OXIDATION OF 1-BENZOYLPYRROLE AND 1-AROYLINDOLES BY PALLADIUM ACETATE

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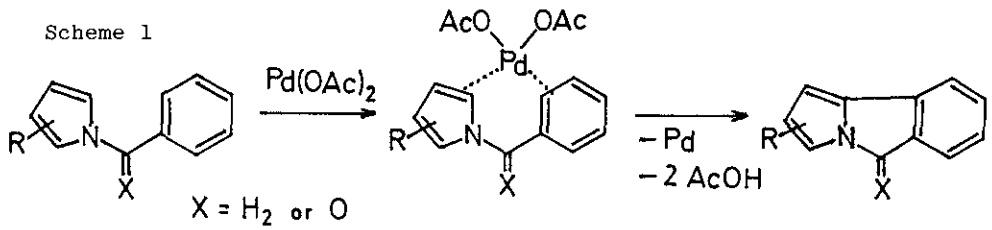
Abstract - Oxidation of 1-benzoylpyrrole and 1-aroylindoles by palladium acetate in acetic acid gave the corresponding ring-closed products and dimerized compounds.

Oxidative coupling of arenes and olefins by palladium(II) salts is well known as a useful method for synthesis of aryl-substituted olefins.[1] Oxidation of olefinic compounds linked through carbon unit to aryl groups by palladium(II) salts is, therefore, expected to result in intramolecular ring-closure. The reaction is applicable to synthesis of polycyclic heterocycles. Furthermore, we have already reported the intermolecular oxidative coupling of aromatic heterocycles such as 1-substituted pyrroles and indoles and arenes by palladium(II) acetate.[2] These observations led us to examine ring-closure of 1-benzyl- and 1-benzoylpyrrole and indoles by palladium(II) acetate, depicted in Scheme 1.

Scheme 1

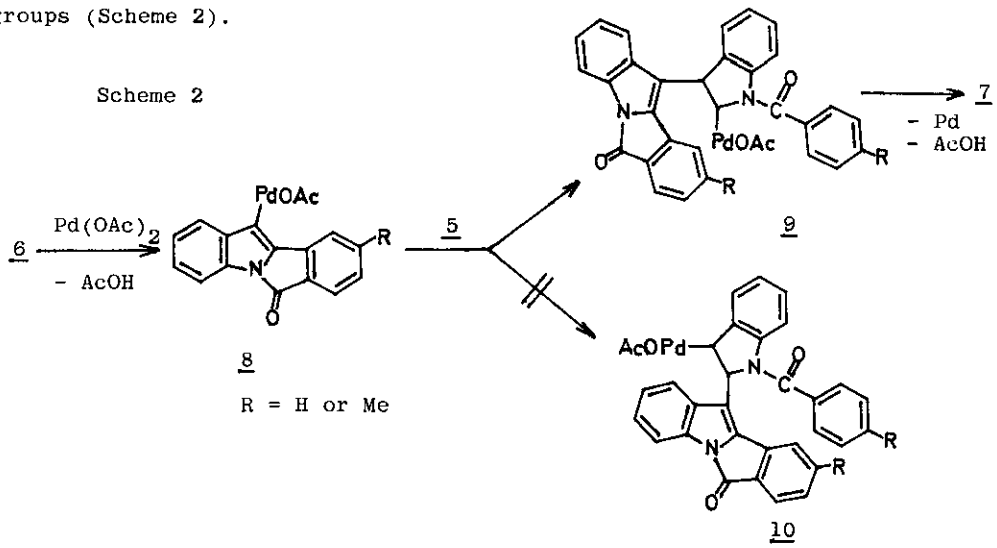


Although oxidation of 1-benzylpyrrole and -indole by palladium acetate in acetic acid gave complex reaction mixtures, the treatment of 1-benzoylpyrrole and 1-aroylindoles gave expected ring-closed products together with dimerized compounds. This paper describes the oxidation of 1-benzoylpyrrole and 1-aroylindoles such as 1-benzoyl-, 1-(4-methylbenzoyl)-, 1-(1-naphthoyl)-, and 1-(2-naphthoyl)-indoles. Treatment of 1-benzoylpyrrole (1) with palladium acetate in acetic acid gave a ring-closed product (2),[3] dimerized compounds (3)[2] and (4), and benzoic acid.

Similar treatment of 3 gave 4, providing an evidence for the structure of 4. Reaction of 1-benzoylindole (5a) with palladium acetate in acetic acid gave a ring-closed product (6a),[4] a dimerized compound (7a), and benzoic acid. The compound 6a had previously been prepared by the irradiation of N-(2-methylphenyl)-phthalimide[5] and of 1-(2-iodobenzoyl)indole[6]. The structure of 7a was confirmed by the elemental analysis, the molecular weight (mass spectrometry), and nmr and ir data. The nmr spectrum showed no indole C-3H signal and ir showed two types of CO absorption at 1715 and 1690 cm^{-1}, while that of 5a[4] is 1680 and 6a[4] is 1720 cm^{-1}. These data suggest that the structure of the dimerized compound is 7a. Under similar conditions, the oxidation of 1-(4-methylbenzoyl)indole (5b) also gave (6b),[4] (7b), and 4-methylbenzoic acid.

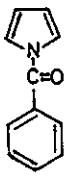
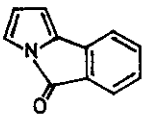
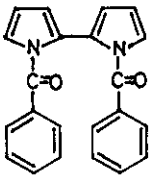
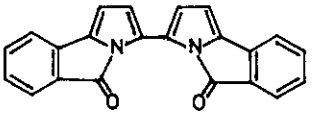
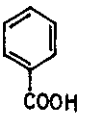
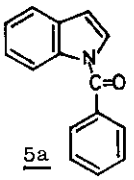
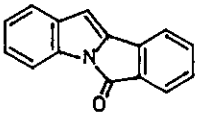
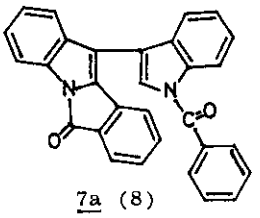
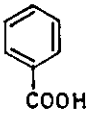
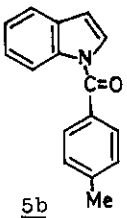
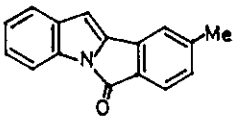
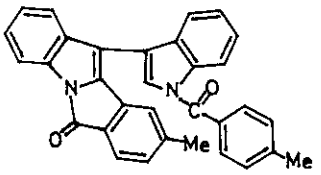
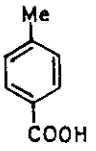
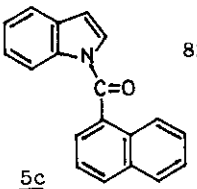
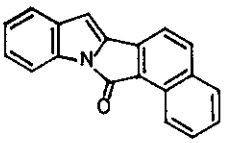
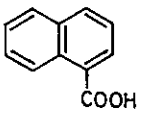
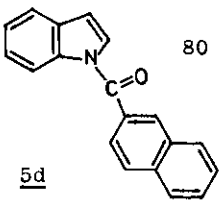
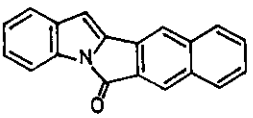
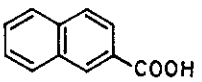
We reported that the alkenylation of 1-substituted indoles with olefins and palladium acetate occurred at the 3-position of indoles[7] while the reaction of 1-acetylindole with palladium acetate in the presence of arenes resulted in arylation at 2-position of the indole[2]. The oxidation of 1-benzoylindoles with palladium acetate gave 3,3'-dimerized compounds 7a and 7b, although 2,2'-dimerized products were obtained from 1-benzoylpyrrole. A plausible mechanism for the formation of 7 is as follows; a palladium σ-complex (8) formed from 6 and $Pd(OAc)_2$ reacts with 5 to give (9) but not (10) because of steric effects[8] of 1-aroyl groups (Scheme 2).

Scheme 2



Ring-closure of 1-(1-naphthoyl)indole (5c) and 1-(2-naphthoyl)indole (5d) was further investigated. The oxidation of 5c with palladium acetate gave an expected ring-closed compound (6c) and 1-naphthoic acid. The reaction of 5d also gave (6d)

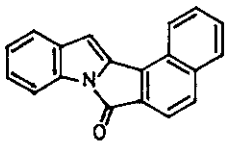
Table 1. Oxidation of 1-Benzoylpyrrole and 1-Aroylindoles by Palladium Acetate[a)]

Substrate	Conv. %	Products (yield based on substrate consumed, %)			
 1	87	 2 (28)	 3 (15)	 4 (3)	 (44)
 5a	85	 6a (45)	 7a (8)		 (40)
 5b	88	 6b (43)	 7b (8)		 (35)
 5c	82	 6c (34)		 (37)	
 5d	80	 6d (34)		 (52)	

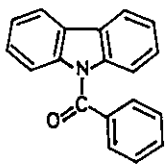
a) Conditions used in all experiments: substrate (1 mmol) and $Pd(OAc)_2$ (1 mmol) in AcOH (40 ml) at 100-110 °C for 7 h under nitrogen.

and 2-naphthoic acid. The nmr data suggest that the ring-closed product from 5d is 6d but not (6e). These results are summarized in Table 1.

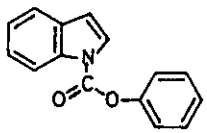
Under similar conditions, no reaction occurred in the case of 1-benzoylcarbazole (11). On the other hand, 1-phenoxycarbonylindole (12) reacted with palladium acetate to give complex reaction mixtures.



6e



11



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EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Proton magnetic resonance spectra were obtained with a JEOL PMX60A spectrometer with tetramethylsilane as an internal standard. Infrared spectra were measured with a JASCO IRA-1 spectrometer. Mass spectra were obtained with a JEOL JMS-D300 spectrometer. The elemental analyses were performed by the Analytical Center of Kyoto University. 1-Benzoylpyrrole (1),[9] 1-benzylpyrrole,[10] 1-benzoylindole (5a),[4] 1-(4-methylbenzoyl)indole (5b),[4] 1-benzylindole,[11] and 1-benzoylcarbazole (11)[12] were prepared according to the procedure described before.[2,4,7,8]

1-(1-Naphthoyl)indole (5c)

To a stirred solution of indole (50 mmol) and sodium hydride (50 mmol) in dimethylformamide (DMF) (150 ml), 1-naphthoyl chloride (50 mmol) in DMF (50 ml) was added under nitrogen atmosphere. The solution was heated at 70 °C for 20 h. The reaction mixture was poured into water and extracted with benzene. The benzene extract was dried with sodium sulfate and evaporated to give a brown oily residue. The residue was chromatographed on a silica gel with hexane/benzene to give 5c (41 % yield); mp 84.5-85.5 °C: IR (Nujol) 1690 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ 6.47(d, 1H, J=4 Hz), 6.95 (d, 1H, J=4 Hz), 7.23-8.1(m, 10H), 8.4-8.6(m, 1H). Anal. Calcd for $C_{19}H_{13}NO$: C, 84.11; H, 4.83; N, 5.16. Found: C, 84.34; H, 4.72; N, 5.21.

1-(2-Naphthoyl)indole (5d)

This compound was prepared in 68 % yield from indole and 2-naphthoyl chloride according to the procedure described above; mp 156.5-157.5 °C: IR (Nujol) 1680 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ 6.59(d, 1H, J=4 Hz), 7.16-8.06(m, 10H), 8.20(s, 1H), 8.3-8.5 (m, 1H). Anal. Calcd for $C_{19}H_{13}NO$: C, 84.11; H, 4.83; N, 5.16. Found: C, 84.37;

H, 4.72; N, 5.08.

1-Phenoxycarbonylindole (12)

To a stirred solution of indole (50 mmol) and sodium hydride (50 mmol) in DMF (150 ml), phenyl chloroformate (50 mmol) in DMF (50 ml) was added under nitrogen. The solution was heated at 70 °C for 20 h. The reaction mixture was poured into water and extracted with benzene. The extract was evaporated to give a brown oily residue. The residue was chromatographed on silica gel with hexane/benzene to give 12 (52 % yield); mp 95-96 °C: IR (Nujol) 1755 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ6.67 (d, 1H, J=5 Hz), 7.16-7.7(m, 8H), 7.75(d, 1H, J=5 Hz), 8.17-8.41(m, 1H). Anal. Calcd for $C_{15}H_{11}NO_2$: C, 75.93; H, 4.67; N, 5.90. Found: C, 76.07; H, 4.79; N, 5.81.

General Procedure for Oxidation of 1-Benzoylpyrrole and 1-Aroylindoles by Palladium Acetate

A solution of 1-benzoylpyrrole or 1-aroylindoles (1 mmol) and palladium acetate (1 mmol) in acetic acid (40 ml) was heated at 100-110 °C under nitrogen for 7 h. The reaction mixture was evaporated to give an oily residue which was then chromatographed by silica gel TLC, developed with benzene or chloroform, to give ring-closed products and dimerized compounds. These results are summarized in Table 1. The products 3,[2] 6a,[4] and 6b[4] were already reported. The spectral and analytical data of the other products are given below.

5H-Pyrrolo[2,1-a]isoindol-5-one (2)

Mp 86-86.5 °C: IR (Nujol) 1760, 1615 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ6.18(s, broad, 2H), 6.9-7.75(m, 5H): MS m/z (%) 170(M^++1, 13), 169(M^+, 100), 140(19), 114(21). Anal. Calcd for $C_{11}H_7NO$: C, 78.09; H, 4.17; N, 8.28. Found: C, 78.09; H, 4.08; N, 8.32.

3,3'-Bis(5H-pyrrolo[2,1-a]isoindol-5-one) (4)

Mp >300 °C: IR (Nujol) 1750, 1720(sh), 1610 cm^{-1}: MS m/z (%) 338(M^++2, 4), 337 (M^++1, 25), 336(M^+, 100), 279(13), 168(13). Proton nmr data could not obtained because 4 was not sufficiently soluble in $CDCl_3$, CD_3COCD_3, CD_3SOCD_3, and C_6D_5N. Anal. Calcd for $C_{22}H_{12}N_2O_2$: C, 78.56; H, 3.60; N, 8.33; O, 9.51. Found: C, 78.18; H, 3.64; N, 8.35; O, 9.12.

11-(1-Benzoylindol-3-yl)-6H-isoindolo[2,1-a]indol-6-one (7a)

Mp 194-196 °C: IR (Nujol) 1715, 1690, 1610 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ6.8-7.9(m, 17H), 8.15-8.45(m, 1H): MS m/z (%) 439(M^++1, 12), 438(M^+, 36), 106(8), 105(100), 77(22). Anal. Calcd for $C_{30}H_{16}N_2O_2$: C, 82.55; H, 3.69; N, 6.42. Found: C, 82.09; H, 3.90; N, 6.30.

9-Methyl-11-[1-(4-methylbenzoyl)indol-3-yl]-6H-isoindolo[2,1-a]indol-6-one (7b)

Mp 203-205 °C: IR (Nujol) 1710, 1675, 1610 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ 2.10(s, 3H), 2.39 (s, 3H), 6.63(d, 2H, J=8 Hz), 6.96-7.83(m, 13H), 8.04-8.25(m, 1H): MS m/z (%) 467 (M^++1, 14), 466(M^+, 38), 119(100), 91(23). Anal. Calcd for $C_{32}H_{22}N_2O_2$: C, 82.38; H, 4.75; N, 6.01. Found: C, 82.11; H, 4.60; N, 5.99.

6H-Naphtho[1',2':3,4]pyrrolo[1,2-a]indol-6-one (6c)

Mp 216-218 °C: IR (Nujol) 1710, 1595 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ 6.57(s, 1H), 7.03-8.04 (m, 9H), 8.8-9.03(m, 1H): MS m/z (%) 270(M^++1, 21), 269(M^+, 100), 240(18), 135(12). Anal. Calcd for $C_{19}H_{11}NO$: C, 84.74; H, 4.12; N, 5.20. Found: C, 84.61; H, 3.99; N, 5.21.

6H-Naphtho[2',3':3,4]pyrrolo[1,2-a]indol-6-one (6d)

Mp 246-248 °C: IR (Nujol) 1725 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ 6.67(s, 1H), 7.1-8.1(m, 8H), 7.89(s, 1H), 8.26(s, 1H): MS m/z (%) 270(M^++1, 22), 269(M^+, 100), 240(20), 135(13). Anal. Calcd for $C_{19}H_{11}NO$: C, 84.74; H, 4.12; N, 5.20. Found: C, 84.56; H, 3.87; N, 5.25.

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