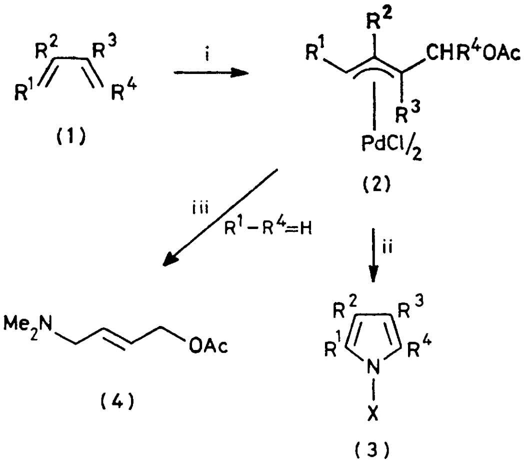
Palladium-promoted 1,4-Cycloamination of 1,3-Dienes to Pyrroles

By JAN-E. BÄCKVALL* and JAN-E. NYSTRÖM

(*Department of Organic Chemistry, Royal Institute of Technology, S-*100 44 *Stockholm, Sweden*)

Summary 1,3-Dienes react with palladium(II) chloride and acetic acid with the formation of 4-acetoxy-alk-2-enylpalladium complexes (**2**), which on reaction with primary amines give *N*-alkylpyrroles.

WE have recently been concerned with palladium-promoted functionalization of alkenes and 1,3-dienes involving carbon–nitrogen bond formation to give amino-alcohol derivatives, aziridines and diamines.[1–3] The 1,4-diamination of buta-1,3-diene proceeds through an intermediate 4-aminobut-2-enylpalladium complex, which under the reaction conditions adds a second molecule of amine to give the 1,4-diaminobut-2-ene.[3] By a similar route 1-alkoxy-4-amino-2-alkenes were obtained.[3,4] We have now found that 1,3-dienes can be transformed into 1-acetoxy-4-amino-2-alkenes in an analogous palladium-promoted reaction and, more importantly, when primary amines are utilized, the resulting amino-acetates undergo a spontaneous palladium-catalysed cyclization to pyrroles.



Scheme 1. Reagents: i, $PdCl_2$, HOAc, $CuCl_2$; ii, XNH_2, $AgBF_4$ (1 equiv.), PPh_3 (0·1 equiv.), $Cu(BF_4)_2$ (1 equiv.); iii, $AgBF_4$, Me_2NH.

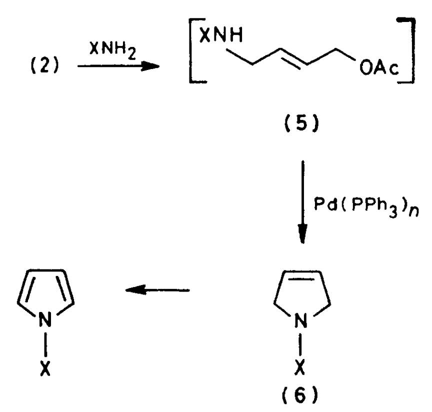
Reaction of the dienes (**1**) with palladium(II) chloride and copper(II) acetate in acetic acid gave the stable π-allylpalladium complexes (**2**) in high yield.† Treatment of (**2**; R^1—R^4 = H) with $AgBF_4$ (−30 °C) in tetrahydrofuran (THF), followed by reaction with dimethylamine (0 °C), gave (*E*)-1-acetoxy-4-dimethylaminobut-2-ene (**4**) in 40% yield. A small amount of 1,4-bis(dimethylamino)but-2-ene (4%) was also formed, most likely *via* a palladium-catalysed substitution of the acetoxy-group in (**4**) by amine.[5] When triphenylphosphine was present in the reaction mixture the diamine was the sole product. When (**2**, R^1—R^4 = H) was treated with a primary amine in the presence of 1 equiv. of AgBF and 0·1 equiv. of triphenylphosphine, neither amino-acetate nor diamine could be isolated but the main product in this case was the pyrrole (**3**, R^1—R^4 = H) (Scheme 1). Results for cycloamminations of various dienes (**1**) are given in the Table.

Table. 1,4-Cycloamination of the dienes (**1**) with the amines XNH_2 *via* the π-allylpalladium complexes (**2**).[a]

R^1	R^2	R^3	R^4	% Yield of (**2**)	X	% Yield of (**3**)[b]
H	H	H	H	100	$PhCH_2$	54 (45)[c]
					Et	40
H	Me	H	H	95	$PhCH_2$	20[c]
					Et	13
H	Me	Me	H	88	$PhCH_2$	14
Me	H	H	Me	70	,,	22
Me	H	H	H	85	,,	24

[a] To the appropriate π-allyl complex (**2**) (1 mmol on Pd) in THF (4 ml) at −30°C were added PPh_3 (0·1 mmol), $PhCH_2NH_2$ (4 mmol), and $AgBF_4$ (1 mmol); upon allowing the mixture to warm to room temperature, palladium black was formed. After 1 h $Cu(BF_4)_2$ (1 mmol) and $PhCH_2NH_2$ (2 mmol) were added and the mixture was stirred for another hour. The isolated products were obtained after concentration and kugelrohr distillation of the mixture. [b] Based on the corresponding π-allyl complex (**2**), and determined by g.l.c. unless otherwise stated. [c] Isolated yield after kugelrohr distillation and filtration through a short column of silica.

The reactions of (**2**) to give the pyrroles (**3**) most probably proceed through a 4-amino-acetate (**5**) which is the expected product from nucleophilic addition of amine to the allyl group.[3,6] If the nucleophile is a secondary amine, *e.g.* dimethylamine, the amino-acetate (**4**) can be isolated. It is well known that allylic acetates react with amines in the presence of palladium(0) catalysts to give allylic amines.[5] Thus, an intramolecular reaction of this type with amine (**5**) would result in cyclization to the pyrroline (**6**) which in fact was detected by g.l.c.–mass spectroscopy in some of the reactions. The pyrroline is then oxidized, probably by palladium(II), to the pyrrole. If no other oxidant is used the yield of pyrrole, based on palladium(II), is theoretically limited to 50%. Addition of co-oxidants, *e.g.* $Cu(BF_4)_2$, increases the yield of pyrrole in most cases.



Scheme 2.

For steric reasons it seems that cyclization of (**5**) would require a (*Z*)-configuration around the double bond. Since (**5**) formed by amination of (**2**) is most likely to be present mainly as the (*E*)-isomer, (*E*) to (*Z*) isomerization of the double bond probably occurs. An alternative explanation is that *syn–anti* isomerization takes place in the intermediate π-allylpalladium complex, presumably formed in the cyclization of (**5**).

N-Benzylpyrrole has been prepared from (*Z*)-but-2-ene-1,4-diol and benzylamine in a palladium-catalysed reaction (Pd black; 120 °C).[7] At first glance there appears to be some resemblance between the mechanism of this reaction and the cyclization presented here. However, two different mechanisms are probably operating in the two systems: a dehydrogenation to aldehyde in the butenediol case[7] and a π-allylpalladium complex formation in our case.

Pyrroles are an important class of heterocyclic compounds for which there is a demand for simple synthetic methods.[8] Most procedures for their preparation, however, start from 1,4-dicarbonyl systems.[8]‡ The simple starting materials used here, 1,3-dienes, should make the present

---

† The procedure described by Rowe and White was used: J. M. Rowe and D. A. White, *J. Chem. Soc.*, 1967, 1451.

‡ Recently, a method starting from 1,2-diones, *via* palladium-catalysed reactions was reported: B. M. Trost and E. Keinan, *J. Org. Chem.*, 1980, **45**, 2741.

procedure useful for pyrrole synthesis, expecially in view of the great number of recently developed simple 1,3-diene syntheses.[9]

We thank the Swedish Natural Science Research Council and 'Stiftelsen Bengt Lundqvists minne' for financial support.

(*Received*, 20*th October*, 1980; *Com.* 1129.)

[1] J. E. Bäckvall and E. E. Björkman, *J. Org. Chem.*, 1980, **45**, 2893; J. E. Bäckvall, *Tetrahedron Lett.*, 1975, 2225.

[2] J. E. Bäckvall, *Tetrahedron Lett.*, 1978, 163; *J. Chem. Soc., Chem. Commun.*, 1977, 413.

[3] B. Åkermark, J. E. Bäckvall, A. Löwenborg, and K. Zetterberg, *J. Organomet. Chem.*, 1979, **166**, C33.

[4] B. Åkermark, J. E. Bäckvall, and K. Zetterberg, unpublished results.

[5] K. E. Atkins, W. E. Walker, and R. M. Manyik, *Tetrahedron Lett.*, 1970, 3821; K. Takahashi, A. Miyake, and G. Hata, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 230; B. M. Trost and J. P. Gênet, *J. Am. Chem. Soc.*, 1976, **98**, 8516.

[6] B. Åkermark and K. Zetterberg, *Tetrahedron Lett.*, 1975, 3733.

[7] S. Murahashi, T. Shimamura, and I. Moritani, *J. Chem. Soc., Chem. Commun.*, 1974, 931.

[8] R. A. Jones and G. P. Bean, 'The Chemistry of Pyrroles,' Academic Press, London, 1977.

[9] R. C. Larock and B. Riefling, *J. Org. Chem.*, 1978, **43**, 1468 and references cited therein; V. V. R. Rao, C. V. Kumar, and D. Devaprabhakara, *J. Organomet. Chem.*, 1979, **179**, C7; J. B. Cambell, Jr. and H. C. Brown, *J. Org. Chem.*, 1980, **45**, 549; B. M. Trost and J. M. Fortunak, *J. Am. Chem. Soc.*, 1980, **102**, 2841; I. Shimizy, T. Yamada, and J. Tsuji, *Tetrahedron Lett.*, 1980, **21**, 3199 and references cited therein.