substitution on the aromatic ring of **4**.

A slight drawback of this procedure is the production of minor products when electron-releasing groups are present on the aromatic ring.[8] These materials, however, are easily removed by column chromatography.

The general experimental procedure for the production of pyrrolones **2** is as follows. To a stirred solution of 2 mmol (0.28 mL, 0.356 g) of diethyl (diazomethyl)-phosphonate (**3**), 1 mmol of 2-oxopropanamide **4**, and 2 mL of acetonitrile at 0 °C was added powdered potassium *tert*-butoxide (1.5 mmol, 0.18 g) over a period of 1.5 h. After 2 min, the reaction mixture was quenched with 10 mL of water, and extracted with five 15-mL portions of ethyl acetate. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to yield the crude products. Purification was achieved by high-pressure liquid chromatography.

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Registry No. **2a**, 72788-60-4; **2b**, 104422-25-5; **2c**, 104422-26-6; **3**, 25411-73-8; **4a**, 61110-50-7; **4b**, 61110-54-1; **4c**, 61110-53-0; **5**, 104422-27-7; **6**, 104422-28-8.

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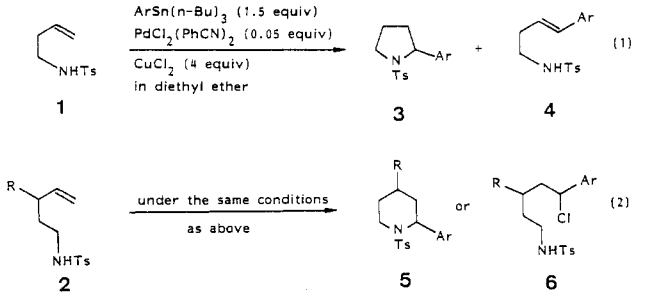
Synthesis of Five- and Six-Membered Nitrogen Heterocycles via a Palladium(II)-Catalyzed Cyclization of Unsaturated Amides

Summary: Palladium(II)-catalyzed arylation of *N*-4-pentenyl-*p*-toluenesulfonamides **2** with $ArSn(n\text{-}Bu)_3$ under oxidative conditions ($CuCl_2$ in ether) provides either 2-arylpiperidines **5** or *N*-(chloro-5-arylpentyl)-*p*-toluenesulfonamides **6** depending on the kind of arylating agents. Under the similar conditions, *N*-3-butenyl-*p*-toluenesulfonamides (**1**) are converted to a mixture of 2-arylpyrrolidines **3** and *N*-(4-aryl-3-butenyl)-*p*-toluenesulfonamides **4**.

Sir: Palladium(II) usually mediates addition reactions at the vicinal positions of olefins.[1] For example, Heck reaction selectively provides 1,2-arylchlorination[2] or 1,2-oxyarylation products.[3] In separate papers, 1,1-difunctionalization has been noted in some special cases.[4,5]

Recently we have found that a slight modification of conditions of Heck reaction (catalytic $PdCl_2(PhCN)_2$, ArHgCl or $ArSn(n\text{-}Bu)_3$, $CuCl_2$ in diethyl ether) dramatically alters the reaction pattern, and 1,1-difunctionalization becomes the main course of the reaction as exemplified by the formation of 2-aryltetrahydropyrans from 4-pentenols.[6] In this paper, we describe the first example of the palladium(II)-catalyzed regiospecific 1,1-arylamination of unsaturated amides, which provides 2-arylated five- and six-membered nitrogen heterocycles (eq 1 and 2). These products share the partial structure with many interesting alkaloids.[7]



A typical reaction was performed as follows: Into an argon-purged and ice-cooled flask, containing $PdCl_2(PhCN)_2$ (0.05 mmol) and $CuCl_2$ (4 mmol), was introduced a solution of 4-pentenyl-*p*-toluenesulfonamide (**1**, R = H, 1 mmol) in 20 mL of dry ether. Then $4\text{-}MeOC_6H_4Sn(n\text{-}Bu)_3$ was added via a syringe in one portion, and the heterogeneous mixture was stirred at 0 °C for 5 h, during which the color of the mixture turned from dark brown to gray and finally to light brown. The mixture was diluted with 20 mL of ether and washed thoroughly with three portions of 10 mL of saturated KF and then with 10 mL of 2 N HCl, followed by 5 mL of saturated $NaHCO_3$. The ethereal layer was dried over anhydrous $MgSO_4$ and condensed to leave a sticky oil, which was subjected to flash column chromatography over silica gel (benzene–ethyl acetate gradient) to provide *N*-tosyl-2-(*p*-methoxyphenyl)piperidine (**5b**, 70%). **5b**: mp 116.9–117.1 °C (hexane–benzene); IR (KBr disk) 2940, 1615, 840, 815 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11–1.82 (m, 6 H), 2.40 (s, 3 H), 3.04 (m, 1 H), 3.75 (s, 3 H), 3.77 (m, 1 H), 5.22 (br s, 1 H), 6.82 (d, J = 9.0 Hz, 2 H), 7.24 (m, 4 H), 7.72 (d, J = 8.3 Hz, 2 H) [the resonances at δ 3.04, 3.77, and 5.22 collapse to d (J = 13.7 Hz), d (J = 13.7 Hz), and s by irradiation at δ 1.42, respectively]; ^{13}C NMR ($CDCl_3$) δ 18.9, 21.4, 24.3, 27.3, 41.7, 54.8, 55.2, 113.9, 127.0, 128.1, 129.5, 130.8, 138.8, 142.7, 158.4.

The results examined with *N*-3-butenyl- (**1**) and *N*-4-pentenyl-*p*-toluenesulfonamides (**2**) according to the procedure described above are summarized in Table I. From this table the following points readily emerge. First, the present reaction is applicable not only for the formation of 2-arylpiperidines **5** but also for the formation of 2-arylpyrrolidines **3**. However, we have not succeeded yet in the formation of 2-aryl-1-azacycloheptanes using *N*-5-hexenyl-*p*-toluenesulfonamide as a substrate. Second, all the reactions are complete at 0 °C or room temperature within 5–8 h with a Pd^{II} catalyst as small amount as 5 mol %. Arylmercuric chlorides may be used as arylation agents instead of aryltins (**6a** was obtained in 60% yield by the use of PhHgCl, cf. run 4, Table I). Third, depending on the structure of substrate and the substituent on the aromatic ring of the arylating agent, the course of the reactions dramatically changes. Thus, 2-arylpyrrolidines **3** are formed as major products together with **4** from *N*-3-butenyl-*p*-toluenesulfonamides (**1**), irrespective of the kind of the arylating agents. On the other hand, *N*-4-pentenyltosylamides **2** give either 2-arylpiperidines **5** or *N*-(5-aryl-5-chloropentyl)-*p*-toluenesulfonamides **6**. Aryltins with electron donating substituents provide **5**, and

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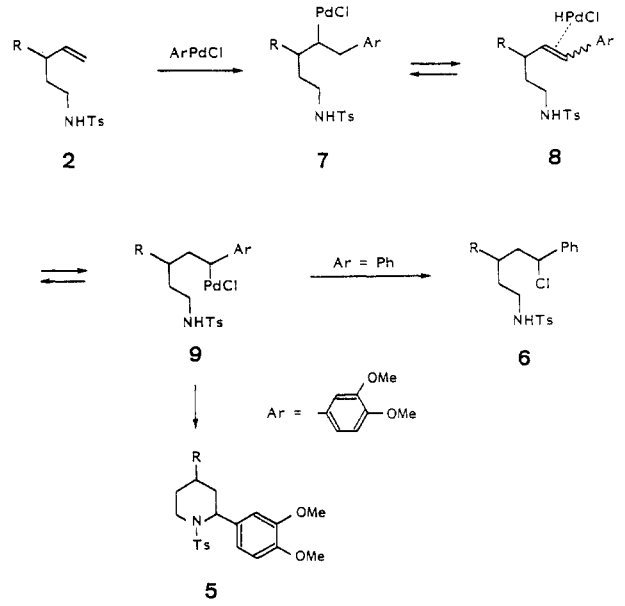
Table I. Terminal *gem*-Arylamination and Arylchlorination of *N*-3-Butenyl- and *N*-4-Pentenyl-*p*-toluenesulfonamides Catalyzed by Pd^{II}

	starting amide[a] 1 or 2	arylating agent $ArSn(n\text{-}Bu)_3$, Ar	reacn[b] conditions T, °C	reacn[b] conditions t, h	product (yield,[c] %)
1	1	C_6H_5	0	6	**3a** (65) **4a** (35)
2	1	$4\text{-}MeC_6H_4$	0	7	**3b** (72) **4b** (21)
3	1	$3,4\text{-}(MeO)_2C_6H_3$	0	8	**3c** (63) (11)[d]
4	2 (R = H)	C_6H_5	0	5	**6a** (69)
5	2 (R = H)	$4\text{-}(MeO)C_6H_4$	0	5	**5b** (70)
6	2 (R = H)	$3,4\text{-}(MeO)_2C_6H_3$	0	8	**5c** (78)
7	2 (R = Me)	C_6H_5	0	8	**6d** (65)
8	2 (R = Me)	$4\text{-}(MeO)C_6H_4$	0	7	**5e** (58)[e]
9	2 (R = Ph)	C_6H_5	0	6	**6f** (77)
10	2 (R = Ph)	$4\text{-}(MeO)C_6H_4$	0	5	**5g** (55)[f]
11	2 (R = OAc)	$4\text{-}(MeO)C_6H_4$	*h*	5	**5h** (77)

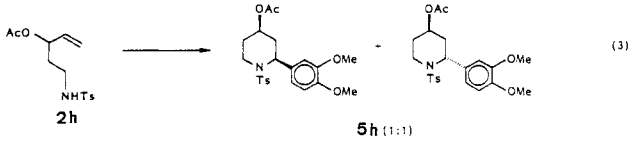
[a] For the structures of 1, 3, and 4 and for those of 2, 5, and 6, see eq 1 and 2, respectively. [b] The mixture consisting of 1 or 2 (1 mmol), $PdCl_2(PhCN)_2$ (0.05 mmol), $ArSn(n\text{-}Bu)_3$ (1.5 mmol), $CuCl_2$ (4 mmol), and dry ether (20 mL) was stirred under argon for the period indicated. [c] All the products, isolated by column chromatography, showed satisfactory spectral (^1H and ^{13}C NMR, IR) and analytical data (high-resolution MS). Yield refers to the isolated one for the spectroscopically homogeneous compound. No entry data signifies that the expected product could not be detected by ^1H NMR and TLC monitoring of the crude reaction mixture. [d] *N*-3-Chloro-4-[(3,4-dimethoxyphenyl)butyl]-*p*-toluenesulfonamide was obtained. [e] *cis*- and *trans*-*N*-tosyl-2-*p*-anisyl-4-methylpiperidines were obtained in 47% and 11% yields, respectively. [f] A mixture of stereoisomers was obtained. [g] See eq 3. [h] Room temperature.

Scheme I



phenyltin gives **6** specifically.[8]

We suggest that **5** and **6** may proceed through a common intermediate **9**, which is derived from a primary arylpalladation intermediate **7** via sequential elimination–addition of a hydridopalladium species (Scheme I). Interestingly no 1,2-regioisomers derived from **7** (e.g., *N*-(5-aryl-4-chloropentyl)-*p*-toluenesulfonamides or *N*-tosyl-2-(arylmethyl)pyrrolidines) were detected.[10] Finally, the formation of **5h** from 3-acetoxy-4-pentenyl-*p*-toluenesulfonamide (**2h**, eq 3) in high yield is noteworthy. Although the structural arrangement of **7** (R = OAc) is ready to undergo deacetoxypalladation,[11] the reaction still prefers to take the course of dehydropalladation to give **9**.



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(8) It is premature to discuss the distribution of the cyclized and noncyclized products. The mechanism of the $CuCl_2$-assisted Pd–C bond cleavage is still controversial,[9] and the distribution of products is rather complicated and dependent on the ring sizes to be formed. However, it may be suggested that the more stable the carbonium ion generated by heterolytic cleavage of the Pd–C bond in an intermediate **9** (Scheme I), the higher the proportion of cyclized products.

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(10) For the explanation about this point, see ref. 6.

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Chirality Transfer in Stereoselective Synthesis. A Highly Stereocontrolled Synthesis of 22-Hydroxylated Steroid Side Chains via the [2,3]-Wittig Rearrangement[1]

Summary: An efficient approach toward 22-oxygenated steroid side chains has been accomplished utilizing the [2,3]-Wittig rearrangement of the dianion derived from the (*E*)-17(20)-ethylidene-16α-(carboxymethyl)oxy steroid.

Sir: Despite the recent considerable success in the construction of steroid side chains,[2] the efficient, highly stereocontrolled synthesis of 22-hydroxylated steroids remains a formidable challenge. Interestingly, all of the known physiologically significant 22-oxygenated steroids, with the notable exception of the plant hormone brassinolides[3] (e.g., **2**), possess the C-22 configuration shown in

(1) This work was presented in part at the 190th National Meeting of the American Chemical Society, Chicago, September, 1985 (Abst ORGN 145) and at the International Symposium on Organic Chemistry of Medicinal Natural Products (IUPAC), Shanghai, November, 1985 (Abst C-50).

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