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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-2phenylindoles.

ARVL-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 $olefins^5$ 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-benzoylpyrroles.⁸ We now report that the oxidation of 1-benzoylpyrroles and 1acetylindoles 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 ringclosed 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.

Substrate (1 mmol)	Pd(OAc) ₂ /mmol	AcOH ml	Arene (ml)	t/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	$C_{e}H_{e}$ (25)	14	88	(3), 8: (5), 25; (6a), 20
(1)	1.0	25	$p - Me_2 C_6 H_4$ (25)	14	90	(3),12; (6b),28
(1)	1.0	40	$p - Cl_2 C_8 H_4 (10)$	14	90	(3),18; (6c),15
(7)	1.5	25	$C_{B}H_{B}(25)$	14	83	(9a),81
(7)	1.0	25	$p - Me_2C_6H_4$ (25)	14	72	(8b),12°; (9b),36°
(7)	1.0	40	p-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.



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 Pd(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 Pd(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 Pd(OAc)₂ in AcOH-benzene gave the expected product (9a), m.p.

137-138 °C, in high yield (81%) and no ring-closed compounds were obtained. Similarly, treatment of (7) with Pd(OAc)₂ in AcOH-p-xylene and in AcOH-p-dichlorobenzene gave any lated 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-phenoxycarbonylpyrrole, and 1-methylpyrrole with Pd(OAc)₂ in AcOH-benzene gave complex reaction mixtures.



Oxidation of 1-benzoylindole with Pd(OAc), in AcOHbenzene gave a ring-closed compound⁸ but no phenylated products were obtained. On the other hand, treatment of 1-acetylindoles (10) with $Pd(OAc)_2$ 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-2arylpyrroles 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 2,5diphenylpyrrole, providing additional evidence for the structure of (9a).

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