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# Palladium-catalyzed Cross-coupling of Pyrrolyl Anions with Organic Halides

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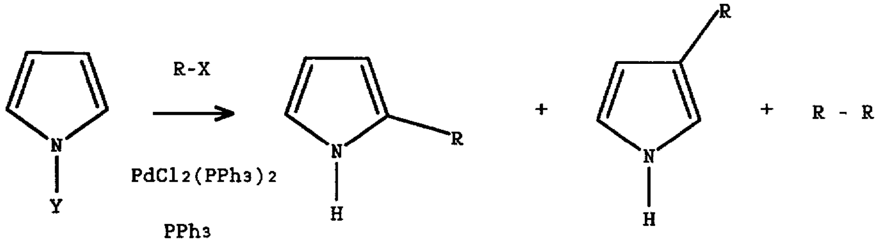
*Key Words:* pyrrolyl anion; palladium catalysis; perfluoroalkylpyrroles

**Abstract:** *Ambident pyrrolyl anions react with aromatic halides, as well as perfluoroalkyl iodides, in the presence of a palladium catalyst.*

Palladium catalysis is a very useful tool for the introduction of organic groups into pyrroles[1]. Both the Heck reaction of pyrrolyl iodides[2] and the cross-coupling between 1-methylpyrrol-2-ylzinc chloride with organic halides[3] are well known.

We have found that pyrrol-1-yl-zinc halides, prepared "in situ" from pyrrol-1-ylsodium and Zinc(II) halides, undergo coupling with organic halides in the presence of a palladium salt and phosphine (Table 1):[4]



(I) (II) (III) (IV)

2-Phenylpyrrole is obtained from bromobenzene in NMP at 140°C in good-to-poor yields depending on the nature of the zinc halides, the major by-product being biphenyl.

Pyrroles are known ambident anions, whose reactivity towards electrophiles is well explained by HSAB theory[5]. A soft counterion will result in the formation of mostly N-substituted derivatives, while a harder one will promote C-substitution.

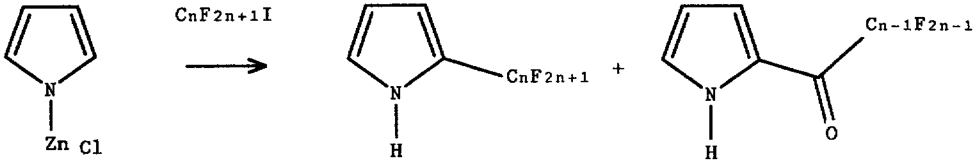
In the present work, the σ-phenylpalladium complex does not react at all with pyrrol-1-ylsodium, while affording C-phenyl (mainly 2-) pyrroles on treatment with pyrrol-1-ylzinc bromide and, even better, with pyrrol-1-ylzinc chloride, in accordance with the increase of "hardness" along the series (run 1-3).

Table 1. Palladium catalyzed coupling of pyrrol anions with organic halides [a)]

| Run | R | X | Y | %Conversion [b)] | yield II(%) | yield III(%) | yield IV(%) |
|---|---|---|---|---|---|---|---|
| 1 | $C_6H_5$- | Br | Na | 100 | 0 | 0 | 100 |
| 2 | $C_6H_5$- | Br | ZnBr | 70 | 40 | 10 | 50 |
| 3 | $C_6H_5$- | Br | ZnCl | 100 | 75 | 5 | 15 |
| 4 | $C_{12}F_{25}$ | I | ZnCl | 100 | 75 (c) | 0 | 0 |
| 5 | $C_{10}F_{21}$ | I | ZnCl | 100 | 80 (d) | 0 | 0 |
| 6 | $C_8F_{17}$ | I | ZnCl | 100 | 72 (e) | 0 | 0 |

a) Yields were determined by GLC.
b) Conversion after 2 hours at 140°C.
c) 2-Perfluorododecanoylpyrrole (18%) was also found.
d) 2-Perfluorodecanoylpyrrole (15%).
e) 2-Perfluoroctanoylpyrrole (20%).

As σ-perfluoroalkylpalladium iodides react like σ-arylpalladium halides [6], we used this procedure for the introduction of a perfluoroalkyl moiety into a pyrrole. According to the present nonoptimized procedure, a perfluoroalkyl iodide gives a mixture of 2-perfluoroalkylpyrrole and 2-perfluoroalkanoylpyrrole, the latter probably arising from partial hydrolysis[7] of some of the former compound (run 6-7-8).



Therefore, this method may provide a pratical route to 2-perfluoroalkylpyrroles, as an alternative to radical methods[8].

A typical procedure is as follows. A solution of pyrrolylsodium in N-methylpyrrolidone (10 ml), prepared from pyrrole (0.18 g; 2.7 mmol) and NaH (0.064 g; 2.7 mmol), was treated with $ZnCl_2$ (0.36 g; 2.7 mmol) portionwise. After 2 hours at room temperature, perfluorododecyl iodide (1.0 g; 1.3 mmol), $PdCl_2(PPh_3)_2$ (0.18g; 0.27 mmol) and $PPh_3$ (0.15 g; 0.57 mmol) were added, then the mixture was stirred at 140°C for 2 h. GLC analysis of a hydrolysed sample showed the formation of 2-perfluorododecyl pyrrole in 75% yield[9].

## References and notes

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9) Identified by GC/MS (M+: 150) and H-NMR spectroscopy: δ(CDCl3) 6.2 (1 H, m), 6.5 (1H, m), 6.9 (1H, m), 8.9 (1H, s).

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