



Isatin α -chloride에 의한 인디고계 염료의 합성

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The Synthesis of Indigoid-Type Dyes Based on Isatin α -Chloride

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(Received: May 11, 2007/Revised: June 8, 2007/Accepted: June 18, 2007)

Abstract— The indigoid-type dyes based on isatin α -chloride were synthesized and the dyes were discussed with relevance to the “H-chromophore” or “cross-conjugated chromophore.” The color-changed properties of the dyes were also investigated by means of visible absorption spectra. The novel dyes from isatin α -chloride are of theoretical interest and such dyes can be used as continuous pH indicators in acid/base titrimetric analyses.

Keywords: *indigoid dyes, H-chromophore, cross-conjugated chromophore, pH indicator*

1. Introduction

1.1 H-chromophore

Cross-conjugated chromophores describe; a basic color-producing system consists of a C=C double bond substituted by two opposing donor group and two opposing acceptor groups. The inherent cross conjugation of the molecule has been recognised as being responsible for high bathochromicity of these systems, and Klessinger¹⁻⁴⁾ has expanded this system a “H-chromophore” because of its structural geometry. In general indigo (Fig. 1) is the classical example of a dye containing a cross conjugated chromophore⁵⁻⁷⁾.

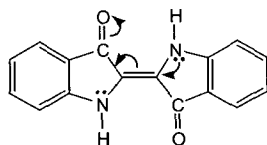


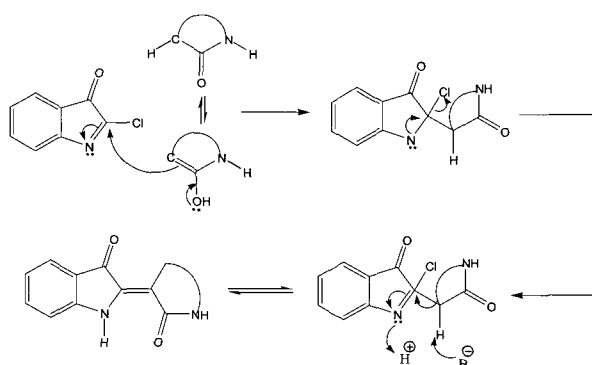
Fig. 1. A classical example of cross conjugated chromophore for indigo.

Another such H-chromophore types are isatin dyes and the series of these dyes were easily synthesized by the way of a Knoevenagel reaction, (Scheme 1) i.e. the condensation of aldehydes or ketones, usually not containing an hydrogen, with compounds of the form Z-CH₂-Z' or Z-CHR-Z' is called the Knoevenagel reaction,⁸⁾ where Z and Z' may be CHO, COR, COOH, COOR, CN, NO₂, SOR, SO₂R, SO₂OR, or similar groups.

1.2 Dyes as a pH Indicator

A pH indicator dye can be defined as; a dye or dye precursor whose visible absorption spectrum alters perceptibly and reversibly in response to a change in the pH of the molecular environment. Such dyes can be used as indicators in acid-base titrimetric analyses. This end point of titration is made evident by a color change of the indicator, and ideally the color change takes place over as narrow an interval of added titrant as possible.

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Scheme 1. The synthesis of isatin dyes by way of a Knoevenagel reaction.

For example, the color change in an acid metric-titration would ideally occur over an interval of about 1.2 to 2.2 pH units. Otherwise the pH value of the mid-point of the color change corresponds to the pKa value of the conjugate acid.

Generally, good pH indicator dyes should;⁹⁾

- be readily soluble in water, dilute acids and other common titration media
- be stable in light, air
- exhibit a color change that is pronounced, rapid and fully reversible
- not react with other species encountered in the titrimetric reaction

1.3 Dyes as a redox Indicator

In some cases dyes have an ability to change color in redox system, and it was noted from the very earliest days of synthetic dye chemistry that dyes could be reduced with hydrogen and then this resulted in loss of color. In many cases, but not all, the reduction process was reversible and on exposure to air or more powerful oxidizing agents, the color of the dyes could be restored. In fact, such reversible reduction-oxidation processes have been used for thousands of years in the vat dyeing of textiles with natural indigo and quinonoid dyes. Color change could also be brought about more subtly with some dyes, by the reversible action of acids and bases, and this led to the concept of acid-base indicators. These oxidation-reduction behaviour of dyes has been used for analytic indicator or color-forming recording media. The first successful redox behaviour was

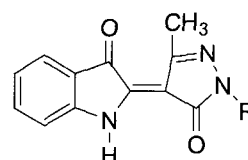
diphenylamine, introduced by Knop in 1924 for titrating ferrous solution with dichromate¹⁰⁾.

In the present paper the synthesis of a number of isatin-type dyes with containing cross conjugated chromophores are discussed. Also, acid-base sensitivities and oxidation-reduction reversible processes of isatin-type dyes are examined, especially, their color change behaviour.

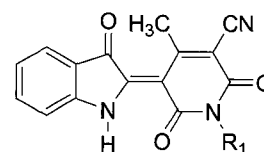
2. Experimental

2.1 Novel Dyes from Isatin α -Chloride

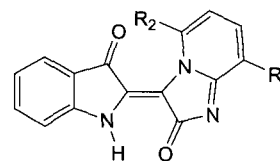
Fig. 2 shows the series of dyes which were successfully synthesized.



A: R = H
B: R = Ph



C: R₁ = CH₂CH₃
D: R₁ = CH₂CH₂CH₂OCH₃



E: R₁, R₂ = H
F: R₁ = H, R₂ = OH
G: R₁ = H, R₂ = Me

Fig. 2. Synthesized H-chromophore typed isatine dyes.

2.2 Synthesis of isatin α -chloride

Isatin (5.0 g, 0.03 mole) was refluxed with phosphorous pentachloride (7 g, 0.03 mole) in dry toluene (20 ml) for 3 hours in a flask fitted with a calcium chloride drying tube. (All solvent were dried over anhydrous magnesium sulfate for at least 48 hours before a reaction was commenced).

The reaction was followed by t.l.c. The reaction mixture was then allowed to cool, the resulting

precipitate was filtered off, and washed with ligroin (100/120) two times. The product was dried in a desiccator over calcium chloride for 24 hours (3.9 g, 78 %). Mass Spectrum (FAB): found 166 (M/Z); required for $C_8H_5N_1O_1Cl$, $M = 166$

3-methyl-4-(3-oxoindolin-2-ylidene)-2-pyrazolin-5-one (A); 2-Chloroisatine (1.7 g, 1 mmole) and 3-methyl-5-pyrazolone (1.74 g, 1 mmole) were dissolved in dry dichloromethane (20 ml) in a flask fitted with a calcium chloride drying tube. The reaction mixture was refluxed at this stage for 6 hour with checking the reaction by t.l.c. for disappearance of the 2-chloroisatine and appearance of new product. Reaction mixture was cooled to room temperature and the solvent was then removed by rotary evaporation. The product recrystallized from ethanol and dried in a vacuum desiccator. 3-methyl-4-(3-oxoindolin-2-ylidene)-2-pyrazolin-5-one was obtained as a red solid (1.17 g, 52 %) m.p. 178-181 °C. Mass Spectrum (FAB): found 228 (M/Z); required for $C_{12}H_9N_3O_2$, $M + H = 228$. Elemental analysis: found C 64.1, H 4.15, N 17.70; $C_{12}H_9N_3O_2$ requires C 63.4, H 3.96, N 18.48 %. 1H NMR (300 MHz, $CDCl_3$): 2.71 (s, 3H), 7.14 (d, H, $J=7.78$ Hz), 7.22 (t, H, $J=7.8$ Hz), 7.66 (t, H, $J=7.7$ Hz), 7.73 (d, H, $J=7.8$ Hz), 11.40 (s, H), 12.63 (s, H).

1-phenyl-3-methyl-4-(3-oxoindolin-2-ylidene)-2-pyrazolin-5-one (B); 2-Chloroisatine (1.7 g, 1 mmole) and 1-phenyl-3-methyl-5-pyrazolone (0.98 g, 1 mmole) were dissolved in dry tetrahydrofuran (20 ml) in a flask fitted with a calcium chloride drying tube. The reaction mixture was refluxed at this stage for 6 hour and the same experimental procedures were followed to synthesis (A). The 1-phenyl-3-methyl-4-(3-oxoindolin-2-ylidene)-2-pyrazolin-5-one was obtained as a red solid (1.45 g, 48 %) m.p. 215 - 217 °C. Mass Spectrum (FAB): found 304 (M/Z); required for $C_{18}H_{13}N_3O_2$, $M + H = 304$. Elemental analysis: found C 71.1, H 4.45, N 14.01; $C_{18}H_{13}N_3O_2$ requires C 71.28, H 4.32 N 13.85 %. 1H NMR (300 MHz, $CDCl_3$): 2.6 (s, 3H), 7.04 (d, H, $J=7.78$ Hz), 7.13 (t, H, $J=7.7$ Hz), 7.20 (t, H, $J=7.7$ Hz), 7.43 (t, 2H, $J=7.0$ Hz), 7.56 (t, H, $J=6.9$

Hz), 7.7 (d, H, $J=7.7$ Hz), 7.96 (d, 2H, $J=8.15$ Hz), 11.35 (s, H).

3-(3-oxoindolin-2-ylidene)-1-ethyl-4-methyl-2,6-dioxoazine-5-carbonitrile (C); 2-Chloroisatine (1.7 g, 1 mmole) and 1-ethyl-4-methyl-2,6-dioxoazine-5-carbonitrile (1.78 g, 1 mmole) were dissolved in dichloromethane (15 ml) in a flask fitted with a calcium chloride drying tube. The reaction mixture was refluxed at this stage for 6 hours with checking the reaction by t.l.c. for disappearance of the 2-chloroisatine and appearance of new product. Reaction mixture was cooled to room temperature and evaporated the solution using a rotary evaporator. The resultant precipitate was recrystallized from toluene. The new product was filtered off, dried in an oven 50 °C and 3-(3-oxoindolin-2-ylidene)-1-ethyl-4-methyl-2,6-dioxoazine-5-carbonitrile obtained as a purple solid (1.45 g, 47 %), m.p. 177-180 °C. Elemental analysis: found C 66.25, H 4.35, N 13.45; $C_{17}H_{13}N_3O_3$ requires C 66.44, H 4.26, N 13.67 %.

1H NMR (300 MHz, $CDCl_3$): 1.23 (t, 3H, $J=7.0$ Hz), 2.72 (s, 3H), 4.0 (quart, 2H, $J=6.9$ Hz), 6.91 (d, H, $J=7.8$ Hz), 7.60 (t, 2H, $J=8.0$ Hz), 7.70 (d, 2H, $J=7.1$ Hz).

3-(3-oxoindolin-2-ylidene)-N-(3-methoxy)propanoyl-4-methyl-2,6-dioxoazine-5-carbonitrile (D); 2-Chloroisatine (1.7 g, 1 mmole) and 1-ethyl-4-methyl-2,6-dioxoazine-5-carbonitrile (2.2 g, 1 mmole) were dissolved in dichloromethane (15 ml) in a flask fitted with a calcium chloride drying tube. The reaction mixture was heated under reflux at this stage for 6 hours and the same experimental procedures were followed to synthesis (C). The 3-(3-oxoindolin-2-ylidene)-N-(3-methoxy)propanoyl-4-methyl-2,6-dioxoazine-5-carbonitrile was obtained as a purple solid (1.68 g, 48 %), m.p. 195-197 °C. Elemental analysis: found C 65.45, H 5.15, N 11.71; $C_{19}H_{17}N_3O_4$ requires C 65.0, H 4.84, N 11.96 %. 1H NMR (300 MHz, $CDCl_3$): 1.84 (quint, 2H, $J=6.8$ Hz), 2.35 (s, 3H), 3.33 (s, 3H), 3.42 (t, 2H, $J=5.9$ Hz), 4.1 (t, 2H, $J=7.1$ Hz), 7.1 (d, H, $J=7.9$ Hz), 7.25 (t, H, $J=8.0$ Hz), 7.67 (t, H, $J=7.8$ Hz), 7.73 (d,

H, $J=7.7$ Hz), 12.6 (s, H).

6-(3-oxoindolin-2-ylidene)-5,8-diazaindan-7-one (E); 2-Chloroisatine (2.5 g, 15 mmole) and [3,7- α]-diazaindan-2-one (2.0 g, 15 mmole) were dissolved in dichloromethane (15 ml) and the solution was refluxed for 6 hours. The same experimental procedures were followed to synthesis (A). The 6-(3-oxoindolin-2-ylidene)-5,8-diazaindan-7-one was obtained as a red solid (1.8 g, 46 %), m.p. 199-201 °C. Elemental analysis: found C 68.60, H 3.10, N 15.85; $C_{15}H_9N_3O_2$ requires C 68.44, H 3.45, N 15.96 %.

4-hydroxy-6-(3-oxoindolin-2-ylidene)-5,8-diazaindan-7-one (F); 2-Chloroisatine (0.45 g, 2.7 mmole) and 8-hydroxy-[3,7- α]-diazaindan-2-one (0.4 g, 2.7 mmole) were dissolved in dichloromethane (5 ml) and the solution was refluxed for 6 hours. The same experimental procedures were followed to synthesis (A). The 4-hydroxy-6-(3-oxoindolin-2-ylidene)-5,8-diazaindan-7-one was obtained as a red solid (0.6 g, 80 %), m.p. 224-225 °C. Elemental analysis: found C 64.60, H 3.14, N 15.27; $C_{15}H_9N_3O_3$ requires C 64.52, H 3.25, N 15.05 %.

4-methyl-6-(3-oxoindolin-2-ylidene)-5,8-diazaindan-7-one (G); 2-Chloroisatine (0.45 g, 2.7 mmole) and 7-methyl-[3,7- α]-diazaindan-2-one (0.4 g, 2.7 mmole) were dissolved in dichloromethane (5 ml) and the solution was refluxed for 6 hours. The same experimental procedures were followed to synthesis (A). The 4-methyl-6-(3-oxoindolin-2-ylidene)-5,8-diazaindan-7-one was obtained as a red solid

(0.52 g, 70 %), m.p. 153-155 °C. Elemental analysis: found C 69.40, H 4.23, N 15.45; $C_{16}H_{11}N_3O_2$ requires C 69.31, H 4.00, N 15.15 %.

3. Results and Discussion

3.1 The Visible Absorption Spectroscopic Properties for Isatin Dyes

The color change process may involve proton addition/removal or more rarely hydroxide ion addition/removal. Isatin dyes provide examples of the type. At about pH 10 the isatin dye (C) changes from purple to colorless due to formation of the base, which no longer has conjugation between C=C double bond site. The hydroxide ion is lost if the pH is lowered about 3, and the color is restored. The experimental results of the color change properties for isatin dyes were in methanol, dichloromethane and toluene shown in Table 1.

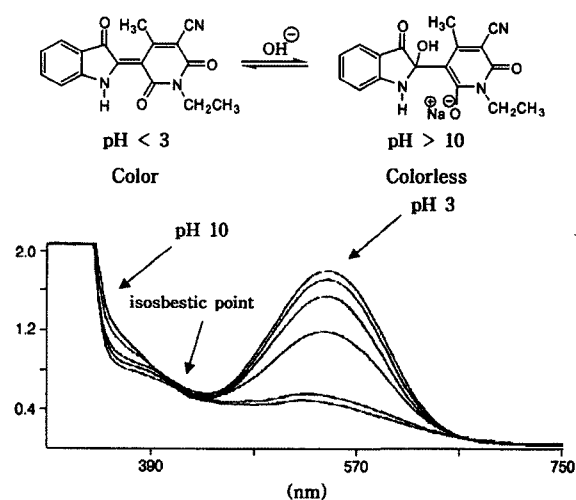


Fig. 3. Absorption spectra of isatin dye (C) in acid-base system in methanol (isosbestic point at ca. 430 nm).

Table 1. Visible Absorption Spectroscopic Data for Isatin Dyes

Compound	Methanol		Dichloromethane		Toluene Neutral
	Acid	Base	Acid	Base	
A	504	colorless	510	colorless	508
B	509	colorless	510	colorless	512
C	541	colorless	545	colorless	548
D	554	colorless	554	colorless	549
E	480	511	496	513	525
F	500	510	516	521	490
G	540	550	560	570	542

3.2 Redox-Indicator for Isatin Dyes

Isatin-type dyes (A - D) are good examples of the redox indicators. On reducing agents such as sodium borohydride, the central carbon to carbon double bond system is transformed to non-conjugation system and then the color (purple) changes to colorless. Otherwise by air or oxidizing agents (ferric chloride or lead dioxide) the reduced leuco compounds readily change to the original colored forms. These redox indicator dyes have certain common characteristics; i) the oxidized products have a visible absorption band, ii) the reduced products have a back to original coloration by air or oxidizing agents, iii) the redox products have a fully reversible at the end point.

The experimental procedure : the determination of the color conversion of the redox indicator dyes was as follow; i) to measure the rate of air oxidation, leuco dye was dissolved in dichloromethane or a mixture of dichloromethane and methanol with solutions of concentration about below $< 1 \times 10^{-4}$ M, ii) to give an absorbance of ca. 0.8 - 1.2 at λ_{\max} in their color form, iii) to give maximum coloration, the dye solution was sealed in a quartz UV cell

and irradiated with UV light at room temperature iv) the absorbance was measured in air with time intervals (every 10 min) and the conversion rate from leuco colorless to color for air oxidation was obtained. Air-oxidation reaction of isatin-type was investigated and their graph of conversion, i.e. fraction vs time, was shown in Fig. 4.

It was demonstrated that the "first order rate constants" (K) was calculated from linear "log(A_0/A_t) vs time" plots at the wavelength of maximum absorbance, i.e the slope of line gave the first order rate constants, K, and half lives, $T_{1/2}$ were measured by using the expression " $T_{1/2} = 0.693 / K$ ".

The electronic absorption spectra of the leuco dyes (A - D) show no absorbance in the visible region, where as after oxidation of the leuco form their dyes have a large ranges of the absorption maximum about 510 - 550 nm in the visible region. We have found that 100 % conversion of the leuco indicator dyes to the color form cannot be completed. The first order rate constant, half-lives and decomposition values of the leuco dyes (A, B, C and D) on air were in methanol investigated Table 2.

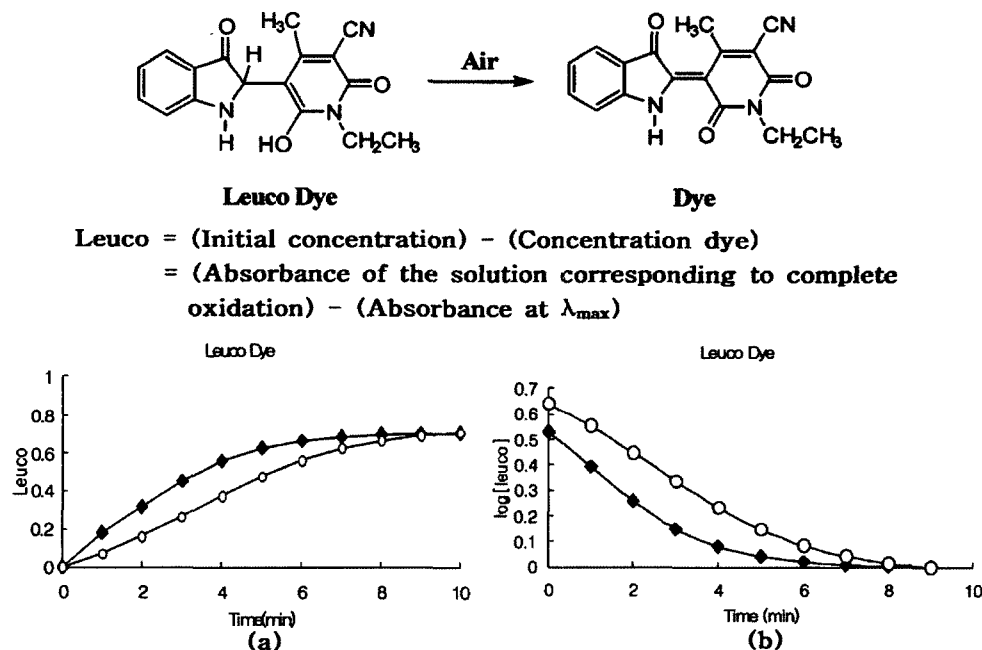


Fig. 4. Color conversion curves of (a) fraction/time plot and (b) log(fraction/time) plot for (◆)leuco 3-(3-oxoindolin-2-ylidene)-1-ethyl-4-methyl-2,6-dioxoazine-5-carbonitrile, (○) leuco 3-(3-oxoindolin-2-ylidene)-N-(3-methoxy)-propanoyl-4-methyl-2,6-dioxoazine-5-carbonitrile.

Table 2. The first order rate constants (K), time for half lives and their decomposition values of pH indicator dyes in methanol solution at room temperature on air

Compound	Decomposition for 1 hour (%)	λ_{\max} (nm) in methanol	Half-lives ($T_{1/2}$, min)	First order rate constant ($K_{\text{sec}^{-1}}$)
A	21	504	9	2.31×10^{-3}
B	24	510	8	2.99×10^{-3}
C	41	540	10	1.16×10^{-4}
D	63	545	13	8.90×10^{-4}

These H-chromophores (E - G) can be exist in E and Z isomeric form. In general, unless there are large differences in the relative stabilities of the two form, separation of these can be very difficult. Computer modelling for (E) based on space-filling consideration that there is a clear distinction between the E-isomer, that can be fully planar, and the Z-isomer, which is distorted from planarity (Fig. 5).

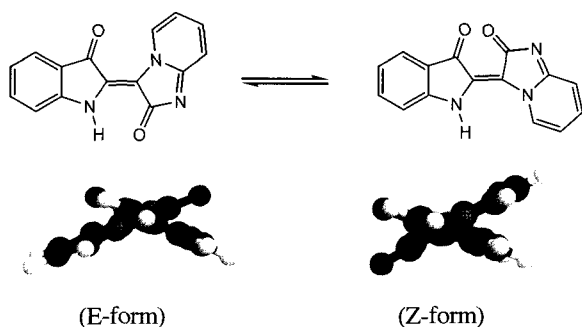


Fig. 5. Conformations and 3-D-representations of geometric isomers of H-chromophore (E).

4. Conclusions

Several new H-chromophores were synthesized with a view to examine their color properties, pH sensitivity and redox behaviour. The unsymmetrical chromophores containing both pyrazolin-5-one and isatine (indoxyl) residue might have been expected to have λ_{\max} (absorption maxima) values midway between those for the symmetrical parent H-chromophores, but in our experiments the observed values were at considerably short wavelengths than this. This effect was even more pronounced in unsymmetrical H-chromophores containing pyrazolin-5-one and isatine terminal groups. The unsymmetrical H-chromophores based on pyrazolin-5-ones and dioxazine-5-carbonitriles were base sensitive, and addition of sodium hydroxide

in solution resulted in complete loss of color. This could be reversed by addition of acid and suggest that these chromophores could be useful as color former and pH indicator. Also, In our results, these H-chromophores were readily reduced to colorless leuco compounds in solution with sodium borohydride, and these could be air-oxidised back to the colored species at room temperature and they are potentially interest as redox indicators.

5. References

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