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PALLADIUM-CATALYZED SYNTHESIS OF PYRROLES

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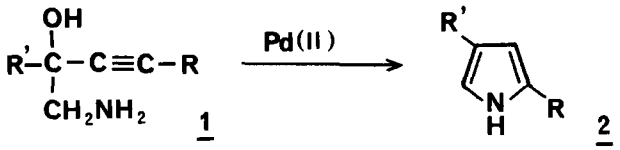
Summary: Pyrrole derivatives are prepared in high yields by the catalytic action of a Pd(II) salt on 1-amino-3-alkyn-2-ols which are obtained from conjugate ynones.

Palladium mediated preparation of pyrroles has been studied.[1-3] This paper describes a Pd(II) catalyzed synthesis of pyrrole derivatives from 1-amino-3-alkyn-2-ols (1) which are obtained from conjugate ynones.



1 2

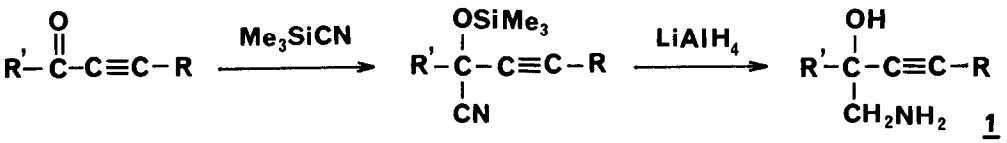
A solution of $PdCl_2$ (7 mg, 0.04 mmol) and 3-aminomethyl-4-undecyn-3-ol (738 mg, 3.8 mmol) in 13.0 ml of acetonitrile was heated at reflux for 3 h. The reaction mixture was worked up with sat. NaCl aq. solution and extracted with ether. The ethereal solution was dried (Na_2SO_4) and distilled affording 4-ethyl-2-hexylpyrrole (560 mg, 3.1 mmol, 84% yield). $Pd(OAc)_2$, in place of $PdCl_2$, gave a similar result but $Pd(PPh_3)_4$ was less effective.[4] Results are summarized in Table 1.

Table 1. Pyrrole 2 from Amino-alkynol 1

Entry	R	R'	Catalyst	(equiv.)	Yield (%)[a]
1	$n\text{-}C_6H_{13}$	Et	$PdCl_2$	(0.01)	84
2	"	"	$PdCl_2$	(0.001)	83
3	"	"	$Pd(OAc)_2$	(0.01)	73[b]
4	"	"	$Pd(PPh_3)_4$	(0.01)	17
5	"	$(CH_3)_3C$	$PdCl_2$	(0.01)	85
6	"	H	$PdCl_2$	(0.01)	88[c]
7	Ph	Et	$PdCl_2$	(0.01)	100[d]

a) Glc yields are quantitative except entries 3 and 4. b) The yield diminished to 70% when benzene was employed as solvent. c) Starting material is methyl ether of 1. d) Yield of a crude product whose nmr is identical to that of authentic one.

The starting materials 1 are produced from easily accessible conjugate ynones. The case of 4-undecyn-3-one is illustrative.



To a mixture of the ynone (5.50 g, 33.1 mmol) and cyanotrimethylsilane (7 ml, 53 mmol), diethylaluminium chloride (0.6 mmol, 0.4 ml of 21% benzene solution) was added and the whole was stirred for 1 h at room temperature.[5] Excess Me_3SiCN was evaporated and the residue was treated with lithium aluminium hydride (1.30 g) in 40 ml of ether at room temperature for 1 h. After usual workup, 3-aminomethyl-4-undecyn-3-ol (5.20 g, 26.4 mmol, 80% yield) was obtained.

Alternatively, 1,1-dimethoxy-2-nonyne (507 mg, 2.8 mmol) was treated with cyanotrimethylsilane (0.4 ml, 3.0 mmol) in the presence of $BF_3 \cdot OEt_2$ (2 drops) at room temperature for 40 min.[6] The reaction mixture was concentrated and treated with lithium aluminium hydride (159 mg) in 12 ml of ether affording 2-methoxy-3-decynylamine (474 mg, 2.6 mmol, 94% yield) after usual workup. Subsequent treatment with catalytic amount of $PdCl_2$ gave 2-hexylpyrrole in 88% yield (Table 1 entry 6).

Both acyclic and cyclic conjugate ynones are easily obtained from trimethylsilylalkynes and acyl chlorides.[7,8] Accordingly synthesis described here constitutes a useful route to this group of heterocycles.

REFERENCES AND NOTES

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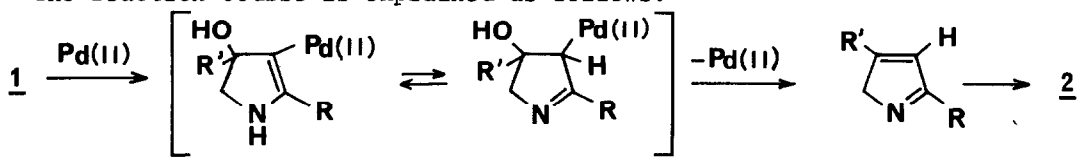
3. J-E. Bäckvall and J-E. Nyström, J. Chem. Soc., Chem. Commun., 59 (1981).
4. The reaction course is explained as follows:



5. Lewis acid catalyzed addition of Me_3SiCN to conjugate ynones will be reported by K. Utimoto, M. Inoue, Y. Wakabayashi, H. Miwa, K. Mizohata, and H. Nozaki.
6. Reaction of acetals with Me_3SiCN gave α-alkoxynitriles: K. Utimoto, Y. Wakabayashi, Y. Shishiyama, M. Inoue, and H. Nozaki, Tetrahedron Letters, accepted for publication.
7. L. Birkofer, A. Ritter, and H. Uhlenbrauck, Chem. Ber., 96, 3280 (1963).
8. K. Utimoto, M. Tanaka, M. Kitai, and H. Nozaki, Tetrahedron Letters, 2301 (1978).

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