Conversion of Alcohols into Unsymmetrical Secondary or Tertiary Amines by a Palladium Catalyst. Synthesis of *N*-Substituted Pyrroles

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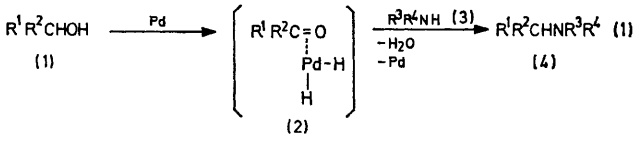
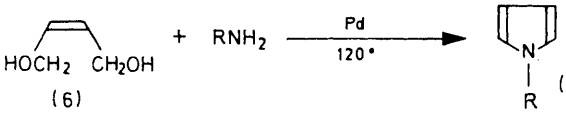
Summary The palladium-induced reaction of arylmethanols or allyl alcohols with amines provides a useful method for synthesis of secondary or tertiary amines; *N*-substituted pyrroles can be prepared by the palladium-catalysed reaction of but-2-ene-1,4-diol with primary amines in excellent yields.

WE recently reported a ready amine-exchange reaction induced by palladium catalyst.[1] We now report an efficient process for synthesis of secondary or tertiary amines from the reaction of arylmethanols or allyl alcohols with primary or secondary amines with a palladium catalyst.



This method has certain advantages over the classical reductive amination of aldehydes and ketones, where high-pressure hydrogenation conditions are normally required, and yields are often low.[2]

Reaction of benzyl alcohol (28 mmol) with n-hexylamine (30 mmol) in the presence of palladium black (0·2 g) under nitrogen at 110° for 6 h gave *N*-n-hexylbenzylamine in 98% yield. Other examples are in the Table.



a; R=CH_2CH_2OH
b; R=cyclo-C_6H_{11}
c; R=n-C_6H_{13}
d; R=Ph

N-Substituted pyrroles (**5**) can be prepared by a similar reaction. The palladium-catalysed reaction of *cis*-but-2-ene-1,4-diol (**6**) with primary amines under mild condition gave the pyrroles (**5**) in excellent yields. Although many methods (*e.g.* condensation of primary amines with 2,5-diketones,[3,4] tetrabromobutanes,[5] and 1,4-diaminobuta-1,3-dienes[6]) have been used for the synthesis of (**5**), they require 2,5-diketones or their derivatives which are normally difficult to be prepared, and the yields are often low.

In a typical case, a mixture of (**6**) (3·5 g), ethanolamine (1·2 g) and palladium black (0·1 g) was stirred at 120° for 18 h. Filtration followed by distillation gave (**5a**) (b.p. 120—130° at 90 mmHg) (87%); ν_{max} 3200 cm^{-1}; δ 6·50 (t, 2H, J 2 Hz), 6·00 (t, 2H), 3·67 (t, 2H, J 7 Hz, N-CH_2) 3·83 (t, 2H, O–CH_2), and 2·13 (s, H).

reaction (1), by analogy with the amine-exchange reaction.[1] Dehydration of the alcohol (**1**) would lead to the intermediate (**2**) which would react with (**3**) to give the corresponding Schiff base. Subsequent hydrogenation of the Schiff base with the palladium-hydride species would afford the product (**4**). The pyrroles (**5**) could be derived

TABLE. Reaction of alcohols with amines with a palladium catalyst

R^1R^2CHOH		R^3R^4NH			Product amine	
R^1	R^2	R^3	R^4	Temp./°C (time/h)	Conversion (%)	Yield (%)
H	Ph	H	n-C_6H_{13}	110(6)	35	98
H	Ph	H	Ph	80(6)	28	44(56)[a]
H	CH_2=CH	H	n-C_6H_{13}	100(12)	40	87[b]
Me	Ph	H	n-C_6H_{13}	120(18)	96	83(7)[c]
Me	Ph	–[CH_2]$_4$–		110(26)	95	83

[a] *N*-Benzylideneaniline. [b] *N*-Propylidenehexylamine. [c] α-Methylbenzylideneamine.

Similarly, reaction of (**6**) (120°; 14—20 h) with cyclohexylamine, n-hexylamine, and aniline gave (**5b**) (89%), (**5c**) (93%), and (**5d**) (46%), respectively. The *trans*-isomer of (**6**) reacts similarly with cyclohexylamine to give (**5b**) in 95% yield.

These reactions can be rationalized by the mechanism in by a similar procedure; palladium-induced intramolecular cyclization of the initially formed 4-aminobut-2-en-1-ol would give (**5**).

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† Satisfactory spectroscopic and analytical data have been obtained for all compounds.

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