes by aromatic halides bearing carbanion-stabilizing groups.[7a] Using the same procedure as used previously for aromatic halides, which is also the same procedure employed here for heteroannulation using vinylic halides, except for the omission of PPh_3, we have been able to effect the carboannulation of allenes. The results are summarized in Table 2, entries 31−36. In one instance, it was found that a higher yield and faster reaction could be obtained by employing KOAc as the base and DMSO as the solvent (entry 35).

The carboannulation process appears to be reasonably general for the formation of six-membered ring carbocycles. Attempts to extend this methodology to the formation of five-membered ring carbocycles has been unsuccessful. Attempted annulation using the following vinylic halide only resulted in cyclization to the corresponding alkylidene cyclopropane (eq 4). This may

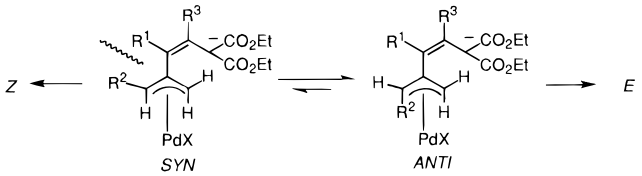


(4)

provide a new method for the synthesis of alkylidene cyclopropanes. This cyclization presumably proceeds by nucleophilic displacement of an intermediate vinylic palladium species, although there appears to be only one previous report of such a reaction.[11] Despite numerous attempts to generalize this type of intramolecular vinylic halide displacement process to the formation of cyclic alkenes containing other ring sizes, we have so far been unsuccessful.

Unlike the reactions involving alcohol, sulfonamide, acid, or amide functionality, but analogous to the reactions of vinylic halides bearing amine functionality (see Table 2, entry 11), the reactions involving carboannulation generally proceed by regioselective attack on the π-allylpalladium intermediate at the less substituted end. However, the regioselectivity is dependent on the nature of the nucleophile, the structure of the allene, and the reaction conditions. For example, the annulation using a malonate and a monosubstituted terminal allene proceeds with a regioselectivity of approximately 90−97% (Table 2, entries 32, 33, and 36), but analogous reactions with the disubstituted terminal allene vinylidene cyclohexane proceed with 100% regioselectivity (Table 2, entry

Scheme 2



31). The addition of 5 mol % PPh_3 to the reaction described in entry 33 (Table 2) resulted in a 53:47 ratio of regioisomers resulting from attack at the less substituted and more substituted ends of the π-allylpalladium system, respectively. This again shows the propensity of the PPh_3-coordinated π-allylpalladium intermediates to undergo attack at the more substituted end of the system, generating the presumably kinetically favored product.

The stereoselectivity of carboannulation is also quite interesting. While alkyl-substituted allenes afforded predominantly the *Z* stereoisomers (Table 2, entries 32 and 34−36), phenylallene gave almost exclusively the *E* isomer (entry 33). Steric hindrance in the π-allylpalladium intermediates appears to be the controlling factor as seen by comparing the ratios of stereoisomers in entries 32, 36, and 33 (Table 2), where the hindrance between R^1 and R^2 = H and ethyl (Table 2, entry 32), methyl and *n*-octyl (Table 2, entry 36), and H and phenyl (Table 2, entry 33) in the *syn*- and *anti*-π-allylpalladium intermediates changes the *Z* to *E* ratio from 98:2 to 85:15 to 3:97 (Scheme 2).[3a,b,i]

Mechanism. These reactions are believed to proceed through palladium acetate reduction to palladium(0), oxidative addition of the vinylic halide to palladium(0), vinylic palladium addition to the allene to initially produce a σ-allylpalladium intermediate, which rapidly equilibrates to *syn*- and *anti*-π-allylpalladium intermediates, which subsequently undergo intramolecular nucleophilic displacement to provide the observed products and regenerate the palladium(0) catalyst (Scheme 3).

The regio- and stereoselectivity of this process arises from the π-allylpalladium displacement step. The regioselectivity is usually quite high with mixtures of regioisomers only generally observed when vinylic halides bearing sulfonamides, carboxylic acids, amides, or carbanions are employed. The mixtures of regioisomers in these cases arise by either low regioselectivity during kinetic attack on the π-allylpalladium intermediates or thermodynamic equilibration through reversible formation of π-allylpalladium intermediates.

In the formation of five-membered heterocyclic rings, alcohol- and sulfonamide-containing vinylic halides preferentially close at the more substituted end of the π-allyl system. When six-membered ring products are formed, alcohol, acid, and amide functionalities are observed to afford predominantly the products of attack at the more substituted end of the π-allylpalladium intermediate. As noted previously,[3d] methoxyallene is observed to give exclusively the product of attack by the nucleophile at the methoxy end of the π-allylpalladium intermediate. On the other hand, six-membered ring formation by amine (Table 2, entry 11), sulfonamide (Table 2, entry 15), and carbanion (Table 2, entries 31−33, and 36) displacements have been observed to occur at the less hindered end of the allylic system, although the sulfonamide reactions are not very regioselective. It is note-

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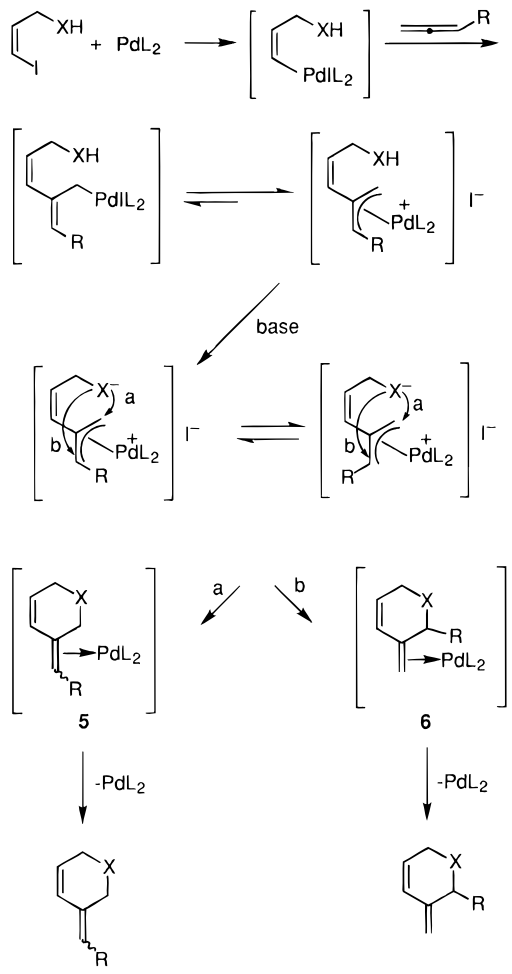
Scheme 3



worthy that one can choose the substitution pattern one desires in the six-membered ring nitrogen heterocycles by choosing either an amine or amide nucleophile (compare entries 11 and 28 of Table 2).

In heteroannulation, the fact that intramolecular nucleophilic attack on the unsymmetrical π-allylpalladium species usually occurs at the more substituted carbon (path b) is in agreement with the need to add PPh_3 to obtain good yields of the products, as well as faster reaction times. The addition of PPh_3 favors the formation of a cationic π-allylpalladium intermediate with the carbocation lying preferentially at the more substituted carbon for electronic reasons. Substitution at that carbon then results in the observed products. The methoxy group of methoxyallene further enhances this regiochemistry. Also, when PPh_3 is added as a ligand, it increases the bulk around the palladium atom. The steric congestion that develops in the transition state for the formation of the initial product of cyclization (complex **5** or **6**) increases the energy of this transition state, favoring nucleophilic attack at the more substituted carbon to form the less congested olefin−palladium π-complex (**6**). In addition, it is known that electron-rich palladium(0)−olefin complexes favor coordination to the more electron-deficient double bond as in complex **6**.[12] It is noteworthy, however, that in six-membered ring formation the more hindered amine, sulfonamide, and carbanion nucleophiles attack preferentially at the less hindered end of the π-allylpalladium intermediates (Table 2, entries 11, 15, 31−33, and 36). Again, the addition of PPh_3 has been observed to reverse this preference as noted above.

This process appears to proceed almost exclusively through *syn*-π-allylpalladium intermediates, except when these become relatively hindered. Only one stereoisomer is observed in entries 3, 9, 10, 12, 13, 16, 18, 21, 25, 30, and 35 (Table 2). The structures of the products in entries 3 and 13 have been established through 2-D NOESY experiments. In each case, the two vinylic protons exhibited no NOE interaction. The product in entry 3 (Table 2) exhibited a strong interaction between the exocyclic vinyl proton and the methylene protons on the more remote *n*-propyl side chain. In the case of entry 13, a strong interaction was evident between the vinyl hydrogen exocyclic to the six-membered ring and its allylic counterpart at the ring junction. The structures of the other stereoisomers have been tentatively assigned assuming that they are identical to these products.

The products of entries 5, 23, 24, 32−34, and 36 in Table 2 were all mixtures of stereoisomers. It appears that such mixtures only arise when the product bears a good allylic leaving group, such as a carboxylate (similar results not included in this paper have been observed for the carboxamide group), or the *syn*- and *anti*-π-allylpalladium intermediates become energetically comparable due to steric hindrance in the syn isomer.[13] The loss of stereospecificity observed with carboxylates suggests that the isomeric mixtures arise by reversible formation of π-allylpalladium intermediates, which equilibrate through mixtures of syn and anti species to give thermodynamic mixtures of products. It is possible, though in our view unlikely, that the malonate derivatives are equilibrating in the same way, since it is known that dienyl malonates can reversibly form π-allylpalladium intermediates.[13] The stereochemistry of the major isomer formed in entry 4 (Table 2) is uncertain.

In one instance (Table 2, entry 7), it appears that the initially formed π-allylpalladium intermediate inserts a second allene and then closes to a seven-membered-ring heterocycle, rather than close to a five-membered ring ether bearing two exocyclic carbon−carbon double bonds. In no other system have we seen products arising by multiple allene insertion.

Conclusion

The palladium-catalyzed coupling of a wide variety of functionally substituted vinylic halides and allenes provides a very versatile synthesis of a variety of five- and six-membered-ring heterocycles and carbocycles. The process is often quite regio- and stereoselective with the selectivity highly dependent on the nature of the incipient nucleophile and the substitution pattern of the resulting π-allylpalladium intermediates.

Experimental Section

Allenes. The following allenes were prepared as indicated. Vinylidene cyclohexane was prepared from (1-chlorocyclohexyl)acetylene using a literature procedure.[14] 1,2-Undecadiene, phenylallene, and 4,5-nonadiene were prepared by treating the

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corresponding 1,1-dibromocyclopropanes with methyllithium according to a literature procedure.[15] Methoxyallene was prepared by the base-catalyzed isomerization of propargyl methyl ether.[16] 1,2-Cyclotridecadiene was generously provided by Professor Richard Johnson, and 1,2-pentadiene is commercially available.

Vinylic Halides. The vinylic halides were prepared as follows. (*Z*)-3-Iodo-2-methyl-2-propen-1-ol was prepared through the copper-catalyzed addition of MeMgI to propargyl alcohol followed by an iodine quench using a literature procedure.[17] (*Z*)-4-Iodo-4-phenyl-3-buten-2-ol was prepared from 4-phenyl-3-butyn-2-ol using a literature procedure[18] involving Red-Al addition and iodination. 2-Iodo-3-methyl-2-butenol was prepared by DIBAL reduction of ethyl 2-iodo-3-methyl-2-butenoate using a literature procedure.[19] 3-Iodo-3-buten-1-ol was prepared by reaction of 3-butyn-1-ol with NaI, Me_3SiCl, water, and acetonitrile according to a literature procedure.[20] (*Z*)-4-Iodo-2-methyl-3,4-diphenyl-3-buten-2-ol was prepared by sequential treatment of (propene)Ti(O-*i*-Pr)2 (formed in situ from Ti(O-*i*-Pr)4 and *i*-PrMgCl) with diphenylacetylene, acetone, and I_2 according to a literature procedure.[21] *n*-Butyl [(*Z*)-3-iodo-2-methyl-2-propenyl]amine was prepared by reacting the tosylate of (*Z*)-3-iodo-2-methyl-2-propen-1-ol with *n*-butylamine. *N*-[(*Z*)-3-Iodo-2-methyl-2-propenyl]aniline was prepared by reacting (*Z*)-1,3-diiodo-2-methyl-1-propene with aniline. 2-Iodo-2-propen-1-ol was prepared by the reaction of propargyl alcohol with NaI, Me_3SiCl, water, and acetonitrile according to a literature procedure.[22] (*Z*)-3-Iodo-1,2,3-triphenyl-2-propen-1-ol was prepared by sequential treatment of Cp_2ZrEt_2 (formed in situ from Cp_2ZrCl_2 and EtMgBr) with diphenylacetylene, benzaldehyde, and I_2 using a literature procedure.[23] All toluenesulfonamides were prepared from the corresponding alcohols by reaction with *N*-BOC-*p*-toluenesulfonamide under the Mitsunobo reaction conditions, followed by the removal of the *N*-BOC group by treatment with trifluoroacetic acid in CH_2Cl_2.[24] (*Z*)-3-Bromo- and (*Z*)-3-iodopropenoic acid were prepared by the reaction of 2-propiolic acid and lithium bromide or lithium iodide in acetic acid according to a literature procedure.[25] 2-Bromocyclohexene carboxylic acid was obtained by saponification of methyl 2-bromocyclohexene carboxylate.[26] *N*-Phenyl-(*Z*)-3-iodoacrylamide was prepared by DCC coupling of aniline and (*Z*)-3-iodopropenoic acid according to a literature procedure.[27] All malonates were formed through the reaction of diethyl sodiomalonate and the mesylate of the corresponding alcohol.

General Procedure for the Palladium-Catalyzed Annulation. After $Pd(OAc)_2$ (5 mol %), PPh_3 where used (5 mol % for heteroannulation, none for carboannulation), *n*-Bu_4NCl (1 equiv, Aldrich Chemical Co., monohydrate), Na_2CO_3 (5 equiv), and the organic halide (0.25 mmol) in 1 mL of anhydrous DMF were stirred for 2 min, the allene (0.50 or 1.25 mmol) was added to the mixture. In a few reactions, KOAc and/or DMSO were used as the base and solvent (see, for example, entry 35 in Table 2). The vial was then capped and suspended in an oil bath at the appropriate reaction temperature for the appropriate period of time. When the reaction was considered complete as determined by TLC analysis, it was allowed to cool to room temperature and directly chromatographed on a silica gel column (230−400 mesh silica gel) with an appropriate elutant. Alternatively, the reaction was diluted with saturated NH_4Cl and extracted with ether (Table 2, entries 5, 6, and 13−18). The extracts were dried over Na_2SO_4 and concentrated prior to chromatography. The desired products were collected, and the solvents were removed by rotary evaporation. When necessary, the isomeric ratio of the products was determined by employing gas chromatography (10 m HP-1 megabore or 25 m DB-1 capillary or 5 m OV 101 packed column; 70−250 °C at a rate of 35 °C/min) and/or ^1H NMR spectral analysis. Most products were sufficiently unstable as to prevent us from obtaining elemental analyses to ascertain purity.

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Supporting Information Available: Copies of ^1H and/or ^{13}C NMR spectra of all new compounds as well as spectral data for all compounds in Tables 1 and 2 (95 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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