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

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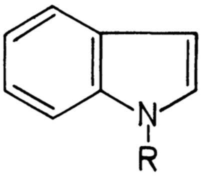
A treatment of 1-acylindoles with palladium acetate and sodium peroxydisulfate under a carbon monoxide atmosphere gave the corresponding 1-acylindole-3-carboxylic acids.

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-indolylmagnesium 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 olefins2) 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.



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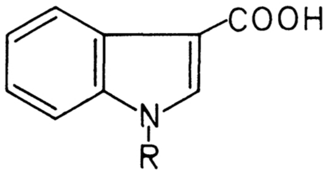

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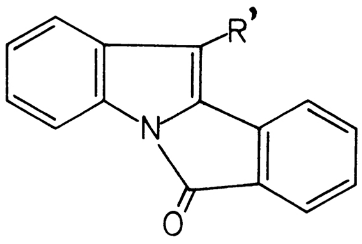
a, R=$COCH_3$
b, R=COC_6H_5
c, R=H

While a treatment of 1-methylindole with palladium acetate under a carbon monoxide atmosphere gave a complex reaction mixture, treatments of 1-acetylindole (1a) and of 1-benzoylindole (1b) under similar conditions resulted in a carboxylation at 3-position of 1a and of 1b 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 1a and of 1b 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 1b 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 2a with NaOH in EtOH-H_2O at 70° for 4h gave indole-3-carboxylic acid (2c), dec. 218-223° (lit.1) dec. 220-224°), at 95% yield, providing an additional evidence for the structure of 2a. Furthermore, a treatment of 2-substituted 1-acylindole such as (3)$^{6)}$ with palladium acetate and sodium peroxydisulfate under a carbon monoxide atmosphere afforded the corresponding indole-3-carboxylic acid such as (4)$^{5)}$.



3, R'=H

4, R'=COOH

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

Indoles (mmol)	$Na_2S_2O_8$ mmol	Recovered Indoles and Products (mmol)	Yields of 2 or 4 % yield$^{b)}$ (Conv. %):	% yield$^{c)}$
1a (2)	——	1a (1.30), 2a (0.10)	14 (35)	10
1a (2)	3	1a (0.48), 2a (0.56)	37 (76)	56
1b (2)	——	1b (1.52), 2b (0.38)	79 (24)	38
1b (2)	3	1b (0.42), 2b (1.24)	78 (79)	124
3 (1)	1	3 (0.18), 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 1 or 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(Nujol) 3300-2300, 1740, 1700 cm^{-1}; ^1H-NMR(CD_3SOCD_3) δ 2.79(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(Nujol) 3300-2300, 1695, 1675 cm^{-1}; ^1H-NMR(CD_3SOCD_3) δ 7.30-8.06(m, 7H), 8.24-8.60(m, 3H); MS m/e 265(M^+), 105. 4: mp.>280°; IR(Nujol) 3300-2300, 1760-1720, 1680 cm^{-1}; ^1H-NMR(CD_3SOCD_3) δ 7.35-8.54 (m, 8H); MS m/e 263(M^+), 219, 190.

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