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SYNTHESIS AND PROPERTIES OF 6H-BENZO[hi]PYRROLO[2,1,5-cd]INDOLIZIN-6-ONES[1]

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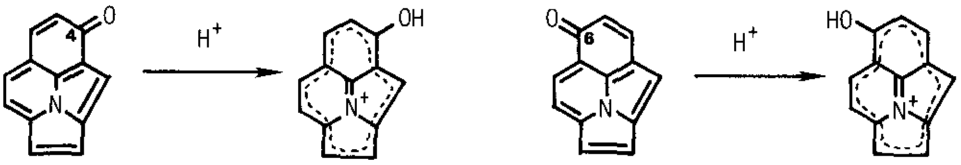
Abstract —— The electronic features and chemical behaviors of 3-phenyl-6H-benzo[hi]pyrrolo[2,1,5-cd]indolizin-6-one (**1**) were discussed comparing with those of 4-one regio-isomer, 3-phenyl-4H-benzo[hi]pyrrolo[2,1,5-cd]indolizin-4-one (**2**).

In the course of our studies on iso π-electronic isomers of 1H-phenalen-1-one, we recently reported some interesting properties of 4H-benzo[hi]pyrrolo[2,1,5-cd]indolizin-4-one (**A**); *e.g.*, i) a highly polarized structure in the ground state, ii) the exsistence of a peripheral [12]annulene system in its protonated species **B**, iii) a significant stabilization of the excited state in **B**.[1b] Therefore, it is of interest to investigate the properties of 6H-benzo[hi]pyrrolo[2,1,5-cd]indolizin-6-one (**C**), a regio-isomer of **A**.

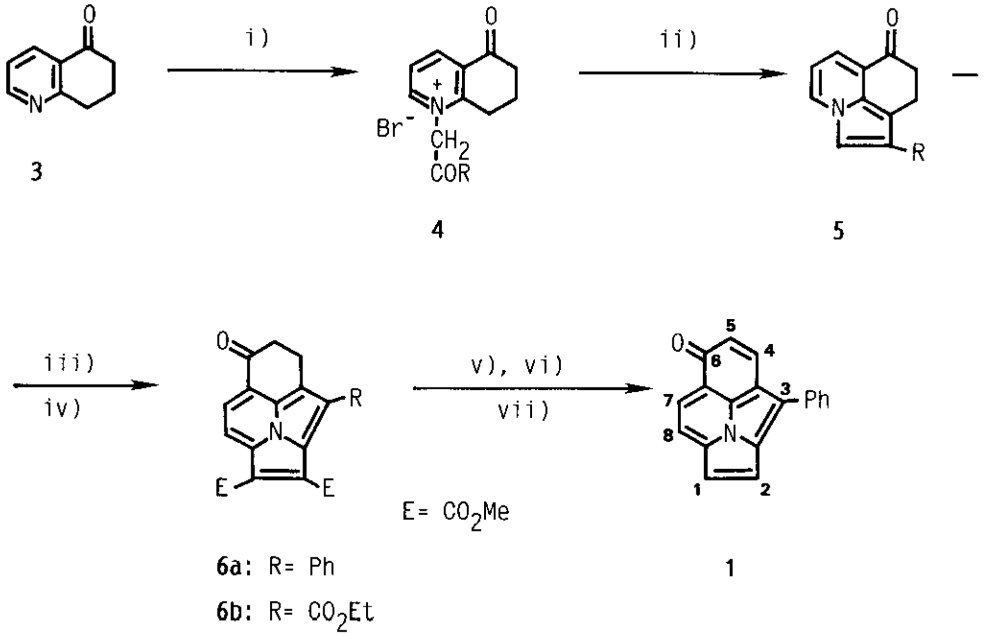


A **B** **C** **D**

In this paper we discuss the properties of 3-phenyl-6H-benzo[hi]pyrrolo[2,1,5-cd]indolizin-6-one (**1**) comparing with those of 3-phenyl-4H-benzo[hi]pyrrolo[2,1,5-cd]indolizin-4-one (**2**).[1b]
At first, the MO calculations for **C** and its protonated species **D** using MNDOA method[2] revealed that both molecules have planar structures and that **C** is less polarized than **A** at the ground state (calculated dipole moment: 3.75 D for **C** and 4.26 D for **A**). However, the polarization of **C** was enhanced by the protonation at the carbonyl oxygen, *i.e.* in molecule **D**. The resulting positive

charge is delocalized over the peripheral linkage and more stabilization than **B** is predicted because of lowering the LUMO of D (Figure 2).

6*H*-Benzo[*hi*]pyrrolo[2,1,5-*cd*]indolizin-6-one derivatives **6a,b** were prepared in three steps from 7,8-dihydro-5(6*H*)-quinolone (**3**) (Scheme 1). The saponification of **6a** follwed by the decarboxylation gave 3-phenyl derivative **1**. However, the efforts to convert **6b** into the unsubstituted molecule **C** had been unsuccessful.



Scheme 1. Reagents and Conditions: i) RCOCH$_2$Br, acetone, reflux, 20 h; ii) NaHCO$_3$, EtOH, reflux, 6 h; iii) DMAD, toluene, room temperature, 0.5 h; iv) DDQ, toluene, reflux, 2 h; v) KOH, MeOH, reflux, 10 h; vi) conc. HCl; vii) Cu powder, quinoline, 160 °C, 0.5 h

The carbonyl absorption of **1** in the ir spectrum is observed at 1600 cm^{-1}, which is slightly lower than that of 4-one isomer **2** (1606 cm^{-1}). The effects of protonation to **1** were examined by ^{1}H nmr spectroscopy. The ^{1}H nmr spectral data for 3-pentadeuteriophenyl derivative **1-d_5** in deuteriochloroform (CDCl$_3$) and in trifluoroacetic acid (CF$_3$COOD) are listed in Table 1. The positive charge resulting from the protonation causes a small downfield shift for the protons ($\Delta\delta$: less than -0.6). Interestingly, a small upfield shift for 1-, 2-, and 8-H in CF$_3$COOD is observed. This means that the ring current due to the peripheral [12]annulene would offset the downfield shift caused by the positive charge of protonation. The averaging of the coupling constants in CF$_3$COOD indicates that the bond-alternation of this peripheral π-system is less significant.

Table 1. ^{1}H Nmr Spectral Data of 1-$\underline{d}_5$ in $CDCl_3$ and CF_3COOD

	δ /ppm						J/Hz		
Solvent	1-H	2-H	4-H	5-H	7-H	8-H	1-2	4-5	7-8
$CDCl_3$[a)]	6.89	7.53	7.60	6.13	8.07	7.67	4.3	9.8	8.4
CF_3COOD[a)]	6.84	7.44	8.08	6.67	8.53	7.63	5.1	8.2	8.6
Δδ[b)]	0.05	0.09	-0.48	-0.54	-0.46	0.04			

a) 0.01M Solution. b) $\Delta\delta = \delta CDCl_3 - \delta CF_3COOD$.

The characteristic feature of 1 was observed in its electronic spectra. Compound **1** is blue in the crystalline state or in the solutions of nonpolar solvents such as cyclohexane. The color of the solution changed to green in chloroform or methanol in contrast with the 4-one derivative **2**, which showed the same color (reddish violet) in most solvents.

The longest absorption maximum in chloroform is observed at 613 nm, which is at 86 nm longer wavelength than that of **2** (537 nm). The absorption maxima of **1** were shifted to longer wavelength beyond 750 nm as degree of the protonation onto the carbonyl oxygen increaes (Figure 1) and these changes were reversible.

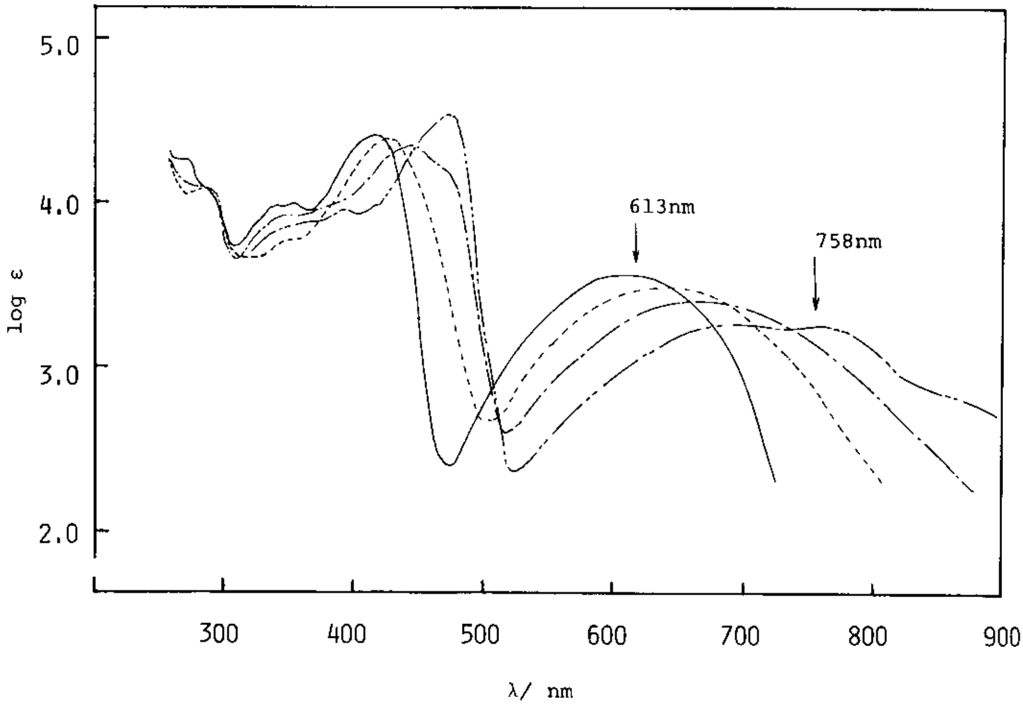


Figure 1. **Change of the Electronic Spectra of 1 with Acid Concentrations** : (————) in $CHCl_3$; (--------) in $CHCl_3/CF_3COOH$= 100/1; (—·—·—·) in 50/1; (—··—··—) in 3/2.

As same as the results of 2, the spectra of 1 in acidic media depended neither on the concentrations of 1 nor on the addition of aromatic compounds such as 1,4-dimethoxybenzene and 1,4-dimethoxynaphthalene, which have strong an electron-donating nature.

From these and previously reported observations,[1b] it might be concluded that these interesting properties of 1 and 2 are representative of the natures of **A** and **C** and, especially, that their behaviors in acidic media are arisen from **B** and **D**, the [12]annulene systems perturbed by an internal azomethinium ion.

EXPERIMENTAL[3]

Preparation of 3-substituted 1,2-bis(methoxycarbonyl)-6H-benzo[hi]pyrrolo[2,1,5-cd]indolizin-6-ones (6). General procedure: A solution of 7,8-dihydro-5(6H)-quinolone (3)[4] (50 mmol) and phenacyl bromide (1.2 equiv.) in dry acetone (50 ml) was heated under reflux for 20 h. After cooling, the resultant quinolinium salt **4a** was collected by filtration in 66% yield. The treatment of **4a** (40 mmol) with sodium hydrogencarbonate (3.0 equiv) in refluxing ethanol for 6 h gave indolizinone **5a** in 63% yield.

1-Phenyl-8,9-dihydro-7H-pyrrolo[3,2,1-ij]quinolin-7-one (5a): orange plates (ethanol); mp 128-129 °C; ir(KBr) cm^{-1}: 1656(CO); ^{1}H nmr(CDCl$_3$) : 2.94(t, J= 7 Hz, 2H, 8-H), 3.37(t, J= 7 Hz, 2H, 9-H), 6.52(t, J= 6 Hz, 1H, 5-H), 7.1-7.8(overlapping, 7H, 2-H, 6-H, and phenyl), 7.98(d, J= 6 Hz, 1H, 4-H); ms m/z: 247(M$^+$). Found: C, 82.66; H, 5.39; N, 5.79. Calcd for $C_{17}H_{13}NO$: C, 82.57; H, 5.30; N, 5.66.

1-Ethoxycarbonyl-8,9-dihydro-7H-pyrrolo[3,2,1-ij]quinolin-7-one (5b): yield: 38% from **3**; orange plates (ethanol); mp 162-163 °C; ir(KBr) cm^{-1}: 1718, 1652(CO); ^{1}H nmr(CDCl$_3$) : 1.44(t, J= 7 Hz, 2H, -CH$_3$); 3.01(t, J= 6.5 Hz, 2H, 8-H), 3.52(t, J= 6.5 Hz, 2H, 9-H), 4.46(q, J= 7 Hz, 2H, -CH$_2$-), 6.73(t, J= 7 Hz, 1H, 5-H), 7.22(d, J= 7 Hz, 1H, 4-H), 7.96(s, 1H, 2-H), 8.03(d, J= 7 Hz, 1H, 6-H); ms m/z: 243(M$^+$) . Found: C, 69.10; H, 5.48; N, 5.87. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76.

The solution of **5a** (1.2 mmol) and dimethyl acetylenedicarboxylate (1.5 equiv.) in dry toluene (20 ml) was stirred at room temperature for 0.5 h. After confirming the complete consumption of **5a** by tlc, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (4.0 equiv.) was added portionweise to the mixture. The mixture was heated under reflux for 2 h. The resulting hydroquinone was filtered off and the filtrate was concentrated to dryness. The residue was subjected to a column chromatography on neutral alumina to give **6a** (chloroform/ethyl acetate: 20/1) in 92% yield.

1,2-Bis(methoxycarbonyl)-3-phenyl-6H-benzo[hi]pyrrolo[2,1,5-cd]indolizin-6-one (6a): violet needles (ethanol); mp 221-222 °C; ir(KBr) cm^{-1}: 1716, 1612(CO); ^{1}H nmr(CDCl$_3$) : 3.96, 3.99(2s, 3H each, $-CH_3$), 6.24(d, J= 9.8 Hz, 1H, 5-H), 7.4-7.9(overlapping, 6H, 4-H and phenyl), 8.1(overlapping, 2H, 7-H and 8-H); ms m/z: 385(M^+). Found: C, 71.65; H, 3.93; N, 3.88. Calcd for $C_{23}H_{15}NO_5$: C, 71.68; H, 3.92; N, 3.64.

3-Ethoxycarbonyl-1,2-bis(methoxycarbonyl)-6<u>H</u>-benzo[<u>hi</u>]pyrrolo[2,1,5-<u>cd</u>]indolizin-6-one (6b): yield: 98%; blue needles (ethanol); mp 209-210 °C; ir(KBr) cm^{-1}: ^{1}H nmr($CDCl_3$) : 1.47(t, J= 7 Hz, 3H, $-CH_3$), 4.03, 4.15(2s, 3H each, $-CH_3$), 4.48(q, J= 7 Hz, 2H, $-CH_2-$), 6.26(d, J= 10 Hz, 1H, 5-H), 7.76(d, J= 10 Hz, 1H, 4-H), 8.3(overlapping, 2H, 7-H and 8-H); ms m/z: 381(M^+). Found: C, 63.07; H, 4.03; N, 4.00. Calcd for $C_{20}H_{15}NO_7$: C, 62.99; H, 3.97; N, 3.67.

Compound **6a** (420 mg, 1.10 mmol) was heated under reflux in 5% methanolic potassium hydroxide (25 ml) for 10 h and the methanol was evaporated to dryness. The residue was made acidic with conc. hydrochloric acid. The resultant diacid was filtered, dried, and subjected to the next decarboxylation without further purification. A solution of the diacid in quinoline (20 ml) was heated at 160 °C for 0.5 h in the presence of copper powder (50 mg). The copper was filtered off and the filtrate was evaporated to give a residue. The residue was dissolved in benzene (50 ml) and washed with 0.5 M hydrochloric acide (3 x 30 ml) in oder to remove the quinoline. The organic layer was dried over anhydrous magnesium sulfate and evaporated to dryness. The residue was subjected to a chromatography on alumina to afford **1** (chloroform) in 64% yield from **6a**.

3-Phenyl-6<u>H</u>-benzo[<u>hi</u>]pyrrolo[2,1,5-<u>cd</u>]indolizin-6-one (1): dark blue needles (ethanol); mp 114-115 °C; ir(KBr) cm^{-1}: 1600(CO); ^{1}H nmr($CDCl_3$) : 6.13(d, J= 9.8 Hz, 1H, 5-H), 6.89(d, J= 4.3 Hz, 1H, 1-H), 7.4-7.7(overlapping, 8H, 2-H, 4-H, 8-H, and phenyl), 8.07(d, J= 8.4 Hz, 1H, 7-H); ms m/z: 269(M^+). Found: C, 84.66; H, 4.28; N, 5.01. Calcd for $C_{19}H_{11}NO$: C, 84.74; H, 4.12; N, 5.20. Electronic spectra: λ max(cyclohexane) nm(logε): 252(sh, 4.34), 265(4.22), 281(4.08), 339(4.02), 352(4.03), 402(4.36), 589(3.56), 613(3.52); λ max($CHCl_3$): 240(sh, 4.23), 253(4.33), 270(sh, 4.25), 288(sh, 4.10), 342(3.97), 355(4.00), 416(4.40), 613(3.54); λ max(MeOH): 252(4.25), 268(sh, 4.17), 286(4.04), 354(3.90), 419(4.37), 622(3.47).

Similarly, the pentadeuteriophenyl derivative **1-$\underline{d}_5$** was obtained from **3** in the total yield of 24%.

REFERENCES AND NOTES

1. a) Studies on Nitrogen-bridged Heterocycles. VII. b) Part VI in this series: M. Noguchi, T. Yamamoto, S. Kajigaeshi, K. Saito, and T. Arai, <u>Bull. Chem. Soc. Jpn.</u>, 1988, **61**, 423.
2. The calculations were carried out using the ACOS system 1000 computer in the Computation Center of Osaka University. For an optimization of the structure, the initial structure was taken as follows: for the geometries of the cyclazine moiety of **C**, the X-ray analytical data for 1,4-

dibromopyrrolo[2,1,5-cd]indolizine[5] were used. Those of the enone part were estimated using the molecular models fused by the above cyclazine system. The distance of the C=O bond was taken from that of acrylaldehyde (1.23 Å). A structure optimization was performed for the bond length and valence and dihedral angles of all the atoms of **C**, except for the hydrogen atoms. The structural optimization for **D**, the protonated species of **C**, was performed using the attained geometries for **C** as an initial structure. Among the results, the net atomic charges and bond lengthes for **C** and **D** are demonstrated in Figure 2.

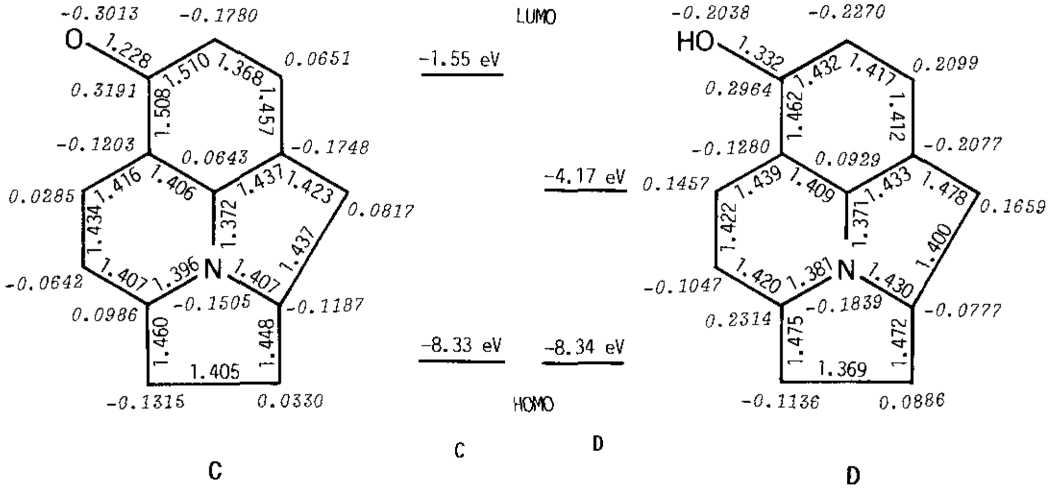


Figure 2. Net atomic charge and atomic distance (Å) of C and D by MNDOA.

3. All melting points are uncorrected. The ir spectra were measured on a JASCO IRA-1 spectrophothometer. The ^{1}H nmr spectra were measured on JEOL JMN-MH-100 and/or Hitachi R-600 spectrometers. Chemical shifts are expressed in parts per million (ppm) downfield from tetramethylsilane. The mass spectra were determinded with a JEOL JMS-D spectrometer at 75 eV using a direct inlet method. The electronic spectra were taken by a Hitachi 220 spectrophotometer. The elemental analyses were performed on a Hitachi 026 CHN analyzer. Most of the reactions were monitored by thin-layer chromatography (Silica Gel 60F-254, Merck). Wakogel C-200(Wako Pure Chemical Industries LTD) and Aluminium Oxide 90(Merck) were used for preparative column chromatography.
4. M. G. Hicks, G. Jones, and H. Sheikh, J. Chem. Soc., Perkin Trans. 1, 1984, 2297.
5. A. W. Hanson, Acta Crystallogr., 1961, **14**, 124.

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