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PALLADIUM- OR NICKEL-CATALYZED REACTION OF ALKYNES WITH TRIMETHYLSILYL CYANIDE. A NEW SYNTHESIS OF 5-AMINOPYRROLE-2-CARBONITRILES

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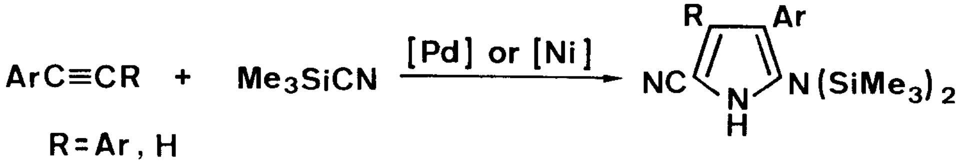
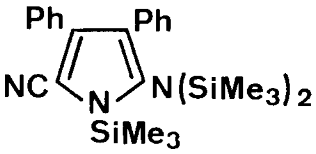
Summary: The reaction of alkynes with trimethylsilyl cyanide (**1**) in the presence of a palladium or nickel catalyst gave 5-aminopyrrole-2-carbonitriles in high yields with high regioselectivity.

In the study of a new palladium-catalyzed reaction of (**1**),[1] we have already reported that the reaction of arylacetylenes with (**1**) in the presence of $PdCl_2$/pyridine resulted in addition of (**1**) to carbon-carbon triple bond to give β-cyanoalkenylsilanes with high regio- and stereoselectivity.[2] This reaction represents the first example of the addition of (**1**) across a carbon-carbon multiple bond. We now report a new and regioselective conversion of alkynes into 5-aminopyrrole-2-carbonitriles by a palladium- or nickel-catalyzed reaction of (**1**).



In a typical procedure, a mixture of 2.5 mmol (0.45 g) of diphenylacetylene (**2a**), 15 mmol (2.0 mL) of (**1**), and 4 mol% of $PdCl_2$ (18 mg) was heated under reflux under nitrogen for 20 h. After evaporation of unreacted silyl cyanide (**1**), the residue was chromatographed on silica gel (n-hexane/EtOAc=9/1) to give 850 mg (yield 84%) of the colourless solid (**3a**)[3,4] (mp 186-187° C, from n-hexane). Product (**3a**) might have been produced by desilylation of (**4**), the initial product, through the isolation procedure. Compound (**4**) apparently consists of one molecule of diphenylacetylene and three molecules of (**1**). The use of a solvent (e.g., toluene, DMF, CH_3CN) resulted in reduced yield. The reaction without a solvent gave the best results. Although $PdCl_2$/DIBAH (i-Bu_2AlH) was not effective, other palladium complexes such as $PdCl_2$ (84%), $PdBr_2$



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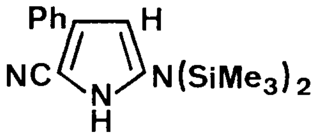

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(71%), Pd(OAc)$_2$ (79%), PdCl$_2$/pyridine (86%), (PPh$_3$)$_2$PdCl$_2$ (48%), Pd(PPh$_3$)$_4$ (62%) showed a catalytic activity. Ni(0) catalysts, NiCl$_2$/DIBAH (87%) and NiCl$_2$/Et$_3$Al (80%), were also found to be effective for this reaction, but NiCl$_2$ alone had no catalytic activity.

The results obtained for some substituted diphenylacetyles are shown in Table 1. In each case, 5-aminopyrrole-2-carbonitrile derivative was obtained in a high yield. To examine the regioselectivity of the construction of pyrrole ring, (p-methoxyphenyl)-phenylacetylene (**2d**) was employed. The reaction of (p-methoxyphenyl)phenylacetylene (**2d**) with **1** was less selective. Two regioisomers (**3d**) and (**3e**) were formed in a ratio of ca. 1:1. The reaction of di(2-thienyl)-acetylene (**2f**) gave (**3f**) in a high yield.

The palladium-catalyzed reaction of phenylacetylene (in toluene as a solvent) proceeded to produce selectively β-cyanoalkenylsilane, an addition product as previously reported.[2] In contrast, when the reaction was conducted with Ni(0) catalyst (no solvent), 5-aminopyrrole-2-carbonitrile (**3g**)[5] was obtained as a single product in a good yield (Table 2). No regioisomer (**5**) was detected in the crude reaction mixture. The regiochemistry was confirmed by the examination of ^{1}H n.m.r. (δ 6.98 ppm, =CH).[6a] As shown in Table 2, 4-aryl-5-aminopyrrole-2-carbonitriles were obtained with exclusive regioselectivity by the reaction of substituted phenylacetylenes with (**1**) with the aid of NiCl$_2$/DIBAH. In the case of 2,4,6-trimethylphenylacetylene, no reaction occured.

In summary, from the synthetic point of view, the present reaction provides a novel and regioselective method for the construction of pyrrole ring[6,7] containing useful functional groups. In contrast to the extensive studies on the Lewis acid-mediated reactions of (**1**),[8] very few studies have been carried out the transition metal-mediated reactions of (**1**).[9]

Acknowledgement

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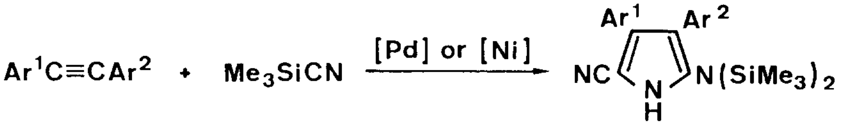
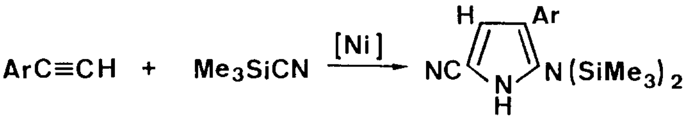
Table 1. Pd- or Ni-Catalyzed Reaction of Diarylacetylenes with Me_3SiCN (**1**)[a]



entry	Ar^1	Ar$_2$		catalyst		yield (%)[b]
1	C_6H_5	C_6H_5	(**2a**)	$PdCl_2$	(**3a**)	84
2	C_6H_5	C_6H_5	(**2a**)	$NiCl_2$/DIBAH	(**3a**)	87
3	C_6H_5	C_6H_5	(**2a**)	$NiCl_2/Et_3Al$	(**3a**)	80
4	p-$CH_3OC_6H_4$	p-$CH_3OC_6H_4$	(**2b**)	$PdCl_2$	(**3b**)	83
5	p-ClC_6H_4	p-ClC_6H_4	(**2c**)	$PdCl_2$	(**3c**)	82
6	p-$CH_3OC_6H_4$	C_6H_5	(**2d**)	$PdCl_2$	(**3d**)(**3e**)	82[c]
7	C_4H_3S	C_4H_3S	(**2f**)	$PdCl_2$	(**3f**)	75

[a] All reactions were carried out on a scale as described in the text. [b] Isolated yields based on the acetylene. [c] The ratio of the regioisomers was 46:54 as determined by GLC.

Table 2. Nickel-catalyzed reaction of arylacetylenes with Me_3SiCN (**1**)[a]



entry	Ar		catalyst		yield (%)[b]
1	C_6H_5	(**2g**)	$NiCl_2$/DIBAH	(**3g**)	58
2	C_6H_5	(**2g**)	$NiCl_2/Et_3Al$	(**3g**)	66
3	p-$CH_3OC_6H_4$	(**2h**)	$NiCl_2$/DIBAH	(**3h**)	66
4	o-$CH_3OC_6H_4$	(**2i**)	$NiCl_2$/DIBAH	(**3i**)	54
5	p-ClC_6H_4	(**2j**)	$NiCl_2$/DIBAH	(**3j**)	52

[a] In a 20 mL reaction flask was placed $NiCl_2$ (0.1 mmol, 13 mg), and then 1N DIBAH (i-Bu_2AlH) in hexane (0.2 mmol, 0.2 mL) was added. The color of the catalyst turned to black. The silyl cyanide (**1**) (15 mmol, 2.0 mL) and an arylacetylene (2.5 mmol) were added. The mixture was stirred under reflux for 20 h. The product was isolated by column chromatography on a silica gel.
[b] Isolated yields based on the acetylene.

References and Notes

(1) For a previous paper of this series; N. Chatani, T. Takeyasu, and T. Hanafusa, *Tetrahedron Lett.*, **1986**, *27*, 1849.

(2) N. Chatani and T. Hanafusa, *J. Chem. Soc., Chem. Commun.*, **1985**, 883.

(3) All new compounds reported here gave satisfactory spectral data and elemental analyses.

(4) (**3a**): mp 186-187 (n-hexane); ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 18H, SiMe), 7.09-7.27 (m, 10H, Ph), 8.80 (brs, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 1.59 (SiMe), 92.71 (CN); IR (nujol) 3330 (NH), 2200 (CN); m/z, 403 (M^+); Anal. Calcd for $C_{23}H_{29}N_3Si_2$; C, 68.43; H, 7.24; N, 10.41. Found: C, 68.66; H, 7.10; N, 10.42.

(5) (**3g**): mp 129-130 (n-hexane); ^{1}H NMR ($CDCl_3$) δ 0.08 (s, 18H, SiMe), 6.98 (d, J=3.0 Hz, 1H, =CH), [7.21 (t, J=7.3 Hz, 1H), 7.34 (t, J=7.3 Hz, 2H), 7.55 (t, J=7.3 Hz, 2H), Ph], 8.71 (brs, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 1.64 (SiMe), 94.78 (CN), 119.87 (=CH); IR (nujor): 3320 (NH), 2220 (CN); m/z, 327 (M^+); Anal. Calcd for $C_{17}H_{25}N_3Si_2$: C, 62.33; H, 7.69; N, 12.83. Found: C, 61.96; H, 7.58; N, 12.61.

(6) For recent methods for the preparation of 5-aminopyrrole-2-carbonitriles; (a) M. Jautelat and K. Ley, *Synthesis*, **1970**, 593. (b) R. Verhe, N. De Kimpe, M. Tilley, and N. Schamp, *Tetrahedron*, **1980**, *36*, 131. (c) Recently, Kusumoto, Hiyama, and Ogata have found a similar reaction independently.

(7) C. W. Bird and G. W. H. Cheesemann, 'Comprehensive Heterocyclic Chemistry', A. R. Katritzky and C. W. Rees, Eds., Pergamon Press, Oxford, 1984, Vol. 4.

(8) E. W. Colvin, 'Silicon in Organic Synthesis', Butterworths, London, 1981. W. P. Weber, 'Silicon Reagents for Organic Synthesis', Springer-Verlag, Berlin, 1983.

(9) J. J. Eisch, A. A. Aradi, and K. I. Han, *Tetrahedron Lett.*, **1983**, *24*, 2073.

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