

A Dual Pathway in the Solid-State Photoreaction of Nitrobenzaldehydes with Indole

Ji-Ben Meng, Da-Ming Du, Guo-Xiang Xiong, Wen-Guang Wang and Yong-Mei Wang

Department of Chemistry, Nankai University
Tianjin, China

Hideko Koshima

PRESTO, Research Development Corporation of Japan (JRDC)
2-5-2 Nagatacho, Chiyodaku, Tokyo 100

Teruo Matsuura*

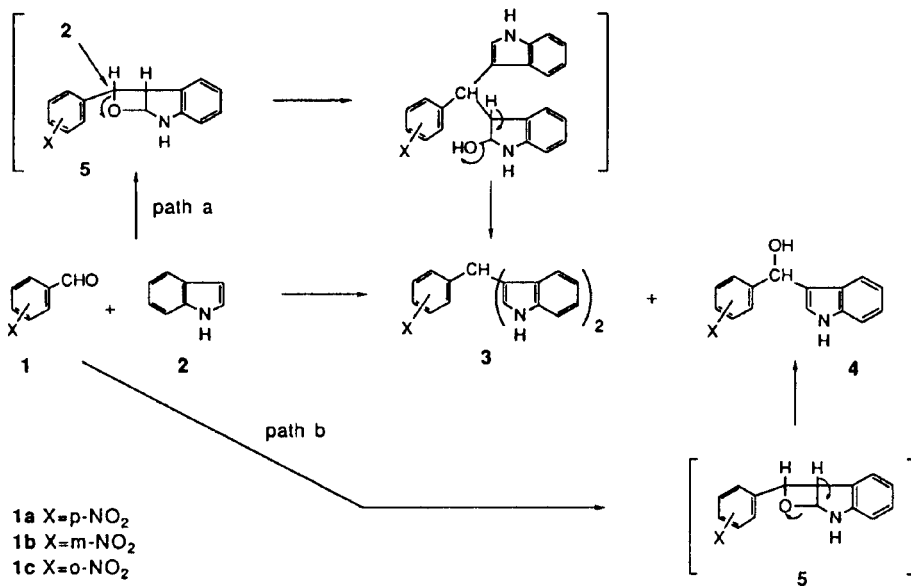
Department of Materials Chemistry,
Faculty of Science and Technology, Ryukoku University
Seta, Otsu 520-21, Japan
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The solid-state photoreaction of the mixed crystals between nitrobenzaldehydes and indole was found to give nitrophenyl-(bis-3-indolyl)methane (**3**) and nitrophenyl-(3-indolyl)methanol (**4**). The structure of the *ortho* isomer **4c** was established by X-ray crystallographic analysis. A dual pathway from an oxetane intermediate **5** is proposed for the formation of **3** and **4**.

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In a previous report [1, 2], it has been demonstrated that the solid-state irradiation of the mixed crystals between an aromatic aldehydes **1** and indole (**2**) gives a photocondensation product **3** as shown in equation 1. In a continuation of this work, we have recently found that the mixed crystals between nitrobenzaldehydes (**1a**, **1b** and **1c**) and indole gave two photoproducts under the same irradiation conditions.

The mixed crystals between nitrobenzaldehyde (**1**) and indole (**2**) were prepared by melting a 1:3 molar mixture of **1** and **2** followed by the resolidification of the melt and were irradiated with a high-pressure mercury lamp with Pyrex housing (>290 nm) in the solid state under ice-cooling. The mixed crystals between *p*-, *m*- and *o*-nitrobenzaldehydes (**1a**, **1b** and **1c**) and indole gave **4a** (17%), **4b** (28%) and **4c** (34%), respectively, in addition



1a X=*p*-NO₂
1b X=*m*-NO₂
1c X=*o*-NO₂

to the formation of **3a** (25%), **3b** (20%) and **3c** (36%), respectively. The structures of **4a**, **4b** and **4c** were deduced from their spectroscopic and microanalytical data and confirmed by the X-ray crystallographic analysis of **3c**. It should be noted that compound **3c** exhibits a high inclusion ability towards carbon tetrachloride. When a solution of **3c** in 1:1 (v/v) ethanol-carbon tetrachloride

was gradually evaporated at room temperature, a 2:1 inclusion compound between **3c** and carbon tetrachloride crystallized. The inclusion compound had an infrared band at 780 cm⁻¹ assignable to the absorption of a C-Cl bond.

We have previously shown that there are two classes of mixed crystals between two different organic compounds

Table 1
Fractional Coordinates and Equivalent Isotropic Thermal Parameters
for Non-hydrogen Atoms with Estimated Standard Deviation in Parentheses.

Atom	X	Y	Z	Beq.(Å ²)	Atom	X	Y	Z	Beq.(Å ²)
O1	0.2982(5)	-0.0179(5)	0.4690(4)	4.3(1)	C17	0.5097(7)	0.1143(6)	0.5061(5)	2.6(1)
O2	0.747(1)	-0.2822(9)	0.4191(8)	15.0(3)	C18	0.6003(8)	0.2004(8)	0.4633(5)	3.6(2)
O3	0.770(1)	-0.134(1)	0.4995(6)	19.2(4)	C21	0.4641(8)	-0.0051(7)	0.4712(6)	3.3(2)
N1	0.6064(6)	0.3029(6)	0.5151(4)	3.6(1)	C22	0.5343(8)	-0.0309(7)	0.3702(5)	3.3(2)
N2	0.7298(9)	-0.1746(7)	0.4316(6)	6.6(2)	C23	0.4711(8)	0.0263(8)	0.2906(6)	4.2(2)
C11	0.5249(8)	0.2874(7)	0.5986(5)	3.2(2)	C24	0.522(1)	0.0034(9)	0.1963(6)	5.5(2)
C12	0.4955(9)	0.3623(7)	0.6759(6)	4.0(2)	C25	0.645(1)	-0.0812(9)	0.1826(6)	5.8(2)
C13	0.4054(9)	0.3253(8)	0.7520(6)	5.1(2)	C26	0.710(1)	-0.1388(8)	0.2579(6)	5.8(2)
C14	0.3443(9)	0.2074(8)	0.7519(5)	4.8(2)	C27	0.6523(9)	-0.1149(7)	0.3521(6)	4.3(2)
C15	0.3725(8)	0.1291(7)	0.6761(5)	3.5(2)	HO1	0.777	0.609	0.520	4.0
C16	0.4635(8)	0.1698(7)	0.5970(5)	3.1(2)	HN1	0.693	0.389	0.500	1.4

Anisotropically refined atoms are given in the form of the equivalent isotropic thermal parameter defined as: $(4/3) \cdot [a^2 \cdot \beta(1,1) + b^2 \cdot \beta(2,2) + c^2 \cdot \beta(3,3) + ab(\cos \gamma) \cdot \beta(1,2) + ac(\cos \beta) \cdot \beta(1,3) + bc(\cos \alpha) \cdot \beta(2,3)]$.

Table 2
Bond Distances (Å) and Angles (°) between Non-hydrogen Atoms with Estimated Standard Deviation in Parentheses.

O1-C21	1.422(8)	C11-C12	1.38(1)	C16-C17	1.44(1)	C23-C24	1.39(1)
O2-N2	1.22(1)	C11-C16	1.41(2)	C17-C18	1.361(9)	C24-C25	1.43(1)
O3-N2	1.09(1)	C12-C13	1.36(2)	C17-C21	1.464(9)	C25-C26	1.33(1)
N1-C11	1.348(9)	C13-C14	1.42(1)	C21-C22	1.53(2)	C26-C27	1.41(2)
N1-C18	1.344(9)	C14-C15	1.38(2)	C22-C23	1.37(1)		
N2-C27	1.44(1)	C15-C16	1.406(9)	C22-C27	1.39(2)		
C11-N1-C18	108.5(6)	C13-C14-C15	121.7(8)	O1-C21-C17	113.1(6)	C22-C23-C24	122.1(7)
O2-N2-O3	119(1)	C14-C15-C16	118.2(8)	O1-C21-C22	110.5(6)	C23-C24-C25	118.4(9)
O2-N2-C27	114(1)	C11-C16-C15	119.5(7)	O1-C21-H21	110.4(7)	C24-C25-C26	121.5(9)
O3-N2-C27	127(1)	C11-C16-C17	107.9(6)	C17-C21-C22	111.1(6)	C25-C26-C27	118.3(9)
N1-C11-C12	132.1(8)	C15-C16-C17	132.5(8)	C17-C21-H21	107.1(6)	N2-C27-C22	120.6(9)
N1-C11-C16	107.4(6)	C16-C17-C18	103.0(6)	C22-C21-H21	106.4(6)	N2-C27-C26	116.6(8)
C12-C11-C16	120.5(7)	C16-C17-C21	126.6(6)	C21-C22-C23	118.4(7)	C22-C27-C26	122.7(9)
C1-C12-C13	120.9(8)	C18-C17-C21	130.4(6)	C21-C22-C27	124.5(8)		
C12-C13-C14	119.3(9)	N1-C18-C17	113.1(6)	C23-C22-C27	117.0(7)		

Hydrogen bonding

HO1-O1	1.05(2)	HN1-N1	1.23(2)
HO1...O2'	1.85(2)	HN1 O1b	1.75(2)
C21...O1-HO1	105.2(9)	O1-HO1...O2'	140.5(9)
C21...O1 HN1C	115.0(9)	C11-N1-HN1	126.5(9)
HO1...O1 HN1C	132.8(9)	C18-N1-HN1	123.7(9)
N2-O2...HO1d	123.6(9)	N1-HN1...O1b	155.5(9)

Symmetrical transformations: a = (-.5 + x, -.5 - y, 1 - z); b = (.5 + x, .5 - y, 1 - z); c = (-.5 + x, .5 - y, 1 - z); d = (.5 + x, -.5 - y, 1 - z).

prepared by the melting-resolidification process. One forms a molecular compound and the other is a simple mixture of the microcrystals of the components [2-4]. For example, 5-formyl-1,3-dimethyluracil and antipyrine formed a molecular compound, which was characterized by powder X-ray diffraction (PXRD) and differential scanning calorimetry (DSC), while *p*-hydroxybenzaldehyde and indole formed a mixture of the microcrystals of the components [2]. We tried the PXRD and DSC measurements of the mixed crystals of **1a**, **1b** or **1c** and **2**. However all of the mixed crystals were a partly crystallized liquid at room temperature and we failed to obtain reliable data.

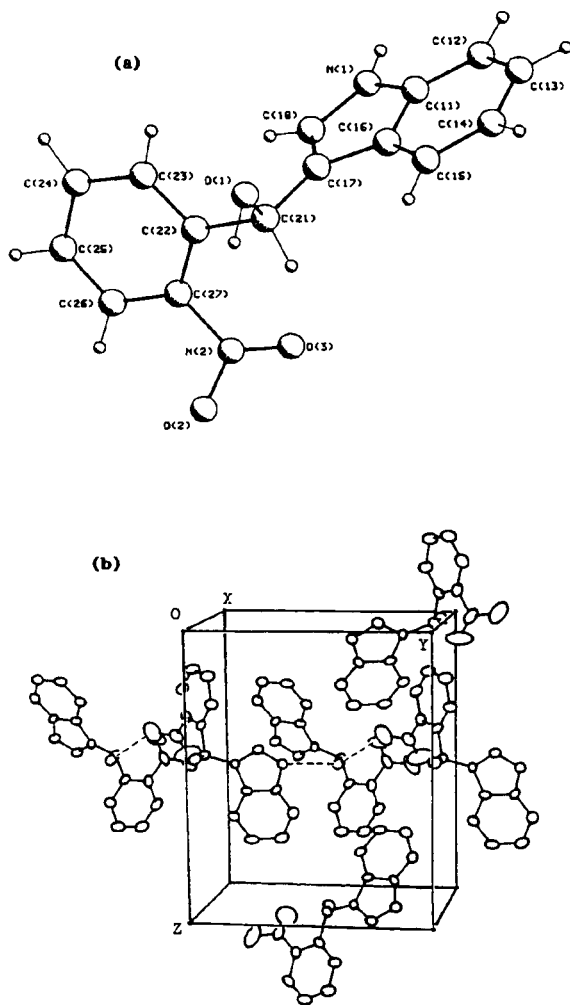


Figure 1. X-Ray Crystal Structures of **4c**: (a) Molecular Structure and (b) Crystal Packing.

For the formation of **3**, we proposed a mechanism (path a in equation 1) involving the intermediate formation of an oxetane **5** [1,2]. D'Auria proposed the intermediacy of 3-indolylphenylmethanol **4** ($X = H$) in the photochemical formation of **3** ($X = H$) from benzaldehyde (**1**, $X = H$) and

indole (**2**) in a concentrated solution [5]. In order to evaluate the D'Auria's mechanism, a control experiment was carried out. We did not observe any reaction to give **3c** on irradiation or heating of the mixed crystals between **4c** and indole (**2**), indicating that **4c** is not an intermediate for the formation of **3c**.

In conclusion, we propose a dual mechanism involving the oxetane intermediate **5** which undergoes bond breaking in two ways to give **3** and **4** (path a and path b in equation 1, respectively).

EXPERIMENTAL

All melting points are uncorrected. The ^1H -nmr and mass spectra were measured on a JEOL PMX-60 and a 7070E-HE spectrometers respectively. The ir spectra were measured on a PYE Unicam SP3-300 spectrometer. Powder X-ray diffraction spectra were taken on a Rigaku ROTAFLEX RU-200B. Differential scanning calorimetry (DSC) was accomplished on a Shimadzu differential scanning calorimeter DSC-50. Column chromatography and preparative tlc were carried out on silica gel of Qing Tao 300 and Merck F₂₅₄ respectively. All of the starting materials were commercially available.

Solid-State Photoreaction of 4-Nitrobenzaldehyde (**1a**) and Indole (**2**). 4-Nitrophenyl-(bis-3-indolyl)methane (**3a**) and 3-Nitrophenyl-(3-indolyl) methanol (**4a**).

The mixed crystals were prepared by melting a mixture of **1a** (75.5 mg, 0.50 mmole) and **2** (170 mg, 1.45 mmole) followed by resolidifying the melt with cooling. The pulverized mixed crystals were irradiated with a 450 W high pressure mercury lamp under nitrogen for 48 hours, with ice-cooling as described previously [2]. The irradiated mixture was dissolved in dichloromethane and the insoluble solid was removed by filtration. The filtrate was evaporated and the residue was dissolved in dioxane. Dilution of the dioxane solution with petroleum ether gave **3a** (45 mg, 25%) as crystals, mp 220-222°; ir (potassium bromide): 3340, 3025, 1590 and 1340 cm^{-1} ; ^1H -nmr (hexadeuterioacetone): δ 6.08 (s, 1H, CH-proton), 6.90-7.48 (m, 12H, aromatic protons), 7.65 (d, 2H, aromatic protons), 8.16 (d, 2H, aromatic protons); ms: m/z 367 (M^+), 320, 251, 245.

Anal. Calcd. for $\text{C}_{23}\text{H}_{17}\text{N}_3\text{O}_2$: C, 75.19; H, 4.66; N, 11.44. Found: C, 75.32; H, 4.51; N, 11.56.

The mother liquor from **3a** was evaporated and the residue was submitted to column chromatography. Elution with 2: 2: 1 (v/v/v) chloroform/petroleum ether/ethyl acetate afforded **4a** (23 mg, 17%) as crystals, mp 154-156°; ir (potassium bromide): 3380, 3300, 1600 and 1349 cm^{-1} ; ^1H -nmr (deuteriochloroform): δ 2.64 (s, 1H, OH-proton), 6.00 (s, 1H, CH-proton), 6.64-8.48 (m, 10H, aromatic proton); ms: m/z 268 (M^+), 250, 220, 151.

Anal. Calcd. for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_3$: C, 67.15; H, 4.51; N, 10.44. Found: C, 67.21; H, 4.48; N, 10.17.

Solid-State Photoreaction of 3-Nitrobenzaldehyde (**1b**) with Indole (**2**). 3-Nitrophenyl-(bis-3-indolyl)methane (**3b**) and 3-Nitrophenyl-(3-indolyl)methanol (**4b**).

The mixed crystals prepared from **1b** (151 mg, 1.00 mmole) and **2** (351 mg, 3.00 mmole) as above were irradiated for 10

hours in the same manner as described above. The irradiated mixture was dissolved in chloroform and subjected to column chromatography eluting with petroleum 10:1 (v/v) ether/ethyl acetate to give **3b** (36 mg, 20%) and **4b** (38 mg, 28%). Compound **3b** had mp 82-85°; ir (potassium bromide): 3381, 3049, 1619 and 1454 cm^{-1} ; $^1\text{H-nmr}$ (hexadeuteriodimethyl sulfoxide): δ 5.95 (s, 1H, CII-proton), 6.60 (m, 1H, NH-proton), 6.80-8.20 (m, 14H, aromatic protons); ms: m/z 367 (M^+), 337, 320, 245.

Anal. Calcd. for $\text{C}_{23}\text{H}_{17}\text{N}_3\text{O}_2$: C, 75.19; H, 4.66; N, 11.44. Found: C, 75.29; H, 4.53; N, 11.17.

Compound **4b** had mp 135-136°; ir (potassium bromide): 3520, 3250, 1350 and 1000 cm^{-1} ; $^1\text{H-nmr}$ (hexadeuteriodimethyl sulfoxide): δ 4.00 (s, 1H, OH proton), 5.90 (s, 1H, CH-proton), 6.70-8.60 (m, 9H, aromatic proton); ms: m/z 268 (M^+), 250, 203, 176.

Anal. Calcd. for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_3$: C, 67.15; H, 4.51; N, 10.44. Found: C, 66.94; H, 4.19; N, 10.14.

Solid-State Photoreaction of 2-Nitrobenzaldehyde (**1c**) with Indole (**2**). 2-Nitrophenyl-(bis-3-indolyl) methane (**3c**) and 2-Nitrophenyl-(3-indolyl) methanol (**4c**).

The mixed crystals prepared from **1c** (75 mg, 0.50 mmoles) and **2** (176 mg, 1.50 mmoles) as above were irradiated for 10 hours in the same manner as described above. The irradiated mixture was dissolved in dichloromethane and subjected to column chromatography. Elution with 2:1 (v/v) petroleum ether/ethyl acetate yielded the starting materials. Elution with 2:2:1 (v/v/v) petroleum ether/chloroform/ethyl acetate gave **3c** (65 mg, 36 %) as an oil and **4c** (46 mg, 34%) as crystals. The product **3c** crystallized from ethanol/carbon tetrachloride as an inclusion complex, mp 140-142°; ir (potassium bromide): 3350, 3050, 1617 and 780 cm^{-1} ; $^1\text{H-nmr}$ (deuteriochloroform): δ 6.40 (s, 1H, CH-proton), 6.50 (m, 2H, NH-proton), 6.70-8.20 (m, 12H, aromatic proton); ms: m/z 367 (M^+), 350, 319, 159.

Anal. Calcd. for $\text{C}_{23}\text{H}_{17}\text{N}_3\text{O}_2 \cdot 1/2\text{CCl}_4$: C, 63.53; H, 3.85; N, 9.45; Cl, 15.93. Found: C, 63.43; H, 3.69; N, 9.40; Cl, 15.44.

Compound **4c** had mp 196-198°; ir (potassium bromide): 3480, 3280, 1520 and 980 cm^{-1} ; $^1\text{H-nmr}$ (hexadeuteriodimethyl sulfoxide): δ 4.00 (s, 1H, OH-proton), 6.56 (s, 1H, CH-proton), 6.70-8.10 (m, 9H, aromatic proton), 10.92 (s, 1H, NH-proton); ms: m/z 268 (M^+), 250, 205, 165.

Anal. Calcd. for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_3$: C, 67.15; H, 4.51; N, 10.44. Found: C, 67.01; H, 4.26; N, 10.30.

Photoreaction of Nitrobenzaldehydes **1** with Indole **2** in Solution.

The photoreaction was carried out with **1a**, **1b** and **1c** and no reaction was observed in all cases. In a typical run, a solution of **1b** (61 mg, 0.40 mmole) and **2** (180 mg, 1.54 mmoles) in acetonitrile (30 ml) was externally irradiated with a 300 W high-pressure mercury lamp for 10 hours at room temperature under a nitrogen atmosphere. The irradiated mixture was found to consist of the starting materials by tlc analysis.

Solid-State Photo and Thermal Reactions of 2-Nitrophenyl(3-indolyl)methanol (**4c**) with Indole (**2**).

The mixed crystals prepared from **4c** (0.10 g, 0.37 mmole) and **2** (0.10 g, 0.85 mmole) by melting and resolidification were irradiated with a 300 W high-pressure mercury lamp under nitrogen for 10 hours in the same manner as described above. Analysis (tlc) of the irradiated mixture showed no spot of **3c**.

Another sample of the mixed crystal was heated at 50-60°C for 10 hours. Analysis (tlc) of the mixture showed only the spots of the starting materials.

X-ray Crystallographic Analysis of **4c**.

A colorless crystal of **4c** having the approximate dimensions of 0.2 x 0.2 x 0.2 mm was mounted on a glass fiber in a random orientation. Preliminary examination and data collection were performed with MoK α radiation ($\lambda = 0.71073 \text{ \AA}$) on an ENRAF-NONIUS CAD4 diffractometer equipped with a graphite crystal, incident beam monochromator. A total of 2508 independent reflections were collected in the range of $2 \leq \theta \leq 25^\circ$ by $w-2\theta$ scan technique at room temperature, in which 1044 reflections with $I \geq 3\sigma(I)$ were considered to be observed and used in the succeeding refinement. The corrections for LP factors and for empirical absorption were applied to the intensity data.

The crystal is orthorhombic, space group $P2_12_12_1$ with $a = 8.523(3)$, $b = 11.122(2)$, $c = 13.689(2) \text{ \AA}$, $V = 1297.6(9) \text{ \AA}^3$, $M_r = 268.27$, $Z = 4$, $D_x = 1.37 \text{ g/cm}^3$, $\mu = 0.91 \text{ cm}^{-1}$, $F(000) = 560$.

The structure was solved by the direct phase determination method (MULTAN 82). Most of non-hydrogen atoms were located on an E-map. The coordinates of the other non-hydrogen atoms were found in the successive difference Fourier syntheses. The hydrogen atoms of carbons were calculated theoretically, while the hydrogen atoms of oxygen and nitrogen atoms were found on the difference Fourier map. All hydrogen atoms were fixed in the refinements and included in the calculations of structure factors. The final refinement by the full matrix least-squares method with anisotropic thermal parameters for non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms was converged with unweighted and weighted agreement factors (R and R_w) of 0.062 and 0.064, and GOF of 1.31. The highest peak on the final difference Fourier map had a height of 0.61 e/\AA^3 . All calculations were performed on a PDP11/44 computer using SDP-PLUS program system. The crystal structures of **4c** are given in Figure 1 and the parameters are given in Table 1 and Table 2.

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- * Author to whom correspondence should be addressed.
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