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The Selective Preparation of *N*-Acylindigo

Yoshimori Omote,* Kiyoko Fujiki,† Hiroshi Awano, Ikuo Kubota,
Takehiko Nishio, and Hiromu Aoyama

Department of Chemistry, The University of Tsukuba, Sakuramura, Niihari, Ibaraki 305
†*Department of Agricultural Chemistry, Faculty of Agriculture, Meiji University, Ikuta, Tama-ku, Kawasaki 214*

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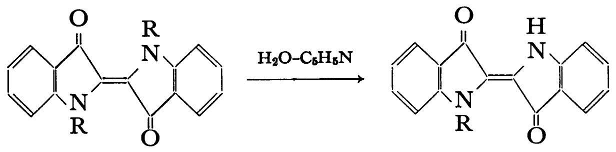
Synopsis. The hitherto unknown *N*-acylindigo has been selectively prepared by heating the corresponding known *N,N′*-diacylindigo in aqueous pyridine. The data of *N*-acetyl, *N*-benzoyl, *N*-(*p*-toluoyl), *N*-(*p*-chlorobenzoyl), *N*-(*p*-nitrobenzoyl), and *N*-(3,5-dinitrobenzoyl)indigo are summarized.

Indigo is a *trans* compound; it is stable and cannot be converted to the *cis*-isomer, not even by irradiation, while *N,N′*-diacetyl[1] and *N,N′*-dimethyl[2] derivatives have been known to show phototropic behavior. Recently we reported the *cis*-to-*trans* isomerization of *N,N′*-diacylindigo (**1**).[3] Therefore, it is of interest to see if *N*-acylindigo (**2**) can isomerize photochemically just like *N,N′*-diacylindigo.



1 R **2**

a: CH_3CO, **b**: C_6H_5CO, **c**: *p*-$CH_3C_6H_4CO$, **d**: *p*-ClC_6H_4CO, **e**: *p*-$NO_2C_6H_4CO$, **f**: 3,5-$(NO_2)_2C_6H_3CO$.

To our surprise, we cannot find any *N*-acylindigo in the literature, although several *N,N′*-diacylindigo have been known. In order to obtain *N*-acylindigo, we attempted to modify the partial acylation of indigo as well as the partial hydrolysis of *N,N′*-diacylindigo, and finally found a facile method of selectively preparing **2** from **1**.

The first trial at the acylation of indigo was as follows. Indigo and an equivalent amount of acetyl chloride were heated in acetic anhydride under reflux. The conditions were similar to those in the preparation of *N,N′*-diacetylindigo (**1a**)[4] except that excess molar acetyl chloride was used in the latter method. The products were found to be indigo and **1a**. The partial hydrolysis of **1a** was then examined. When **1a** was partially hydrolyzed by potassium hydroxide, the products were found to be indigo and **1a**. In neither case could we obtain an economical amount of **1a**. In the next trial, indigo was treated with sodium hydride in hexamethylphosphoric triamide, and then an excess amount of acetyl chloride was added. The product was a mixture of **2a** and **1a**; however, it seemed difficult to regulate the reaction, in which the formation of **2a** was predominant.

Finally, the partial hydrolysis of **1a** which had been heated in aqueous pyridine was found to be successful in giving **2a**. The reaction products were analyzed at time intervals by liquid chromatography and by means of the visible-absorption spectrum. The suitable conditions for the formation of **2a** were established to be as will be shown in the Experimental section.

Table 1. Properties of N-acylindigo (**2**)

R	Mp / °C	$\nu_{C=O}$ / cm^{-1}	ν_{N-H} / cm^{-1}	$\lambda_{max}^{C_6H_6}$ / nm	ε
CH_3CO	185—186	1700 1650	3320	568	12000
C_6H_5CO	268	1690 1655	3300	575	14000
p-$CH_3C_6H_4CO$	276—277	1690 1645	3310	575	15000
p-ClC_6H_4CO	290—291	1690 1660	3310	574	13000
p-$NO_2C_6H_4CO$	> 290	1700 1650	3320	574	12000
3,5-$(NO_2)_2$-C_6H_3CO	> 290	1690 1655	3350	572	9000

The infrared and visible spectra of *N*-acylindigo are summarized in Table 1. The data support the structure of monoacylindigo. Furthermore, the preliminary experiment shows that these examples of *N*-acylindigo do not show any phototropic behavior.

Experimental

N-*Acetylindigo (2a).* *a)*: Sodium hydride (227 mg) was washed with petroleum ether and dispersed in HMPA (15 ml); indigo (500 mg) was then added, and the solution was stirred for 4 h at 0 °C under an argon atmosphere. Then acetyl chloride (725 mg) was added, and the solution was stirred for 15 h. The products were extracted with dichloromethane, dried over anhydrous magnesium sulfate, and chromatographed over silica gel with chloroform–acetone (60 : 1) to give reddish-purple needles (89 mg). Mp 185—186 °C. Found: C, 71.41; H, 4.04; N, 8.91%. Calcd for $C_{18}H_{12}N_2O_3$: C, 71.04; H, 3.97; N, 9.20%.

b): A solution of **1a** (20 mg) in a pyridine–water mixture (80 : 20 v/v, 100 ml) was heated at 88 °C for 120 min. After the pyridine had been removed under reduced pressure, the product was recrystallized from ethyl acetate–hexane. The yield was 37%. Mp 185—186 °C (dec).

N-*Benzoylindigo (2b).* A solution of **1b** (273 mg) in a pyridine–water mixture (60 : 40 v/v, 100 ml) was heated at 88 °C for 80 min. After the pyridine had been evaporated the product was precipitated and recrystallized from chloroform–hexane and then acetone–hexane to give purple needles. Mp 268 °C (dec). 85%. Found: C, 75.35; H, 3.77; N, 7.48%. Calcd for $C_{23}H_{14}N_2O_3$: C, 75.40; H, 3.85; N, 7.64%.

N-*(*p-*Toluoyl)indigo (2c).* *N,N′*-Bis(*p*-toluoyl)indigo (4.0 mg) (**1c**) was dissolved in aqueous pyridine (50 : 50 v/v, 10 ml), and the solution was heated at 70 °C for 4 h. After having been treated with 6 M hydrochloric acid, the reaction mixture was extracted with chloroform, washed with water, and dried over magnesium sulfate. The product was purified by silica gel chromatography using ethyl acetate–benzene. The residue was recrystallized from acetone–hexane, as purple needles. Found: C, 75.42; H, 4.06; N, 7.15%. Calcd for

$C_{24}H_{16}N_2O_3$: C, 75.77; H, 4.23; N, 7.36%.

N-(p-*Chlorobenzoyl)indigo* (**2d**). Fine purple needles. Found: C, 68.78; H, 3.20; N, 6.83%. Calcd for $C_{23}H_{13}N_2O_3Cl$: C, 68.92; H, 3.26; N, 6.98%.

N-*(*p-*Nitrobenzoyl)indigo* (**2e**). Fine purple needles. Found: C, 66.94; H, 3.10; N, 9.86%. Calcd for $C_{23}H_{13}N_3O_5$: C, 67.15; H, 3.18; N, 10.21%.

N-*(3,5-Dinitrobenzoyl)indigo* (**2f**). A solution of **1f** (377 mg) in a pyridine–water mixture (90 : 10 v/v, 100 ml) was heated at 60 °C for 80 min. After the pyridine had been evaporated under reduced pressure, the residue was added to boiling water. The precipitates were collected, dried, and recrystallized from ethyl acetate–hexane and then benzene, as purple plates. Found: C, 60.01; H, 2.68; N, 11.96%. Calcd for $C_{23}H_{12}N_4O_7$: C, 60.53; H, 2.65; N, 12.27%.

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