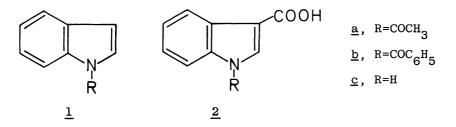
CARBOXYLATION OF 1-ACYLINDOLES WITH CARBON MONOXIDE AND PALLADIUM ACETATE IN THE PRESENCE OF SODIUM PEROXYDISULFATE

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A treatment of 1-acylindoles with palladium acetate and sodium peroxydisulfate under a carbon monoxide atmosphere gave the corresponding l-acylindole-3-carboxylic acids.

Recently increasing interest is being shown in methods for using C_1 compounds such as carbon monoxide and carbon dioxide. It is well known that 1-indoly1magnesium halides react with carbon dioxide to afford indole-3-carboxylic acids. 1) On the other hand, little attention has been paid to carbonylation of indoles with carbon monoxide, although the carbonylation of olefins 2) and aromatic compounds³⁾ with carbon monoxide and palladium(II) salts has been reported. These observations and our interest in connection with reactions of 1-acylindoles⁴⁾ led us to examine a treatment of indoles with carbon monoxide and palladium acetate.



While a treatment of 1-methylindole with palladium acetate under a carbon monoxide atmosphere gave a complex reaction mixture, treatments of 1-acetylindole $(\underline{1a})$ and of 1-benzoylindole $(\underline{1b})$ under similar conditions resulted in a carboxylation at 3-position of \underline{la} and of \underline{lb} to afford 1-acetylindole-3-carboxylic acid $(2a)^{5}$ and 1-benzoylindole-3-carboxylic acid $(2b)^{5}$, respectively. It was further found that sodium peroxydisulfate was remarkably effective for the carboxylation of $\underline{l}\underline{a}$ and of $\underline{l}\underline{b}$ with carbon monoxide and palladium acetate. The reaction was performed as follows. Carbon monoxide was bubbled for 7h at reflux temperature through a solution of <u>1b</u> containing palladium acetate and sodium peroxydisulfate in acetic acid. The reaction mixture was evaporated to give a brown semicrystalline residue which was chromatographed on silica gel to give 1b and 2b. These results are summarized in Table.

A treatment of $\underline{2a}$ with NaOH in EtOH-H₂O at 70° for 4h gave indole-3-carboxylic acid ($\underline{2c}$), dec. 218-223°(lit.) dec. 220-224°), at 95% yield, providing an

additional evidence for the structure of $\underline{2a}$. Furthermore, a treatment of 2-substituted 1-acylindole such as $(\underline{3})^6$ with palladium acetate and sodium peroxydisulfate under a carbon monoxide atmosphere afforded the corresponding indole-3-carboxylic acid such as $(4)^5$.

Table. Carboxylation of 1-acylindoles with palladium acetate and sodium peroxydisulfate under a carbon monoxide atmosphere^{a)}

Indoles	Na ₂ S ₂ O ₈	Recovered Indoles and Products	Yields of $\underline{2}$ or $\underline{4}$
(mmol)	mmol	(mmol)	% yield ^{b)} (Conv. %): % yield ^c
<u>la</u> (2)		<u>la</u> (1.30), <u>2a</u> (0.10)	14 (35) 10
<u>la</u> (2)	3	1a (0.48), 2a (0.56)	37 (76) 56
<u>lb</u> (2)		1b (1.52), 2b (0.38)	79 (24) 38
<u>lb</u> (2)	3	<u>lb</u> (0.42), <u>2b</u> (1.24)	78 (79) 124
<u>3</u> (1)	1	$\underline{3}$ (0.18), $\underline{4}$ (0.55)	67 (82) 55

a) Conditions used in all experiments: indoles, $Pd(OAc)_2$ (1 mmol), AcOH (40 ml), reflux temperature, CO bubbling, 7h reaction. b) Yield based on the substrate $\underline{1}$ or $\underline{3}$ consumed. c) Yield based on $Pd(OAc)_2$ used.

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- 5) Spectral data of 2a, 2b, and 4. 2a: mp. 237-240°, IR(Nujo1) 3300-2300, 1740, 1700 cm⁻¹; 1 H-NMR(CD₃SOCD₃) 52.79(s, 3H), 7.40-7.64(m, 2H), 8.22-8.70(m, 3H): MS m/e 203(M⁺), 161, 144. 2b: mp. 238-241°; IR(Nujo1) 3300-2300, 1695, 1675 cm⁻¹; 1 H-NMR(CD₃SOCD₃) 57.30-8.06(m, 7H), 8.24-8.60(m, 3H); MS m/e 265(M⁺), 105. 4: mp.>280°; IR(Nujo1) 3300-2300, 1760-1720, 1680 cm⁻¹; 1 H-NMR(CD₃SOCD₃) 57.35-8.54(m, 8H); MS m/e 263(M⁺), 219, 190.
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