Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 45 (2004) 9083–9086
Tetrahedron Letters

Thioindigo precursor: control of polymorph of thioindigo

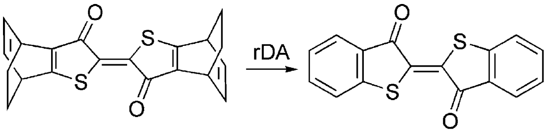
Hidemitsu Uno,[a,*] Kana Moriyama,[a] Takayuki Ishikawa,[b]
Noboru Ono[c] and Hidenori Yahiro[d]

[a] *Division of Synthesis and Analysis, Department of Molecular Science, Integrated Center for Sciences, Ehime University, Bunkyo-cho 2-5, Matsuyama 790-8577, Japan*
[b] *Inkjet Media Design Dept. 2, Inkjet Media Design Div., Inkjet Supply Material Development Center, Canon Inc., 16-1 Shimonoge 3-chome, Takatsu-ku, Kawasaki 213-8512, Japan*
[c] *Department of Chemistry, Faculty of Science, Ehime University, Bunkyo-cho 2-5, Matsuyama 790-8577, Japan*
[d] *Department of Applied Chemistry, Faculty of Engeneering, Ehime University, Bunkyo-cho 3, Matsuyama 790-8577, Japan*

Received 30 April 2004; revised 30 September 2004; accepted 6 October 2004

Abstract—2,2′-Bi[-3(2*H*)-thiophenon]ylidene with two bicyclo[2.2.2]-octadiene moieties was quantitatively converted to thioindigo by the retro-Diels–Alder reaction. The thioindigo solid obtained from the precursor had the $P2_1/c$ structure which was different from the commercial thioindigo samples ($P2_1/n$).

Indigo and thioindigo are known as vat dyestuffs and have been used for coloring textiles since ancient times. Their reduced precursors are called leuco forms and well soluble in alkaline media. When the leuco precursors are exposed to air, they are oxidized to the corresponding insoluble dyes. Although their properties as the vat dyestuffs are very good, the low solubility of the dyestuffs themselves in common solvents limits their use just as coloring material. In order to employ these pigments as functional materials such as materials for memory storage, equivalents of the pigments which can be quantitatively converted to the pigments without any by-product, are required. Morphological control of such dyestuffs is also one of the important problems.[1] We have already succeeded in the conversion of a precursor to tetrabenzoporphyrins for the application of field effect transistors by the thermal retro-Diels–Alder reaction.[2] We planned to utilize the methodology for indigo dyes. In this communication, we discuss about synthesis, thermal behaviors, and crystal structures of the thioindigo equivalent **1** as well as thioindigo itself (Eq. 1).

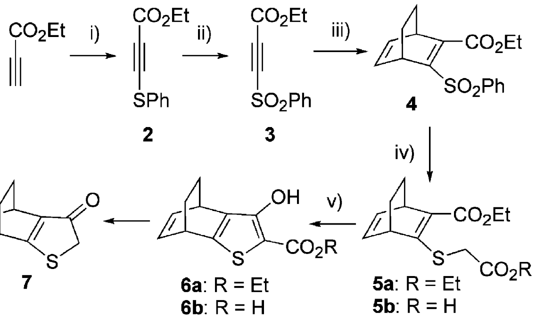


1

Thioindigo

(1)

The targeted equivalent **1** was prepared from commercially available ethyl propiolate in six steps (Scheme 1). In the literature, ethyl phenylsulfonylpropiolate (**3**)



Scheme 1. Reagents, Conditions, and Yields: (i) LiHMDS, $PhSO_2SPh$, THF, −78 °C; 95%. (ii) Dimethyldioxirane, acetone, rt. (iii) 1,3-Cyclohexadiene, $CHCl_3$, rt; 84% (two steps). (iv) Ethyl thioglycolate, NaH, THF, 0 °C; **5a**: 96%; thioglycolic acid, NaH, DMF, rt; **5b**: 88%. (v) NaOEt, toluene, 80 °C; **6a**: 79%; LDA, THF, −78 °C; H_2SO_4 (cat), CH_2ClCH_2Cl, rt; **7**: 74%.

Keywords: Thioindigo; Polymorphism; Retro-Diels–Alder reaction; Soluble precursor.

[*] Corresponding author. Tel.: +81 89 927 9660; fax: +81 89 927 9670; e-mail: uno@dpc.ehime-u.ac.jp

0040-4039/$ - see front matter
doi:10.1016/j.tetlet.2004.10.028

was obtained in good yield from ethyl propiolate by reaction with LDA and *S*-phenyl benzenethiosulfate followed by oxidation with mCPBA.[3] In our hands, however, we encountered low yields and poor reproducibility. In order to suppress the by-product formation derived from nucleophilic addition of diisopropylamine in the first step, LiHMDS was used instead of LDA and ethyl phenylsulfanylpropiolate (**2**) was obtained in 95% yield. Oxidation of **2** with mCPBA gave **3**, but we could isolate **3** in low yields (less than 30%) probably due to highly sensitive nature of **3** toward nucleophiles. We changed the oxidation reagent to dimethyldioxirane[4] and used **3** in the next step without purification. Thus, the Diels–Alder adduct **4**[3] was obtained in good yields (84%). Formation of thiophene ring was achieved by the Diekmann condensation.[5] The Diels–Alder adduct **4** was treated with ethyl thioglycolate and NaH in THF to give **5a** in 96% yield. Treatment of **5a** with NaOEt gave 3-hydroxythiophene-2-carboxylate **6a** in 79% yield. In spite of all our efforts, removal of 2-ethoxycarbonyl group failed due to the thermal instability of **6a** (80 °C, decomp.) and the route was slightly changed. Addition of a disodium salt of thioglycolic acid to **4** in DMF gave acid **5b** in 88% yield. The intramolecular condensation of **5b** directly afforded the 2*H*-thiophen-3-one **7** in 74% yield by an acidic work-up of the initially formed product **6b**.

Oxidative dimerization of **7** to the targeted **1** was next examined under a variety of conditions as shown in Table 1. Two phase oxidation with potassium ferricyanide gave the best result and the targeted compound **1**[6] was obtained as a 1:1 mixture of diastereomers in 75% isolated yield. In this oxidation, only an *E*-isomer of the newly formed double bond was obtained.

Thermal behavior of the thioindigo precursor **1** was examined. The UV spectra were measured during 5 min heating of an orange solution of **1** in diphenyl ether. From this experiment, conversion of **1** to thioindigo started at around 160 °C and completed at 200 °C. The final spectra were completely identical with those of commercially available thioindigo. Heating the solid precursor **1** at 200 °C for 10 min gave analytically pure thioindigo in quantitative yield. From the TG–DTA experiment, almost the same decomposition temperature as in solution was observed; the precursor lost 21.6% of its weight corresponding to two molecules of ethylene between 140 and 195 °C (Fig. 1). Careful inspection of the TG curve (more obvious in DTG curve) revealed that the earlier half of weight loss was sharp (144–160 °C) compared to the latter half (165–195 °C).

Table 1. Oxidative dimerization of **7** to **1**

Conditions	Yield/%
LDA, I_2 (0.5 equiv), THF, rt	23
LDA, I_2 (1.0 equiv), THF, rt	19
t-BuOK, I_2 (0.6 equiv), THF, rt	11
N-Methylmorpholine, I_2 (2.0 equiv), CH_2Cl_2, rt	11
CAN (2.5 equiv), aq MeCN, rt	39
$FeCl_3$–SiO_2, CH_2Cl_2, rt[7]	5
$K_3[Fe(CN)_6]$, H_2O–EtOAc, rt[8]	75

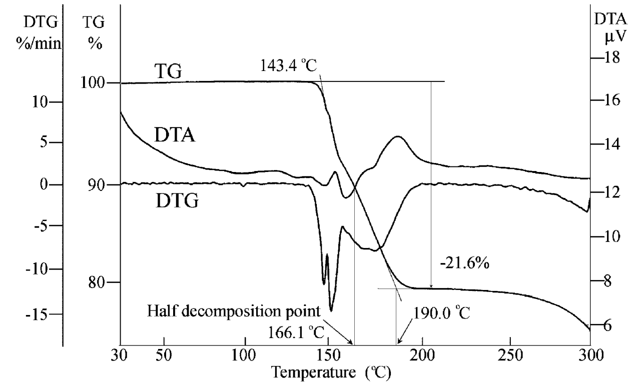


Figure 1. TG–DTA experiment of **1** to thioindigo. The precursor **1** (2.94 mg) was heated at a rate of 20 °C/min under a nitrogen atmosphere.

The XRD experiments of **1**, its thermally decomposed sample (200 °C, 5 min), and commercial thioindigo were carried out and results are shown in Fig. 2. The powder pattern of thioindigo (Fig. 2a) obtained by the thermal decomposition of **1** was quite different from that of commercially available thioindigo (Fig. 2b),[9] and the former and the latter were proven to be the known I ($P2_1/c$) and II ($P2_1/n$) crystal packing types of thioindigo by simulation,[10,11] respectively. Even when the commercial thioindigo sample was heated at 200 °C, the reflection pattern did not change. Thioindigo structure I which is formed by sublimation at 280 °C with partial decomposition[10a] is $P2_1/c$ and the molecules stack along the *b* axis. Therefore, the thioindigo molecules in this crystal system look

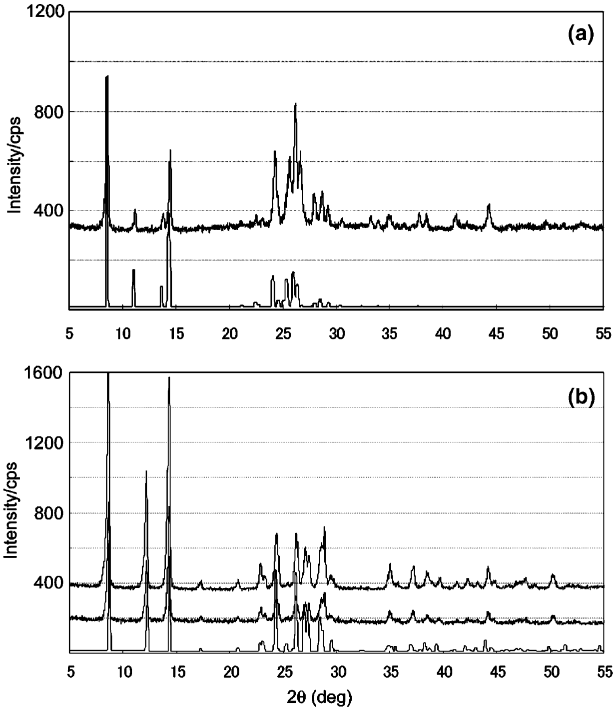


Figure 2. XRD spectra of thioindigo samples. (a) Thioindigo obtained by the pyrolysis (200 °C, 5 min) of **1** (upper) and the simulation pattern of the $P2_1/c$ crystal of thioindigo (lower); (b) commercial thioindigo (upper), commercial thioindigo after 5 min heating at 200 °C (middle), and the simulation pattern of the $P2_1/n$ crystal of thioindigo (lower).

to lie in parallel lines in the *c–a* plane (Fig. 3a). On the other hand, thioindigo structure II which is formed by sublimation at 190 °C[10c] is $P2_1/n$ and the thioindigo molecules stacks along the *a* axis. Therefore, the thioindigo molecules in this crystal system look to lie in zigzag lines in the *b–c* plane (Fig. 3b).

Fortunately, single crystals for the X-ray analysis were obtained by slow diffusion of hexane in a CH_2Cl_2 solution of **1**.[12] The XRD pattern of the powder sample of **1** was proven to be identical with that obtained by simulation. The chromophores stack along the *a* axis, the mean plane distance is 4.62 Å, and the molecules look to lie in parallel lines in the *b–c* plane (Fig. 4). This may explain the formation of thioindigo crystal type I ($P2_1/c$) when **1** is heated to decompose to thioindigo.

In order to examine the transformation mechanism in detail, we measured the DSC–XRD and the results are shown in Figure 5. Each XRD was recorded during the temperature range of ca 8.1 °C. The DSC curve shows the existence of two decomposition periods corresponding to the exothermic peaks at ca 160 and 177 °C during the whole decomposition. The XRD pattern of the precursor **1** remained in the first (lower) decomposition period (Fig. 5a–e), while that of structure I($P2_1/c$) of thioindigo appeared in the second (higher) decomposition period (Fig. 5f–k). In the XRD of the intermediate point (Fig. 5f, 163.8–171.9 °C), a new diffraction pattern (asterisks) was clearly observed as well as that of structure I. This intermediate XRD pattern was observed during almost the whole range of decomposition (Fig. 5c–h; ca 140–188 °C). Taking the result of the TG–DTA experiment (Fig. 1) into an account, the intermediate XRD pattern strongly suggested the existence of an intermediate compound such as mono-ethylene-bridged thioindigo, although further experiments were required for determination. No XRD pattern of structure II or amorphous phase was observed during the decomposition.

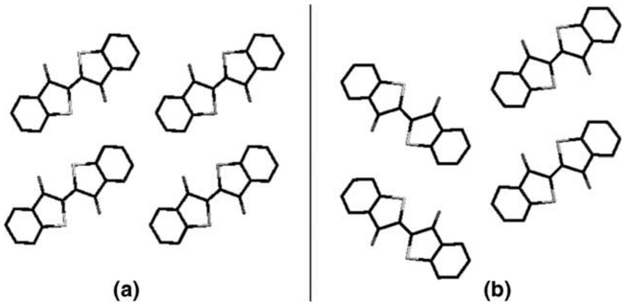


Figure 3. Crystal packing views of thioindigo. (a) Structure I ($P2_1/c$) along *b* axis. (b) Structure II ($P2_1/n$) along *a* axis.

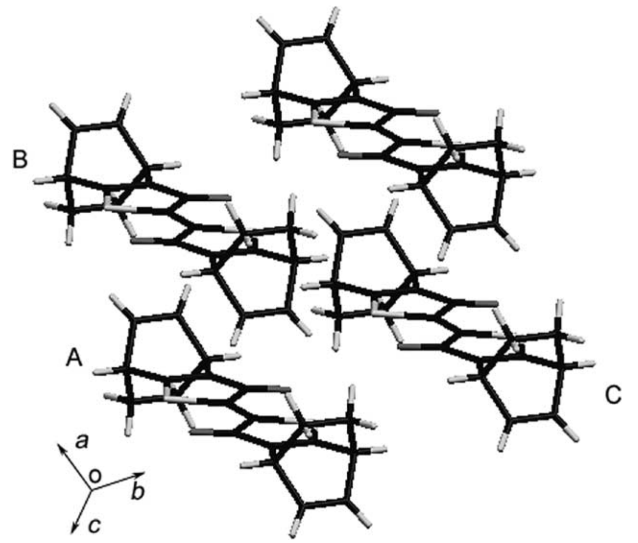


Figure 4. Packing diagram of **1**. The mean plane distances between the chromophores of A, B, and C are 4.62 (A–B) and 2.63 Å (A–C).

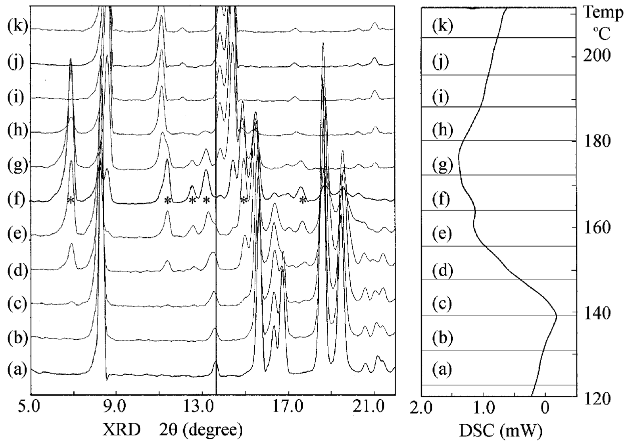


Figure 5. DSC–XRD experiment of **1** to thioindigo. The precursor **1** was heated at a rate of 5 °C/min under a nitrogen atmosphere and the XRDs were measured (Cu*K*α, 2*θ* 5.00–44.99°, 30°/min) during the interval of ca 8.1 °C. (a) 123.0–131.2; (b) 131.2–139.4; (c) 139.4–147.6; (d) 147.6–155.7; (e) 155.7–163.8; (f) 163.8–171.9; (g) 171.9–180.0; (h) 180.0–188.1; (i) 188.1–196.2; (j) 196.2–204.4; (k) 204.4–212.5 °C.

In conclusion, we succeeded in preparation of the thioindigo equivalent which quantitatively gives thioindigo by heating. The crystal packing type of formed thioindigo is only obtained by high temperature sublimation with partial decomposition and is well expected by the crystal packing of the equivalent.

Acknowledgements

We appreciate the partial financial support of Grant-In-Aid for Scientific Research (No. 15655013) from the Ministry of Education, Culture, Sports, Science, and Technology. T.I. thanks Canon Inc. for permission of researching at Ehime University. We thank Mr. Akira Kishi and Ms. Yayoi Taniguchi (Application Laboratory, Rigaku Co.) for their DSC–XRD measurements [RINT-Ultima II (XRD-DSC II)].

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.10.028.

References and notes

1. (a) Fukushima, K.; Nakatsu, K.; Takahashi, R.; Yamamoto, H.; Gohda, H.; Homma, S. *J. Phys. Chem. B* **1998**, *102*, 5986; (b) Mizuguchi, J. *J. Cryst. Soc. Jpn.* **2002**, *44*, 50.
2. (a) Ito, S.; Murashima, T.; Uno, H.; Ono, N. *Chem. Commun.* **1998**, 1661; (b) Uno, H.; Ishikawa, T.; Hoshi, T.; Ono, N. *Tetrahedron Lett.* **2003**, *44*, 5163.
3. Shen, M.; Schultz, A. G. *Tetrahedron Lett.* **1981**, *35*, 3347.
4. Murray, R. W.; Singh, M. *Org. Synth. Coll.* **1998**, *9*, 228.
5. Campaigne, E. Thiophenes and their Benzo Derivatives: (iii) Synthesis and Applications; In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Cheeseman, G. W. H., Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 4, Chapter 3.15.
6. *Spectroscopic data for* **1**: δ_H ($CDCl_3$) 6.47 (2H, m), 6.36 (2H, m), 4.15 (2H, m), 4.01 (2H, m), and 1.63–1.44 (8H, m); δ_C ($CDCl_3$) 184.5, 179.0, 179.0, 136.2, 136.0, 131.7, 40.4, 33.9, 25.8, and 25.4; ν_{max} 2965, 2935, 1632, and 1602 cm^{-1}: λ_{max} (CH_2Cl_2, $\log \varepsilon$) 483 (2.77) nm.
7. Jempty, T. C.; Gogins, K. A. A.; Mazur, Y.; Miller, L. L. *J. Org. Chem.* **1981**, *46*, 4545.
8. Feringa, B.; Wynberg, H. *J. Org. Chem.* **1981**, *46*, 2547.
9. Purchased from Tokyo Kasei Co. Ltd http://www.tokyokasei.co.jp.
10. (a) von Eller, H. *Bull. Chim. Soc. Fr.* **1955**, *106*, 1426; (b) von Eller, H. *Bull. Chim. Soc. Fr.* **1955**, *106*, 1438; (c) Haase-Wessel, W.; Ohmasa, M.; Süsse, P. *Naturwissenschaften* **1977**, *64*, 435, Structure I: monoclinic, $P2_1/c$, $Z = 2$, $a = 7.91(3)$, $b = 3.97(2)$, $c = 20.41(3)$ Å, $\beta = 93(1)°$: Structure II: monoclinic, $P2_1/n$, $Z = 2$, $a = 3.981(3)$, $b = 20.65(2)$, $c = 7.930(7)$ Å, $\beta = 98.84(5)°$.
11. Powder simulation and single cystal analysis were performed by CrystalStructure Ver. 3.6.0 (Rigaku, 3-9-12 Akishima, Tokyo, Japan).
12. *Crystallographic data for* **1**: $C_{20}H_{16}O_2S_2$, orange crystal, triclinic, *P–1*, $Z = 1$ in a cell of dimensions $a = 5.891(1)$, $b = 6.474(2)$, $c = 10.710(2)$ Å, $\alpha = 86.51(2)°$, $\beta = 79.61(1)°$, $\gamma = 84.09(2)°$, $V = 399.26(16)$ Å^3, $D_{calc} = 1.466\,g\,cm^{-3}$. 1835 unique reflections (1996 measured at rt), 1327 with $F^2 > 2\sigma(F^2)$. The final $R_1 = 0.0586$, $_{wR}$ (all) = 0.1629, goodness-of-fit = 1.017 for 110 parameters. The molecule occupies a special position. The crystal is a mixture of two stereoisomers in 1:1 ratio, and the double and single bonds in the bicyclo[2.2.2]-octadiene skeleton could not be distinguished. In the refined structure, hydrogen atoms are formally placed as if the double bonds occupy the *trans* position. The crystallographic data are deposited at Cambridge Crystallographic Data Centre (CCDC 233280).