

Arylation of *N*-Acyl-pyrroles and -indoles with Arenes and Palladium Acetate

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Summary Treatment of 1-benzoylpyrroles with palladium acetate in acetic acid containing benzene gave mixtures of 1-benzoyl-2-phenylpyrroles; similar treatment of 1-acetylindoles gave the corresponding 1-acetyl-2-phenylindoles.

ARYL-PYRROLES and -INDOLES are of interest in connection with the existence of naturally occurring compounds such as 3,4,5-tribromo-2-(3,5-dibromo-2-hydroxyphenyl)pyrrole.¹ However, thus far little attention has been paid to the arylation of pyrroles and indoles as an efficient method for their synthesis; *e.g.*, hardly any reports of *C*-phenylation of pyrroles have, to our knowledge,² been published, except that the reaction of 1-methylpyrrol-2-ylcopper with iodobenzene was reported to afford 1-methyl-2-phenylpyrrole.³ Consequently *C*-aryl pyrroles² and -indoles⁴ have usually been prepared by ring-synthesis. The present paper deals

with a new simple method for the arylation of pyrroles and indoles.

The arylation of olefins⁵ and coupling reactions of aromatic compounds⁶ with palladium(II) salts have been extensively investigated. We have previously reported two oxidations with palladium acetate in acetic acid, namely the 2,2'-dimerization of 1-benzoylpyrroles⁷ and the intramolecular ring-closure of 1-benzoylindoles.⁸ We now report that the oxidation of 1-benzoylpyrroles and 1-acetylindoles with palladium acetate in acetic acid containing arenes resulted in a coupling reaction between the substrates and the arenes.

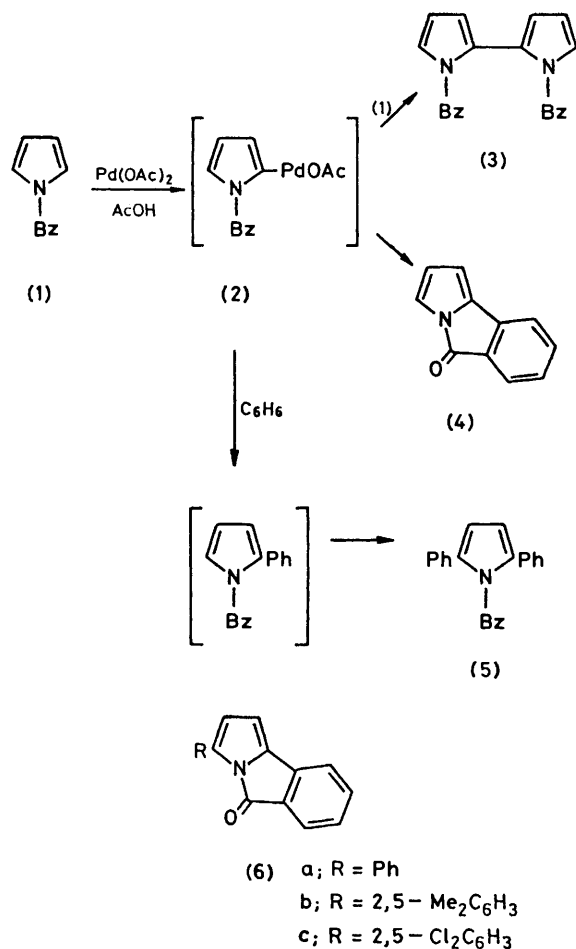
Oxidation of 1-benzoylpyrrole (**1**) in acetic acid with 0.34 equiv. of Pd(OAc)₂ gave the 2,2'-bipyrrole (**3**),⁷ whereas oxidation of (**1**) with 1.0 equiv. of Pd(OAc)₂ gave the ring-closed compound (**4**), m.p. 86–86.5 °C, as the main product.† Furthermore, oxidation of (**1**) in acetic acid

TABLE. Arylation of 1-benzoylpyrroles and 1-acetylindoles with arenes and palladium acetate.^a

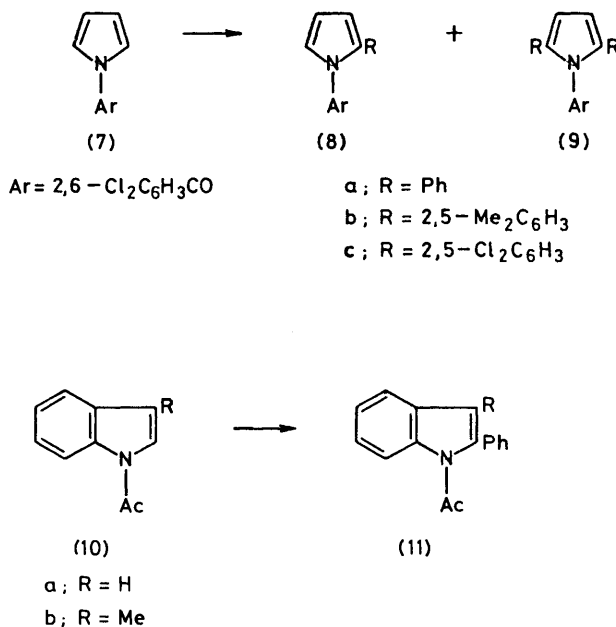
Substrate (1 mmol)	Pd(OAc) ₂ /mmol	AcOH ml	Arene (ml)	<i>t</i> /h	Conversion /%	Products; Isolated yields/% ^b
(1)	0.34	50		10	64	(3),47; (4), trace
(1)	1.0	50		14	92	(3),13; (4), 30
(1)	1.0	25	C ₆ H ₆ (25)	14	88	(3),8; (5),25; (6a), 20
(1)	1.0	25	<i>p</i> -Me ₂ C ₆ H ₄ (25)	14	90	(3),12; (6b),28
(1)	1.0	40	<i>p</i> -Cl ₂ C ₆ H ₄ (10)	14	90	(3),18; (6c),15
(7)	1.5	25	C ₆ H ₆ (25)	14	83	(9a),81
(7)	1.0	25	<i>p</i> -Me ₂ C ₆ H ₄ (25)	14	72	(8b),12 ^c ; (9b),36 ^c
(7)	1.0	40	<i>p</i> -Cl ₂ C ₆ H ₄ (10)	14	70	(8c),30
(10a)	1.0	25	C ₆ H ₆ (25)	14	77	(11a),22
(10b)	1.0	25	C ₆ H ₆ (25)	14	50	(11b),48

^a All reactions performed at reflux temperature. ^b Yield based on pyrroles (**1**) and (**7**), or indoles (**10**) consumed. ^c Yield determined by ¹H n.m.r. spectroscopy.

† All new compounds were fully characterized by ¹H n.m.r., i.r., and mass spectroscopy, and by elemental analysis.



137–138 °C, in high yield (81%) and no ring-closed compounds were obtained. Similarly, treatment of (7) with $\text{Pd}(\text{OAc})_2$ in AcOH -*p*-xylene and in AcOH -*p*-dichlorobenzene gave arylated compounds of the types (8) and (9), *i.e.*, (8b), m.p. 114–115 °C, (8c), m.p. 160–162 °C, and (9b), m.p. 122–123 °C. These results are summarized in the Table. Under our conditions, oxidation of 1-acetylpyrrole, 1-phenoxy-carbonylpyrrole, and 1-methylpyrrole with $\text{Pd}(\text{OAc})_2$ in AcOH -benzene gave complex reaction mixtures.



containing benzene gave the 2-phenylpyrroles (5), m.p. 153–154 °C, and (6a), m.p. 114.5–115.5 °C. A typical reaction was performed as follows. A solution of (1) (1.0 mmol) and $\text{Pd}(\text{OAc})_2$ (1.0 mmol) in acetic acid (25 ml) containing benzene (25 ml) was stirred at 80 °C under nitrogen for 14 h. The mixture was evaporated to give a dark brown oily residue which was chromatographed on silica gel to give (5) and (6a). Treatment of (1) with $\text{Pd}(\text{OAc})_2$ in AcOH -*p*-xylene or in AcOH -*p*-dichlorobenzene gave the ring-closed products (6b), m.p. 99–100 °C, and (6c), m.p. 170–171 °C, respectively, but contrary to our expectation no other arylated compounds were obtained.

In an attempt to avoid ring-closure, the arylation of 1-(2,6-dichlorobenzoyl)pyrrole (7), m.p. 121.5–122.5 °C, was investigated. Treatment of (7) with $\text{Pd}(\text{OAc})_2$ in AcOH -benzene gave the expected product (9a), m.p.

Oxidation of 1-benzoylindole with $\text{Pd}(\text{OAc})_2$ in AcOH -benzene gave a ring-closed compound⁸ but no phenylated products were obtained. On the other hand, treatment of 1-acetylindoles (10) with $\text{Pd}(\text{OAc})_2$ in AcOH -benzene gave the expected corresponding products (11a), oil, b.p. (8 Torr) 200 °C, and (11b), m.p. 80.5–81.5 °C.

We further found that hydrolysis of 1-benzoyl-2-arylpyrroles and 1-acetyl-2-phenylindoles gave the corresponding 2-aryl-1H-pyrroles and 2-phenyl-1H-indoles, respectively, in good yields (55–95%); *e.g.*, treatment of (9a) with NaOH in EtOH-H₂O at 70 °C for 7 h gave 2,5-diphenylpyrrole, providing additional evidence for the structure of (9a).

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² For a review see R. A. Jones and G. P. Bean, 'The Chemistry of Pyrroles,' Academic Press, New York, 1977.

³ N. Gros and S. Gronowitz, *Acta Chem. Scand.*, 1971, **25**, 2595.

⁴ For a review see R. J. Sundberg, 'The Chemistry of Indoles,' Academic Press, New York, 1970.

⁵ P. M. Maitlis, 'The Organic Chemistry of Palladium,' Academic Press, New York, 1971, Vol. 2, pp. 9–16; F. Akiyama, H. Miyazaki, K. Kaneda, and S. Teranishi, *J. Org. Chem.*, 1980, **45**, 2359 and references therein.

⁶ P. M. Maitlis, 'The Organic Chemistry of Palladium,' Academic Press, New York, 1971, vol. 2, pp. 60–70.

⁷ T. Itahara, *J. Chem. Soc., Chem. Commun.*, 1980, 49.

⁸ T. Itahara, *Synthesis*, 1979, 151.