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# Palladium-Catalyzed Coupling of Organic Halides and Tertiary Allylic Amines

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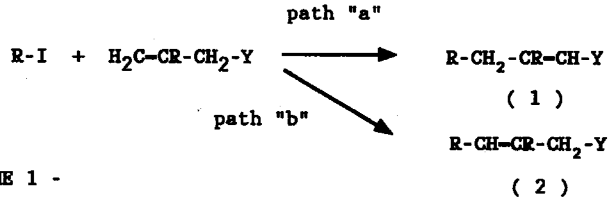
*Key Words:* palladium catalysis, phenyl iodide, perfluoroalkyl iodide, Heck reaction, radical addition.

**Abstract:** *The palladium-catalyzed reaction between aryl or perfluoroalkyl iodides and tertiary allylic amines provides a pratical route to 3-aryl- or 3-perfluoroalkyl-allylic amines. The outcome of the arylation of tertiary allylic amines can be affected by a change of solvent.*

Palladium-catalyzed arylation or vinylation of allylic alcohols afford a convenient synthesis of ß-aryl- or ß-vinyl-carbonyl compounds[1] (Scheme 1, path "a", Y = OH, enolic form). 3-Arylprop-2-enols are obtained when the reaction is carried out in the presence of Ag+ ions[2] (scheme 1, path "b").



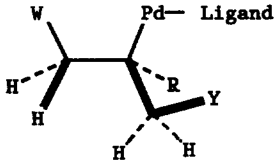
- SCHEME 1 -

On the contrary, tertiary allylic amines and vinyl bromides are reported to give enamines only[3].

The reaction of perfluoroalkyl iodides with either allylic alcohols or unsubstituted, or even N-aryl substituted, allylic amines in alcoholic solvents affords 3-perfluoroalkyl-1,2-epoxides or the corresponding aziridines, respectively[4].

We have found that the reaction between 1-(2-methylprop-2-enyl)-piperidine (2.01 mmol) and phenyl iodide (0.67 mmol), in the presence of $PdCl_2(PPh_3)_2$ (0.02 mmol), $K_2CO_3$ (1.34 mmol), and ethanol (1.5 ml) gave a mixture of 1-(3-phenyl-2-methylprop-2-enyl)piperidine (40%) and 1-(3-phenyl-2-methylprop-1-enyl)piperidine[5] (40%). When ethanol was replaced by DMF, 1-(3-phenyl-2-methylprop-1-enyl)piperidine[5] was the main product (72%). On the contrary, the yield of the allylic derivative was the highest (85%) when the reaction was carried out in the less polar toluene.

This "solvent effect" can be explained by assuming that chelation of palladium by nitrogen in intermediate (3) ($Y = R^1\text{-N-}R^2$, $W = C_6H_5$) hinders cis-elimination of the proton[6] linked to the carbon bearing the heteroatom. This intermediate may be formed by direct addition of a σ-phenylpalladium complex to the olefinic bond, but also by reverse addition of the hydridopalladium halide, as postulated by others[2,3].



( 3 )

The intramolecular coordination should evidently be enhanced by apolar solvents, where the heteroatom would be less solvated and thus readier to chelate the palladium atom[7].

When the reaction was carried out with perfluorododecyl iodide as the organic halide, the best selectivity was obtained in ethanol solution, where a mixture of 1-(3-perfluorododecyl-2-methylprop-2-enyl)-piperidine (70%) and 1-(3-perfluorododecyl-2-methylprop-1-enyl)piperidine (5%) was obtained.

The perfluoroalkylation appears to follow a different reaction pathway, which may involve a palladium(0)-catalyzed, radical addition[8,9] to give a 2-iodo-2-methyl-3-perfluoroalkylpropyl tertiary amine that would subsequently undergo oxidative insertion of palladium(0) and provide intermediate (3) (W = Rf)[10]. This, on the analogy of the arylation of allylic tertiary amines, would be expected to afford only minor amounts of the allylic derivative, which, instead, turns out to be the major product, probably because of the presence of a strongly electron withdrawing perfluoroalkyl group, which should make palladium (II) more electron poor and thus more sensitive to chelation.

As shown in Table 1, since the reaction products can easily be separated by silica gel chromatography, these methods, when the proper solvents are used, may provide a pratical route to 3-aryl- and 3-perfluoroalkyl-allylic amines.

**Table 1:**
*Palladium-catalyzed coupling of allylic compounds with organic iodides* (a).

| Run | W | R | Y | Solvent | Yield in (1) (b) | (2) |
|---|---|---|---|---|---|---|
| 1 | $C_6H_5I$ | Me | piperidino | EtOH | 20 | 60 |
| 2 | $C_6H_5I$ | Me | piperidino | Toluene | 10 | 85 |
| 3 | $C_6H_5I$ | Me | piperidino | DMF | 72 | 2 |
| 4 | $C_6H_5I$ | Me | morpholino | DMF | 75 | 5 |
| 5 | $C_6H_5I$ | Me | morpholino | Toluene | 8 | 80 |
| 6 | $C_6H_5I$ | Me | dimethylamino | toluene | 5 | 70 |
| 7 | $C_{12}F_{25}I$ | Me | piperidino | EtOH | 5 | 70 |
| 8 | $C_{12}F_{25}I$ | Me | morpholino | EtOH | 10 | 75 |
| 9 | $C_{10}F_{23}I$ | Me | piperidino | EtOH | 8 | 80 |
| 10 | $C_{10}F_{23}I$ | Me | morpholino | EtOH | 10 | 82 |
| 11 | $C_{12}F_{25}I$ | Me | dimethylamino | EtOH | 9 | 65 |
| 12 | $C_{10}F_{23}I$ | H | morpholino | EtOH | 20 | 38 |

a) Yields were determined by GLC, after 2 hours at 80°C.
b) E/Z isomer mixture.

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## References and notes

1. a) Chalk, A.J.; Magennis, S.A. *J.Org.Chem.*, **1976**, 41, 273.
   b) Heck, R.F.; Melpolder, J.B. *J.Org.Chem.*, **1976**, 41, 265.
2. Jeffery T. *Tetrahedron Lett.*, **1991**, 32, 2121.
3. Heck, R.F. *Org. React.*, **1982**, 27, 345.
4. Fuchikami, T.; Shibata, Y; Urata H. *Chem. Lett.*, **1987**, 521.
5. After the work up, only the aldehyde was recovered.
6. Heck, R.F. *J.Am.Chem.Soc.*, **1969**, 24, 6707.
7. To a smaller extent, solvents can also affect selectivity of the palladium-catalyzed arylation of allylic alcohols. When the coupling of phenyl iodide and

2-methylprop-2-enol was carried out in toluene, we obtained a mixture of aldehyde and isomeric allylic alcohols or bis-arylated compounds arising from further arylation of allylic alcohols.

8. According to rif.9, the reaction was completely inhibited by nitrotoluene.
9. Chen, Q.Y.; Yang Z.Y.; Zhao C.X.; Qiu Z.M. *J. Chem. Soc. Perkin Trans. I*, **1988**, 563.
10. We have never detected the 2-iodo-2-methyl-3-perfluoroalkylpropyl tertiary amine, but, in our opinion, the 2-hydroxy-2-methyl-3-perfluoroalkylpropyl tertiary amine that we found when the reaction was performed in toluene provides circumstantial evidence that this easily-hydrolysable iododerivative is indeed formed.

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