Palladium-Catalyzed Synthesis of Indoles from 2-Nitrostyrenes

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In the presence of palladium salts, oxidation of 2-nitrostyrenes **1** with nitrous acid alkyl esters **2** resulted in the formation of 2-nitrophenylacetaldehyde dialkyl acetals **3**. Reductive cyclization of the acetals **3** with iron powder in acetic acid afforded indoles **5** in good yield.

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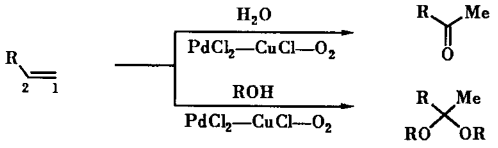
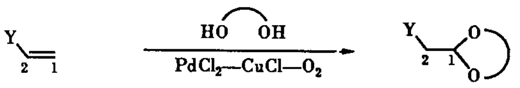
The palladium-catalyzed oxidation of terminal olefins with water, which is well-known as the Wacker reaction, generally produces methyl ketones, and a similar reaction with alcohols leads to the formation of their ketals [1]. These products arise *via* the attack of oxygen nucleophiles at the non-terminal olefinic carbon (C_2) (eq 1). On the other hand, Hosokawa *et al.* [2] reported that terminal olefins bearing electron-withdrawing groups are catalytically acetalized with diols such as ethylene glycol by the use of palladium dichloride catalyst under oxygen atmosphere (eq 2).



(1)



(2)

We also reported that, in the presence of palladium-catalyst and copper(I) chloride in dimethoxyethane, 2-nitrostyrenes are regioselectively acetalized at the terminal carbon (C_1) by propane-1,3-diol under an oxygen atmosphere and following reduction of the produced cyclic acetals leads to the formation of indole derivatives [3]. Meanwhile, Matsui *et al.* [4] have described that, in the presence of nitrous acid alkyl ester, palladium-catalyzed oxidation induces acetalization of alkenes *via* attack of oxygen nucleophiles at the C_1 carbon. For example, the palladium-catalyzed oxidation of acrylonitrile with nitrous acid butyl ester in butanol results in the formation of 4,4-di(butyloxy)butyronitrile in a fairly good yield. Herein, we wish to report the development of palladium-catalyzed reaction for the preparation of indoles **4** from readily obtainable 2-nitrostyrenes **1** by the use of nitrous acid alkyl esters **2**, following by a reductive cyclization. The over-all reaction scheme is presented in Figure 1. As palladium catalysts, disodium tetrachloropalladate(II), palladium(II) acetate, bis(acetonitrile)dichloropalladium(II), and bis(benzonitrile)dichloropalladium(II) were used in place of palladium dichloride because of higher solubility in the solvent (methanol) under an oxygen atmosphere in the absence or presence of a co-catalyst.

In Table 1 are summarized the results of the acetalization of **1** with **2** in the presence of a palladium catalyst. In contrast to the Wacker oxidation, the C_1 carbon of terminal olefins in the compounds **1** is regioselectively acetalized to afford 2-nitrophenylacetaldehyde dialkyl acetals **3**, accompanied by a small amount of 2-nitrophenylacetaldehydes **4**, and catalytic acetalization does not take place in the absence of oxygen. In the reaction of 2-nitrostyrene **1a** with nitrous acid methyl ester **2a**, disodium tetrachloropalladate(II) was shown to be superior to the other palladium catalysts. For example, **1a** was first allowed to react with **2a** in methanol [Na_2PdCl_4/substrate = 1/10, oxygen (1 atmosphere balloon)], and as the result, a fairly good yield (57%, based on **1a**) of 2-(2-nitrophenyl)acetaldehyde dimethyl acetal **3a**, together with 2-(2-nitrophenyl)acetaldehyde **4a** (4%, based on **1a**), was obtained (entry 4). Under similar conditions, the use of palladium(II) acetate, bis(acetonitrile)dichloropalladium(II), or bis(benzonitrile)dichloropalladium(II) as the catalyst decreases the yields of **3a** and increases the catalytic turnover to give **4a** (entries 1, 2, and 3). On the other hand, use of a higher pressure of oxygen (10 or 20 atmospheres) decreased the catalytic turnover to give acetal **3a** in 25% or 8% yield (based on **1a**) (entries 8 and 9). Use of copper(I) chloride or silver(I) acetate as a co-catalyst also decreased the catalytic turnover (entries 13, 14, and 15), however, as co-catalyst, the use of bismuth trichloride combined with lithium chloride in a ratio of 1:1 led to the formation of the acetal **3a** in 52% yield (entry 16). In the place of **2a**, the use of nitrous acid ethyl ester **2b**, butyl ester **2c**, or *t*-butyl ester **2d** decreases the yields of acetals (entries 5, 6, and 7). In a higher concentration of catalyst in methanol [Na_2PdCl_4/substrate = 2/10, oxygen (1 atmosphere, balloon)], the

Table 1

Palladium-Catalyzed Acetalization of 2-Nitrostyrenes 1 with Nitrous Acid Alkyl esters (or alkyl nitrites) 2

Entry	Nitrostyrene	Catalyst	Cocatalyst	Alkyl nitrite	O_2 (atm)	Products (Yield/% [a])	
1	**1a**	$Pd(OAc)_2$ [b]	—	**2a**	1	**3a** (56)	**4a** (12)
2	**1a**	$Pd(CH_3CN)_2$ [b]	—	**2a**	1	**3a** (36)	**4a** (37)
3	**1a**	$Pd(PhCN)_2$ [b]	—	**2a**	1	**3a** (35)	**4a** (27)
4	**1a**	Na_2PdCl_4 [b]	—	**2a**	1	**3a** (57)	**4a** (4)
5	**1a**	Na_2PdCl_4 [c]	—	**2b**	1	**3b** (35)	**4a** (9)
6	**1a**	Na_2PdCl_4 [d]	—	**2c**	1	**3c** (13)	- -
7	**1a**	Na_2PdCl_4 [e]	—	**2d**	1	**3d** (45)	**4a** (20)
8	**1a**	Na_2PdCl_4 [b]	—	**2a**	10	**3a** (25)	**4a** (1)
9	**1a**	Na_2PdCl_4 [b]	—	**2a**	20	**3a** (8)	**4a** (2)
10	**1a**	Na_2PdCl_4 [f]	—	**2a**	1	**3a** (28)	**4a** (49)
11	**1a**	Na_2PdCl_4 [g]	—	**2a**	1	**3a** (81)	**4a** (4)
12	**1a**	Na_2PdCl_4 [h]	—	**2a**	1	**3a** (69)	**4a** (11)
13	**1a**	Na_2PdCl_4	CuCl [i]	**2a**	-	**3a** (10)	**4a** (8)
14	**1a**	$PdCl_2$	CuCl [i]	**2a**	-	**3a** (8)	**4a** (14)
15	**1a**	Na_2PdCl_4	AgOAc [i]	**2a**	1	**3a** (6)	**4a** (2)
16	**1a**	Na_2PdCl_4	$BiCl_3$–LiCl [j]	**2a**	1	**3a** (52)	**4a** (5)
17	**1b**	Na_2PdCl_4	—	**2a**	1	**3e** (65)	- -
18	**1c**	Na_2PdCl_4 [b]	—	**2a**	1	**3f** (50)	**4b** (31)
19	**1d**	Na_2PdCl_4 [b]	—	**2a**	1	**3g** (76)	**4c** (10)
20	**1e**	Na_2PdCl_4 [b]	—	**2a**	1	**3h** (58)	**4d** (10)
21	**1f**	Na_2PdCl_4 [b]	—	**2a**	1	**3i** (64)	- -
22	**1g**	Na_2PdCl_4 [b]	—	**2a**	1	**3j** -	- -

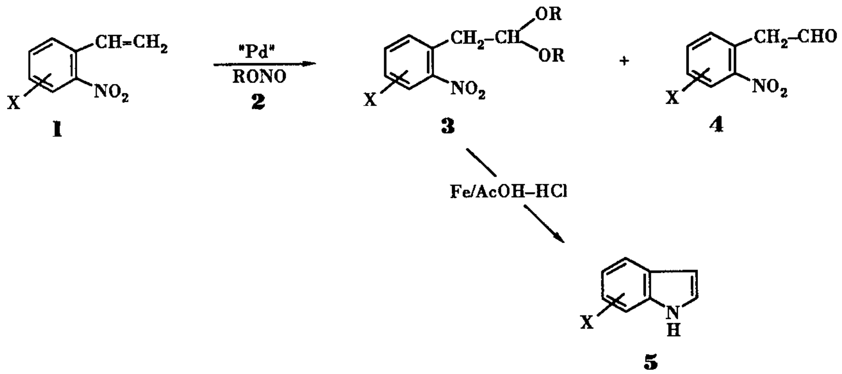
[a] Isolated yield based on the using **1**. [b] The reaction was performed by using **1** (6.19 mmoles), nitrous acid methyl ester **2a**, and catalyst (0.169 mmole) in methanol (64 ml) at room temperature. [c] The reaction was performed by using **1a** (6.19 mmoles), nitrous acid ethyl ester **2b**, and catalyst (0.619 mmole) in ethanol (64 ml) at room temperature. [d] The reaction was performed by using **1a** (6.19 mmoles), nitrous acid butyl ester **2c**, and catalyst (0.619 mmole) in methanol (64 ml) at room temperature. [e] The reaction was performed by using **1a** (6.19 mmoles), nitrous acid *t*-butyl ester **2d**, and catalyst (0.619 mmole) in methanol (64 ml) at room temperature. [f] The reaction was performed by using **1a** (6.19 mmoles), nitrous acid methyl ester **2a**, and catalyst (1.24 mmoles) in methanol (64 ml) at room temperature. [g] The reaction was performed by using **1a** (6.19 mmoles), nitrous acid methyl ester **2a**, and catalyst (1.24 mmoles) in methanol (130 ml) at room temperature. [h] The reaction was performed by using **1a** (6.19 mmoles), nitrous acid methyl ester **2a**, and catalyst (0.619 mmole) in methanol (130 ml) at room temperature. [i] The reaction was performed by using **1a** (6.19 mmoles), nitrous acid methyl ester **2a** catalyst (0.619 mmole) and cocatalyst (0.619 mmole) in methanol (64 ml) at room temperature. [j] The reaction was performed by using **1a** (6.19 mmoles), nitrous acid methyl ester **2a** catalyst (0.619 mmole) bimuth trichloride (0.619 mmole) and lithium chloride (0.619 mmole) in methanol (64 ml) at room temperature.

reaction of **1a** with **2a** decreases the catalytic turnover to give **3a** (entry 10), however, in a low concentration of the catalyst, the reaction of **1a** with **2a** increases the yield of **3a** and **4a** (entries 11 and 12). The reaction of 2-nitrostyrenes **1b**-**1f** with **2a** in methanol [Na_2PdCl_4/substrate = 1/10, oxygen (1 atmosphere balloon)] also afforded the acetals **3e**-**3i** in good yields, accompanied by the **4b**-**4d** (entries 17-21), but the reaction of 6-methyl-2-nitrostyrene **1g** with **2a** did not lead to the formation of the acetal **3j** (entry 22).

The reductive cyclization of the acetals **3** to the corresponding indoles **5** were carried out by using a variety of reagents, including zinc/acetic acid, iron/acetic acid, iron/acetic acid/hydrochloric acid, and iron/hydrochloric acid. We found that the reductive cyclization of **3** to **5** was performed by the reduction with iron powder in acetic acid, followed by treatment with dilute hydrochloric acid (entries 3, 5-12). In Table 2 are summarized the results of the reductive cyclization of **3** to **5**.

EXPERIMENTAL

All melting points were taken with a Gallenkamp melting points apparatus and are uncorrected. The ir spectra were recorded on a Hitachi 260-10 spectrometer, and the ^{1}H nmr spectra were obtained with a Hitachi R-90H spectrometer in deuteriochloroform, using tetramethylsilane as internal standard. Mass spectra were run on a Hitachi RMU-6M mass spectrometer. 2-Nitrostyrene **1a**, 4-methoxy-2-nitrostyrene **1b**, 5-methoxy-2-nitrostyrene **1c**, 4-methyl-2-nitrostyrene **1d**, and 4-methoxycarbonyl-2-nitrostyrene **1e** were prepared as described in the litera-



1a, **4a**, X = H
1b, X = 4-OMe
1c, **4b**, X = 5-OMe
1d, **4c**, X = 4-Me
1e, **4d**, X = 4-COOMe
1f, X = 4-Cl
1g, X = 6-Me

2a, R = Me
2b, R = Et
2c, R = Bu
2d, R = *t*-Bu

3a, X = H, R = Me
3b, X = H, R = Et
3c, X = H, R = Bu
3d, X = H, R = *t*-Bu
3e, X = 4-OMe, R = Me
3f, X = 5-OMe, R = Me
3g, X = 4-Me, R = Me
3h, X = 4-COOMe, R = Me
3i, X = 4-Cl, R = Me
3j, X = 6-Me, R = Me

Figure 1

Table 2

Reductive Conversion of Acetals **3** to Indoles **5**

Entry	Acetals	Reducing agent	Solvent	Temperature (°C)	Time hours	Products (yield, % [a])
1	**3a**	Zn-AcOH [b]	AcOH	85	2	**5a** (20)
2	**3a**	Fe-AcOH [c]	EtOH	75	1	**5a** (30)
3	**3a**	Fe-AcOH [d]	EtOH	70-75	1	**5a** (86)
4	**3a**	Fe-HCl [e]	MeOH	70	5	**5a** (17)
5	**3b**	Fe-AcOH [d]	EtOH	70-75	1	**5a** (82)
6	**3c**	Fe-AcOH [d]	EtOH	70-75	1	**5a** (83)
7	**3d**	Fe-AcOH [d]	EtOH	70-75	1	**5a** (80)
8	**3e**	Fe-AcOH [d]	EtOH	70-75	1	**5b** (84)
9	**3f**	Fe-AcOH [d]	EtOH	70-75	1	**5c** (63)
10	**3g**	Fe-AcOH [d]	EtOH	70-75	1	**5d** (84)
11	**3h**	Fe-AcOH [d]	EtOH	70-75	1	**5e** (73)
12	**3i**	Fe-AcOH [d]	EtOH	70-75	1	**5f** (76)

[a] Isolated yield. [b] The reaction was performed by using **3a** (4 mmoles), and zinc powder (37.5 mmoles) in 80% aceic acid (20 ml) with stirring at 85° for 2 hours. [c] The reaction was performed by using **3a** (4 mmoles), iron powder (37.5 mmoles), and acetic acid (10 ml) in ethanol (10 ml) with stiring at 75° for 1 hour. [d] The reaction was performed by using **3** (4 mmoles), iron powder (37.6 mmoles) and acetic acid (10 ml) in ethanol (10 ml) with stirring. After stirring at 70-75° for 1 hour, 10% hydrocholric acid (10 ml) was added and the resulting mixture was stirred at 85° for 2 hours. [e] The reaction was performed by using **3a** (4 mmoles), iron powder (37.5 mmoles), and 10% hydrochloric acid (10 ml) in methanol (30 ml) with stirring at 70° for 5 hours.

ture [3]. Nitrous acid methyl ester **2a** [5], nitrous acid ethyl ester **2b** [6], nitrous acid butyl ester **2c** [7], and nitrous acid *t*-butyl ester **2d** [8] were prepared according to the literature procedures.

Preparation of 4-Chloro-2-nitrostyrene **1f** and 6-Methyl-2-nitrostyrene **1g**.

The compounds **1f** and **1g** were prepared by the Heck reaction employing a modification of our earlier reported procedure [3]. Spectroscopic and analytical data are as follows:

4-Chloro-2-nitrostyrene **1f**.

This compound was obtained from 4-bromo-3-nitrochlorobenzene and ethylene in the presence of palladium(II) acetate and tri-(*o*-tolyl)phosphine as pale yellow crystals, mp 50-51.5°; ir (potassium bromide): 1520, 1350 (-NO_2), 980, 930 (-CH=CH_2), 3100, 880, 840 cm^{-1} (1,2,4-trisubst Ar-H); ^{1}H-nmr: δ 5.48 (d, 1 H, J = 11 Hz, Ar-C=CH), 5.72 (d, 1 H, J = 17 Hz, Ar-C=CH-), 7.10 (d-d, 1 H, J = 17 an 11 Hz, Ar-CH=C-), 7.53 (m, 2 H, C_5-H + C_6-H), 7.89 ppm (d, 1 H, C_2-H); ms: m/z 183 (M^+).

Anal. Calcd. for $C_8H_6ClNO_2$: C, 52.34; H, 3.29; N, 7.63. Found: C, 52.45; H, 3.36; N, 7.71.

6-Methyl-2-nitrostyrene **1g**.

This compound was obtained from 2-bromo-3-nitrotoluene and ethylene in the presence of palladium(II) acetate and tri(*o*-tolyl)phosphine as a pale yellow oil; ir (neat): 1525, 1350 (-NO_2), 990, 930 (-CH=CH_2), 3100, 780, 750 cm^{-1} (1,2,3-trisubst Ar-H); ^{1}H-nmr: δ 2.37 (s, 3 H, -CH_3), 5.35 (d, 1 H, J = 11 Hz, Ar-C=CH-), 5.68 (d, 1 H, J = 18 Hz, Ar-C=CH), 7.01 (d-d, 1 H, J = 11 and 18 Hz, Ar-CH=C-), 7.42 (t, 1 H, J = 8 Hz, C_5-H), 7.50 (d, 1 H, J = 8 Hz, C_6-H), 8.32 ppm (d, 1 H, J = 8 Hz, C_4-H); ms: m/z 163 (M^+).

Anal. Calcd. for $C_9H_9NO_2$: C, 66.14; H, 5.56; N, 8.38. Found: C, 66.02; H, 5.47; N, 8.29.

General Procedure for the Preparation of 2-Nitrophenylacetaldehyde Dialkyl Acetals **3**.

In a 100 ml flask equipped with a rubber balloon with oxygen, a teflon-coated magnetic stirring bar, and a reflux condenser were placed disodium tetrachloropalladate(II) (0.182 g, 0.619 mmole), 2-nitrostyrene **1** (6.19 mmoles) and methanol (64 ml). To the mixture was introduced a gaseous or liquid nitrous acid alkyl ester **2** which was prepared from sodium nitrite (3.8 g, 55 mmoles) and alcohol (5 ml) in the presence of sulfuric acid (2.5 ml) and water (5 ml) at room temperature, and the resulting mixture was stirred for 24 hours under an oxygen atmosphere. The insoluble materials were removed by filtration, and the filtrate was concentrated under reduced pressure. The products were separated by means of silica gel column chromatography (benzene). The yields of acetals **3** and 2-nitrophenylacetaldehydes **4** are summarized in Table 1. Spectroscopic and analytical data of the products are as follows:

2,2-Dimethoxy-1-(2-nitrophenyl)ethane **3a**.

This compound was obtained from **1a** and **2a**, accompanied by **4a**, as a pale yellow oil; ir (neat): 1530, 1350 (-NO_2), 3090, 760 cm^{-1} (*o*-disubst Ar-H); ^{1}H-nmr: δ 3.20 (d, 2 H, J = 7.0 Hz, -CH_2-), 3.35 (s, 6 H, -CH_3), 4.55 (t, 1 H, J = 7.0 Hz, -CH-), 7.20-7.63 ppm (m, 4 H, Ar-H); ms: m/z 211 (M^+).

Anal. Calcd. for $C_{10}H_{13}NO_4$: C, 56.86; H, 6.20; N, 6.63. Found: C, 56.71; H, 6.08; N, 6.54.

2-Nitrophenylacetaldehyde **4a**.

This compound was obtained as a yellow oil, and the spectroscopic data were identical with those of the authentic sample {lit [9] bp 185° (5 mm/Hg)}.

2,2-Diethoxy-1-(2-nitrophenyl)ethane **3b**.

This compound was obtained from **1a** and **2b**, accompanied by **4a**, as a pale yellow oil; ir (neat): 1530, 1350 (-NO_2), 3100, 740 cm^{-1} (*o*-disubst Ar-H); ^{1}H-nmr: δ 1.13 (t, 6 H, J = 8.0 Hz, -CH_3), 3.25 (d, 2 H, J = 7.0 Hz, Ar-CH_2-), 3.55 (q, 4 H, J = 8.0 Hz, -O-CH_2-), 4.66 (t, 1 H, J = 7.0 Hz, -CH-), 7.21-7.93 ppm (m, 4 H, Ar-H); ms: m/z 239 (M^+).

Anal. Calcd. for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.31; H, 7.27; N, 5.96.

2,2-Dibutyloxy-1-(2-nitrophenyl)ethane **3c**.

This compound was obtained from **1a** and **2c**, as a pale yellow oil; ir (neat): 1530, 1350 (-NO_2), 3100, 750 cm^{-1} (*o*-disubst Ar-H); ^{1}H-nmr: δ 0.98 (t, 3 H, J = 7 Hz, -CH_3), 1.34-1.51 (m, 4 H, -CH_2-CH_2-), 3.36 (m, 4 H, Ar-CH_2- + -O-CH_2-), 4.62 (t, 1 H, J = 7.0 Hz, -O-CH-), 7.23-7.87 ppm (m, 4 H, Ar-H); ms: m/z 239 (M^+).

Anal. Calcd. for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53; N, 4.74. Found: C, 65.18; H, 8.64; N, 4.82.

2,2-Di(*t*-butyloxy)-1-(2-nitrophenyl)ethane **3d**.

This compound was obtained from **1a** and **2d**, accompanied by **4a**, as a pale yellow oil; ir (neat): 1535, 1350 (-NO_2), 3100, 750 cm^{-1} (*o*-disubst Ar-H); ^{1}H-nmr: δ 1.12 (s, 18 H, -CH_3), 3.23 (d, 2 H, J = 7.0 Hz, Ar-CH_2-), 4.64 (t, 1 H, J = 7.0 Hz, -CH-), 7.24-7.87 ppm (m, 4 H, Ar-H); ms: m/z 295 (M^+).

Anal. Calcd. for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53; N, 4.74. Found: C, 64.91; H, 8.44; N, 4.62.

2,2-Dimethoxy-1-(4-methoxy-2-nitrophenyl)ethane **3e**.

This compound was obtained from **1b** and **2a** as a pale yellow oil; ir (neat): 1520, 1350 (-NO_2), 3100, 860, 820 cm^{-1} (1,2,4-trisubst Ar-H); ^{1}H-nmr: δ 3.23 (d, 2 H, J = 7.0 Hz, -CH_2-), 3.38 (s, 6 H, -OCH_3), 3.83 (s, 3 H, Ar-OCH_3), 4.51 (t, 1 H, J = 7.0 Hz, -CH-), 7.26 (d-d, 1 H, C_5-H), 7.37 (d, 1 H, C_6-H), 7.91 ppm (d, 1 H, C_3-H); ms: m/z 241 (M^+).

Anal. Calcd. for $C_{11}H_{15}NO_5$: C, 54.76; H, 6.26; N, 5.80. Found: C, 54.66; H, 6.21; N, 5.73.

2,2-Dimethoxy-1-(5-methoxy-2-nitrophenyl)ethane **3f**.

This compound was obtained from **1c** and **2a**, accompanied by 5-methoxy-2-nitrophenylacetaldehyde **4b**, as a pale yellow oil; ir (neat): 1525, 1350 (-NO_2), 3100, 870, 820 cm^{-1} (1,2,4-trisubst Ar-H); ^{1}H-nmr: δ 3.26 (d, 2 H, J = 7.0 Hz, -CH_2-), 3.89 (s, 1 H, -OCH_3), 4.56 (t, 1 H, J = 7.0 Hz, -CH-), 7.01 (d-d, 1 H, C_4-H), 7.16 (d, 1 H, C_6-H), 7.98 ppm (d, 1 H, C_3-H); ms: m/z 241 (M^+).

Anal. Calcd. for $C_{11}H_{15}NO_5$: C, 54.76; H, 6.26; N, 5.80. Found: C, 54.84; H, 6.34; N, 5.87.

5-Methoxy-2-nitrophenylacetaldehyde **4b**.

This compound was obtained as a yellow oil; ir (neat): 2710, 1725 (-CHO), 1530, 1350 (-NO_2), 3100, 880, 820 cm^{-1} (1,2,4-trisubst Ar-H); ^{1}H-nmr: δ 3.80 (s, 3 H, -OCH_3), 4.17 (d, 1 H, -CH_2-), 7.03 (d-d, 1 H, C_4-H), 7.20 (d, 1 H, C_6-H), 8.10 (d, 1 H, C_3-H), 9.95 ppm (t, 1 H, -CHO); ms: m/z 195 (M^+).

Anal. Calcd. for $C_9H_9NO_4$: C, 55.38; H, 4.64; N, 7.17. Found: C, 55.26; H, 4.54; N, 7.11.

2,2-Dimethoxy-1-(4-methyl-2-nitrophenyl)ethane **3g**.

This compound was obtained from **1d** and **2a**, accompanied by 4-methyl-2-nitrophenylacetaldehyde **4c**, as a pale yellow oil; ir (neat): 1530, 1350 (-NO_2), 3100, 880, 820 cm^{-1} (1,2,4-trisubst Ar-H); ^{1}H-nmr: δ 2.39 (s, 3 H, Ar-CH_3), 3.17 (d, 2 H, J = 5.0 Hz, Ar-CH_2-), 3.33 (s, 6 H, -O-CH_3), 4.53 (t, 1 H, J = 5.0 Hz, -CH-), 7.28 (s, 2 H, C_5-H + C_6-H), 7.67 ppm (s, 1 H, C_3-H); ms: m/z 225 (M^+).

Anal. Calcd. for $C_{11}H_{15}NO_4$: C, 58.65; H, 6.71; N, 6.22. Found: C, 58.53; H, 6.65; N, 6.07.

4-Methyl-2-nitrophenylacetaldehyde **4c**.

This compound was obtained as a pale yellow oil; ir (neat): 2730, 1730 (-CHO), 1530, 1350 (-NO_2), 3100, 880, 825 cm^{-1} (1,2,4-trisubst Ar-H); ^{1}H-nmr: δ 2.37 (s, 3 H, -CH_3), 4.20 (d, 2 H,

-CH_2-), 6.96 (d-d, 1 H, C_5-H), 7.18 (d, 1 H, C_6-H), 7.95 (d, 1 H, C_3-H), 9.97 ppm (t, 1 H, -CHO); ms: m/z 179 (M^+).

Anal. Calcd. for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.81. Found: C, 60.23; H, 4.97; N, 7.77.

2,2-Dimethoxy-1-(4-methoxycarbonyl-2-nitrophenyl)ethane **3h**.

This compound was obtained from **1e** and **2a**, accompanied by 4-methoxycarbonyl-2-nitrophenylacetaldehyde **4d**, as a pale yellow oil; ir (neat): 1720 (-COOMe), 1530, 1360 (-NO_2), 3100, 890, 820 cm^{-1} (1,2,4-trisubst Ar-H); ^{1}H-nmr: δ 3.16 (d, 2 H, J = 7.0 Hz, -CH_2-), 3.94 (-$COOCH_3$), 4.50 (t, 1 H, J = 7.0 Hz, -CH-), 7.43 (d, 1 H, C_6-H), 7.48 (d-d, 1 H, C_5-H), 8.35 ppm (d, 1 H, C_3-H); ms: m/z 269 (M^+).

Anal. Calcd. for $C_{12}H_{15}NO_6$: C, 53.53; H, 5.61; N, 5.20. Found: C, 53.61; H, 5.68; N, 5.32.

4-Methoxycarbonyl-2-nitrophenylacetaldehyde **4d**.

This compound was obtained as a pale yellow oil; ir (neat): 2720 (-CHO), 1725 (-COOMe + -CHO), 1530, 1360 (-NO_2), 3100, 890, 820 cm^{-1} (1,2,4-trisubst Ar-H); ^{1}H-nmr: δ 3.18 (d, 2 H, -CH_2-), 3.96 (-$COOCH_3$), 7.38 (d, 1 H, C_6-H), 7.53 (d-d, 1 H, C_5-H), 8.12 (d, 1 H, C_3-H), 9.97 ppm (t, 1 H, -CHO); ms: m/z (M^+): 225.

Anal. Calcd. for $C_{10}H_{11}NO_5$: C, 53.33; H, 4.92; N, 6.22. Found: C, 53.39; H, 5.08; N, 6.34.

2,2-Dimethoxy-1-(4-chloro-2-nitrophenyl)ethane **3i**.

This compound was obtained from **1f** and **2a** as a pale yellow oil; ir (neat): 1530, 1350 (-NO_2), 3100, 890, 815 cm^{-1} (1,2,4-trisubst Ar-H); ^{1}H-nmr: δ 3.18 (d, 2 H, J = 5.5 Hz, -CH_2-), 3.32 (s, 6 H, -CH_3), 4.52 (t, 1 H, J = 5.5 Hz, -CH-), 7.33 (d, 1 H, C_6-H), 7.47 (d-d, 1 H, C_5-H), 7.82 ppm (d, 1 H, C_3-H); ms: m/z 245, 247 (M^+).

Anal. Calcd. for $C_{10}H_{12}ClNO_4$: C, 48.89; H, 4.92; N, 5.70. Found: C, 48.81; H, 4.81; N, 5.58.

General Procedure for Reductive Cyclization of 2-Nitrophenylacetaldehyde Dialkyl Acetals **3** to Indoles **5**.

Into a solution of 4 mmoles of acetal **3** in 10 ml of ethanol and 10 ml of acetic acid was added 2.1 g (37.6 mmoles) of iron powder in limited amounts at 70-75°. After stirring for 1 hour at the same temperature, 10 ml of 10% hydrochloric acid was added to the reaction mixture and the resulting mixture was stirred at 85° for 2 hours. The insoluble materials were removed by filtration, and the filtrate was concentrated under reduced pressure. The products were separated by means of silica gel column chromatography (benzene). The yields of indoles **5** are summarized in Table 2. All of the indoles **5** prepared by the above procedures had melting points in agreement with literature values and exhibited ir and ^{1}H-nmr spectra consistent with the assigned structure.

Indole **5a**.

This compound was obtained from **3a**, mp 51-53° (lit [10], mp 52-53°).

6-Methoxyindole **5b**.

This compound was obtained from **3e**, mp 89-90° (lit [11], mp 88-90°).

5-Methoxyindole **5c**.

This compound was obtained from **3f**, mp 55-56° (lit [11], mp 54-55°).

6-Methylindole **5d**.

This compound was obtained from **3g**, bp 82-83° (1 mm/Hg) {lit [12], bp 75-78° (1 mm/Hg)}.

Methyl 6-Indolecarboxylate **5e**.

This compound was obtained from **3h**, mp 78-80° (lit [13], mp 78-79°).

6-Chloroindole **5f**.

This compound was obtained from **3i**, mp 87-89° (lit [10], mp 88-89°).

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