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Synthesis and Properties of Cyclohepta[*hi*]pyrrolo-[2,1,5-*cd*]indolizines[1)]

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The oxidation of the methylene moiety of 4,5,6,7-tetrahydrocyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizines with NBS gave 5-bromo-6,7-dihydro- (**4**) and 5-bromo-cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizines. The dehydrobromination of **4** with DBU afforded cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizines in good yields. The characteristic electronic features of these cycloheptapyrroloindolizines are discussed on the basis of the MO calculations and the spectroscopic properties.

Many investigations on cyclazine systems have been reported from synthetic and physicochemical as well as biological viewpoints.[2)] Among them, the cyclazine systems peri-fused by another ring system have attracted our attention regarding the following three points: i) the development of synthetic strategies, ii) the interest for novel chemical and physical properties, and, especially, iii) the investigation on the perturbation of parent nuclei stemmed from the condensation of another ring system.

Recently, we reported that 4*H*-benzo[*hi*]pyrrolo-[2,1,5-*cd*]indolizin-4-ones were synthesized by the regioselective oxidation of 5,6-dihydro-4*H*-benzo[*hi*]-pyrrolo[2,1,5-*cd*]indolizines with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) and that their spectral data implied the exsistence of a peripheral 12 π electronic system in an acidic medium.[3)] As a continuation of our studies, we investigated the synthesis of cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizine, a novel ring system,[4)] which was expected to have a highly polarized structure as predicted from MO calculations.

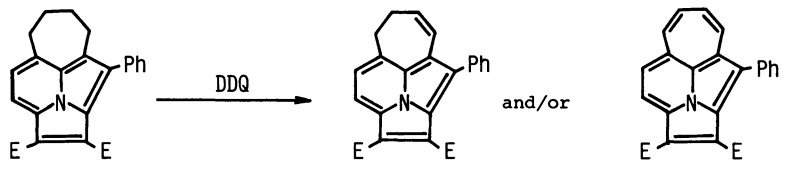
We wish to report here the synthesis of some cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizine derivatives by the oxidation of the methylene moiety of 4,5,6,7-tetrahydrocyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizines with DDQ or *N*-bromosuccinimide (NBS). The interesting electronic features of the cyclohepta-pyrroloindolizines are also discussed.

Results and Discussion

Synthesis of Cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizines. The dehydrogenation of 4,5,6,7-tetrahydro-1,2-bis(methoxycarbonyl)-3-phenylcyclohepta[*hi*]pyrrolo-[2,1,5-*cd*]indolizine (**1a**) with an equimolar DDQ in dry benzene at 5—10 °C gave the 6,7-dihydro derivative **2**[5)] in 31% yield. However, the sequent dehydrogenation of **2** to the expected 1,2-bis(methoxycarbonyl)-3-phenylcyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizine (**3a**) with DDQ or palladium-charcoal under various conditions afforded only unsatisfactory results (see experimental section).

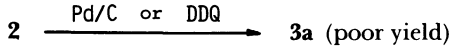
In any event, these findings implied an oxidation of the methylene moiety of **1a** with an appropriate oxidizing agent to provide the full conjugated cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizine system; therefore, we examined the oxidation of **1a** with NBS.

When a solution of **1a** and NBS (2.2 equimolar) in dry carbon tetrachloride was refluxed under irradiation with a tungsten lamp for 6 h, two kinds of colored products, **4a** and **5a**, were obtained in 56 and 33% yields, respectively. The similar oxidation of the pentadeuteriophenyl derivative (**1a**-d_5) with NBS gave



1a **2** **3a**

E: CO_2Me



Scheme 1.

corresponding pentadeuteriophenyl-type products, **4a**-d_5 and **5a**-d_5. The heating of **4a** with an equimolar NBS in carbon tetrachloride afforded **5a** in 64% yield. This means that **4a** is an intermediary product leading to **5a**.

The yellow crystalline **4a** was assigned to 5-bromo-6,7-dihydro- and the reddish crystalline **5a** to 5-bromo-3-phenylcyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizine from the analytical and spectral data in comparison with those of **2** and **3a**.

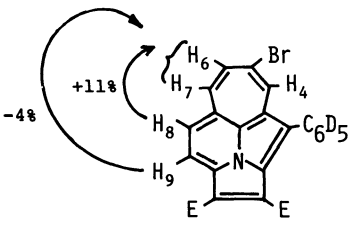
Especially, the regiochemistry of the bromo substituent of **4a** or **5a** was confirmed by measurements of nuclear Overhauser effect (NOE) of **5a**-d_5. As shown in Fig. 1, the irradiation at δ 7.38 (8-H) resulted in an 11% enhancement in the signals at δ 6.65 (superimposed signals due to 6- and 7-H). On the other hand, the irradiation at δ 8.10 (9-H) resulted in a 4% decrease in the signals due to 6- and 7-H.

Similarly, the reaction of 4,5,6,7-tetrahydrocyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizines **1b—d** with NBS gave the corresponding 5-bromo-6,7-dihydro-**4b—d** and 5-bromo-cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]-indolizines **5b—d** in good total yields (Scheme 2). These results as well as electronic spectral data of **4** and **5** are summarized in Tables 1 and 4, respectively.

A reaction of **4a** with an excess of 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) in toluene under reflux gave **3a** in 64% yield. The 3-arylcyclohepta[*hi*]pyrrolo-[2,1,5-*cd*]indolizines **3a**-d_5-**3d** were also obtained by a similar dehydrobromination of the 5-bromo-6,7-dihydro derivatives **4a**-d_3-**4d**. These results as well as the electronic spectral data of **3** are summarized in Tables 2 and 4, respectively.

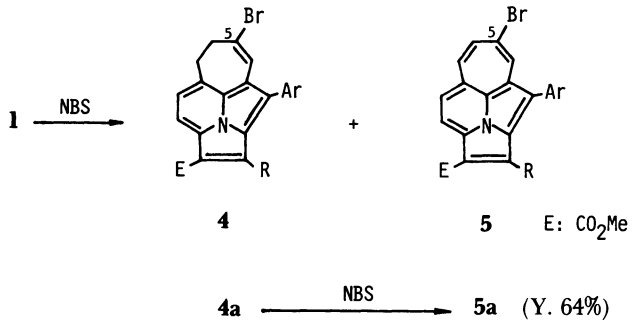
Our attention was then focused on the preparation of 1,2-unsubstituted cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]-indolizines. The saponification of **3a** with 5% methanolic potassium hydroxide followed by acidification afforded the diacid. This was decarboxylated in refluxing quinoline in the presence of copper dust to give the expected 3-phenylcyclohepta[*hi*]pyrrolo-[2,1,5-*cd*]indolizine (**6a**) in 84% yield from **3a**. 3-Pentadeuteriophenyl (**6a**-d_5) and 3-(*p*-bromophenyl)-cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizine (**6d**) as well as 4,5,6,7-tetrahydro-3-phenylcyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizine (**7a**) and its pentadeuteriophenyl derivative **7a**-d_5 were obtained by similar saponification and successive decarboxylation (Scheme 3). However, a similar treatment of **5a** afforded an unseparable mixture of the desired 5-bromo-3-phenylcycloheptapyrrolo-indolizine and **6a**, in which a reductive debromination by copper would occur.

As mentioned above, the full conjugated cyclo-



5a-d_5 E: CO_2Me

Fig. 1. NOE Results for **5a**-d_5.
%: Change of signal area.



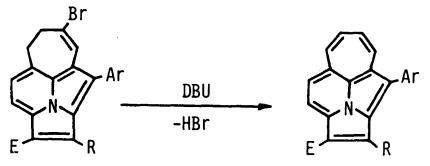
Scheme 2.

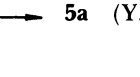
Table 1. Reaction of Tetrahydrocycloheptapyrrolo-indolizines **1** with NBS

Substrate	Ar	R[a]	Yield/%	
			4	**5**
1a	C_6H_5	E	56	33
1a-d_5	C_6H_5	E	55	41
1b	C_6H_5	H	72	28
1c		E	68	25
1d		E	55	38

a) E: CO_2Me.

Table 2. Dehydrobromination of **4** Leading to the Cycloheptapyrroloindolizines **3**



Compd	Ar	R[a]	Yield/%
3a	C_6H_5	E	64
3a-d_5	C_6H_5	E	58
3b	C_6H_5	H	62
3c		E	75
3d		E	60

a) E: CO_2Me.

hepta[*hi*]pyrrolo[2,1,5-*cd*]indolizines **3** and **5** were obtained by the oxidation of the 4,5,6,7-tetrahydro derivative **1** or the dehydrobromination of 5-bromo-6,7-dihydro derivatives **4**. Thus, this oxidation reaction of the methylene moiety turned out to be available for the synthesis of the full conjugated fused [3.2.2]cyclazine systems.

Properties of Cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizines. The Hückel molecular orbital calculations for cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizine (**B**) were carried out using the reported parameters[6] for pyrrolo[2,1,5-*cd*]indolizine (**A**). These results[7] show that the introduction of the cyclohepta moiety into **A** causes a large change in the electronic features of the parent cyclazine nuclei, as follows: The difference of the π-electron densities at the 8- and 9-positions of **B** becomes remarkably large in comparison with that[6] at the 6- and 7-positions of **A**. The π-electron densities at the 1- and 2-positions of **A** are considerably different from one another, while those of **B** are reversed and averaged. As a whole, in cycloheptapyrroloindolizine **B** the seven-membered ring is slightly positively charged and the negative charge is delocalized over the cyclazine system. Therefore, the contribution of the polarized structure, **C** or **D**, to the ground state of **B** is conceivable (Scheme 4).

The electronic spectra of the 6,7-dihydro derivatives of cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizine, **2** and **4**, shift wholly toward longer wavelengths (10—30 nm) compared with that of the tetrahydro derivative **1a** owing to the extention of π-electron system (Table 4). On the other hand, the electronic spectra of 4,5,6,7-tetrahydro-3-phenyl- (**7a**) and 3-phenylcyclohepta-[*hi*]pyrrolo[2,1,5-*cd*]indolizine (**6a**) in chloroform are shown in Fig. 2. Therein, the spectrum of **6a** exhibits fine structures over the range of 490—620 nm; these would be attributed to the proposed dipolar structure.

The ^{1}H NMR spectra of the cycloheptapyrroloindolizines and their dihydro and tetrahydro derivatives were highly dependent on the concentrations of the measuring probes, i.e., the signals of protons of **6a** were observed at higher field as the concentration of the sample is increased. Thus, considerations on the chemical shifts of ring protons are made using a 0.12 M† solution in deuteriochloroform[8] of the corresponding samples. The chemical shifts and coupling constants of the pentadeuteriophenyl derivatives, **6a**-d_5 and **7a**-d_5, are listed in Table 3.

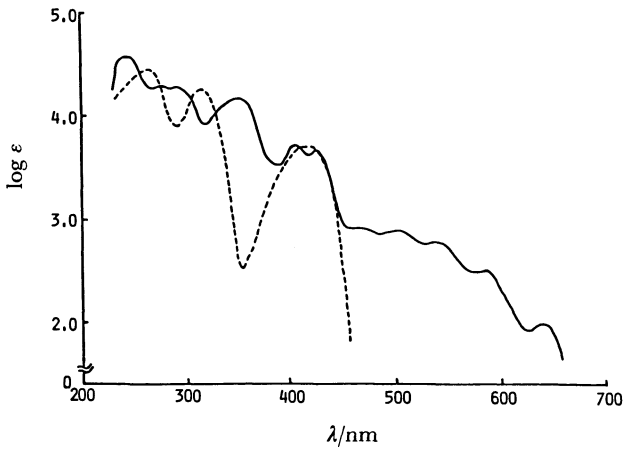
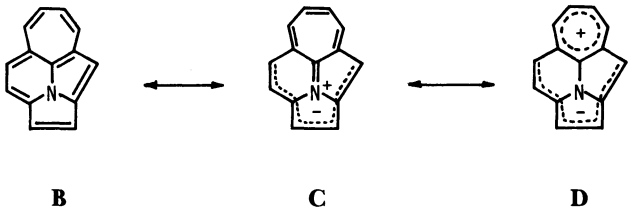
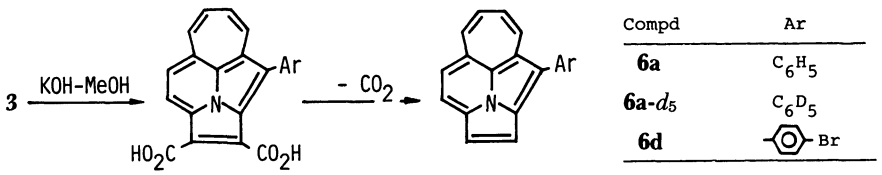


Fig. 2. Electronic spectra of **6a** (——) and **7a** (----) in chloroform.

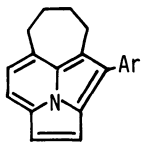


B **C** **D**

Scheme 4.



Compd	Ar
6a	C_6H_5
6a-d_5	C_6D_5
6d	Br



Compd	Ar
7a	C_6H_5
7a-d_5	C_6D_5

Scheme 3.

† 1 M=1 mol dm^{-3}.

The seven-membered ring protons of **6a**-d_5 were observed at a higher field than those of 2-phenylcyclohepta[*hi*]imidazolo[2,3,4-*cd*]indolizine,[9] a 2-aza analog of **6**, and comparable to those of acepleiadiene,[10] tropone,[11] or cycloheptatrienylideneamines.[12] On the other hand, taking the deshielding effect due to the newly-formed polyene system into consideration it is noteworthy that the proton at the 8-position of **6a**-d_5 could be observed at a higher field ($\Delta\delta$=0.26) than that of **7a**-d_5. Probably, the negative charge resulted from a dipolar structure (**C** or **D**) partially located at the carbon atom at the 8-position.

The values of the coupling constants between the protons of seven-membered ring of **6a**-d_5 are almost consistent with those of acepleiadiene,[10] tropone,[11] heptafulvenes,[11] or cycloheptatrienylideneamines.[12] This means an apparent bond-alternation of the seven-membered ring of **6**, while the bond-alternation of the seven-membered ring of 2-phenylcyclohepta-[*hi*]imidazolo[2,3,4-*cd*]indolizine[9] can be scarcely seen.

From these results, we suggest that the resonance for **C** is the most predominant polarized structure contributed to the ground state of cyclohepta[*hi*]-pyrrolo[2,1,5-*cd*]indolizine (**B**).

Further investigations on the properties and chemical reactivities of cyclohepta[*hi*]pyrrolo[2,1,5-*cd*]indolizines are now in progress.

Experimental

General. All melting points are uncorrected. The IR spectra were obtained on a JASCO IRA-1 spectrometer. The ^{1}H NMR spectra were recorded on a JEOL FX-200, FX-100, or JMN-MH-100 spectrometer with tetramethylsilane as an internal standard. The mass spectrometer was equipped with a direct inlet and had at an ionization energy of 75 eV. The elemental analyses were performed on a Hitachi 026 CHN analyzer. For thin-layer and preparative column chromatography, silica gel 60F-254 (Merck) and Wakogel C-300 were used, respectively.

The unknown starting materials **1a**-d_5, **1b**, **1c**, and **1d** were prepared from the reaction of the corresponding cyclohepta-[*hi*]pyrroloindolizines and acetylenes in a similar way to a reported method.[13]

1a-d_5: ^{1}H NMR ($CDCl_3$) δ=2.2 (4H, m, 5- and 6-H), 3.26, 3.46 (2H each, 2t, J=7 Hz each, 4- and 7-H), 3.80, 4.06 (3H each, 2s, $-CH_3$), 7.74 (1H, d, J=8 Hz, 8-H), and 8.34 (1H, d, J=8 Hz, 9-H).

1b: Yellow needles (ethanol); mp 144—146 °C.

Found: C, 80.34; H, 5.78; N, 4.46%. Calcd for $C_{22}H_{19}NO_2$: C, 80.22; H, 5.81; N, 4.25%.

1c: Yellow needles (ethanol); mp 152—153 °C.

Found: C, 71.98; H, 5.59; N, 3.34%. Calcd for $C_{25}H_{23}NO_5$: C, 71.93; H, 5.55; N, 3.36%.

1d: Yellow needles (ethanol); mp 161—162 °C.

Found: C, 61.94; H, 4.28; N, 3.22%. Calcd for $C_{24}H_{20}BrNO_4$: C, 61.81; H, 4.32; N, 3.00%.

Oxidation of 1a with DDQ. A solution of **1a** (500 mg, 1.29 mmol) and DDQ (300 mg, 1.32 mmol) in dry benzene (30 mL) was stirred at 5—10 °C for 24 h under a nitrogen atmosphere. After removing of the resultant hydroquinone by filtration, the filtrate was evaporated to dryness. The residue was subjected to chromatography on silica gel to afforded 155 mg (31%) of **2** together with unreacted **1a** (56%) as chloroform eluents.

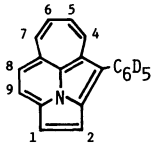
The oxidation of **1a** with 6.4 equiv of DDQ under similar conditions gave an unseparable mixture of **3a** (11%), **2** (33%), and **1a** (36%).

2: Yellow needles (ethanol); mp 191—192 °C; IR (KBr) cm^{-1}: 1730 and 1710 (CO); ^{1}H NMR ($CDCl_3$) δ=2.8—2.9 (2H, m, 6-H), 3.3—3.4 (2H, m, 7-H), 3.78, 4.00 (3H each, 2s, $-CH_3$), 6.1—6.2 (1H, m, 5-H), 6.89 (1H, br d, J=11 Hz, 4-H), 7.4—7.7 (6H, m, 8-H and phenyl protons), and 8.28 (1H, d, J=8 Hz, 9-H); MS m/z (rel intensity): 385 (M^+, base peak), 354 (M^+-OCH_3, 16), 326 ($M^+-CO_2CH_3$, 10), 308 (M^+-Ph, 6), and 267 ($M^+-2\times CO_2CH_3$, 27).

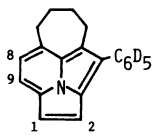
Found: C, 74.51; H, 5.04; N, 3.65%. Calcd for $C_{24}H_{19}NO_4$: C, 74.79; H, 4.97; N, 3.63%.

Oxidation of 2 with Pd/C or DDQ to 3a. A solution of **2** (33 mg) in dry toluene (10 mL) in the presence of 20 mg of

Table 3. Chemical Shifts and Coupling Constants of **6a**-d_5 and **7a**-d_5



6a-d_5



7a-d_5

Compd	Chemical shifts/δ 1-H	2-H	4-H	5-H	6-H	7-H	8-H	9-H
6a-d_5 (δ_1)	7.49	7.74	7.56	6.11	6.38	6.91	7.23	7.89
7a-d_5 (δ_2)	7.24	7.58					7.49	7.81
$\Delta\delta(\delta_1-\delta_2)$	0.25	0.16					−0.26	0.02

Coupling constants for **6a**-d_5 (Hz): $J_{1,2}$=4.2, $J_{4,5}$=11.2, $J_{5,6}$=8.4, $J_{4,6}=J_{5,7}$=1.2, $J_{6,7}$=11.8, $J_{8,9}$=8.4

Coupling constants for **7a**-d_5 (Hz): $J_{1,2}$=4.2, $J_{8,9}$=8.4

10% Pd/C was refluxed for 72 h. After the Pd/C was filtered off, the filtrate was evaporated to dryness. The residue was subjected to column chromatography on silica gel to afford 5 mg (16%) of **3a** as an eluent of chloroform.

Also, the oxidation of **2** with 1.2 equiv of DDQ under similar conditions gave an unseparable mixture of **3a** (24%) and **2** (46%).

3a: Deep red needles (ethanol); mp 189—190 °C; IR (KBr) cm^{-1}: 1740 and 1720 (CO); ^1H NMR ($CDCl_3$) 3.75, 4.04 (3H each, 2s, $-CH_3$), 6.32 (1H, ddd, J=11, 8, and 1 Hz, 5-H), 6.58 (1H, ddd, J=11, 8, and 1 Hz, 6-H), 6.97 (1H, d, J=11 Hz, 4-H), 7.4—7.7 (7H, m, 4- and 8-H and phenyl protons), and 8.36 (1H, d, J=8 Hz, 9-H); MS m/z (rel intensity): 383 (M^+, base peak), 352 (M^+-OCH_3, 24), and 265 ($M^+-2\times CO_2CH_3$, 48).

Found: C, 75.05; H, 4.45; N, 3.74%. Calcd for $C_{24}H_{17}NO_4$: C, 75.18; H, 4.47; N, 3.65%.

Oxidation of 1 with NBS. Typical Procedure: A solution of **1a** (1.00 g, 2.58 mmol) and NBS (1.00 g, 5.62 mmol) in dry carbon tetrachloride (80 mL) was refluxed under the irradiation of a tungsten lamp for 6 h. The resultant succinimide was filtered off and the filtrate was evaporated in vacuo to give a residue. The residue was subjected to column chromatography (silica gel–chloroform) to afford 543 mg (45%) of **4a** and 387 mg (32%) of **5a**. The similar oxidation of **1a**-d_5 with NBS gave the correspoding pentadeuteriophenyl derivatives **4a**-d_5 and **5a**-d_5, respectively.

4a: Yellow needles (ethanol); mp 232—233 °C; IR (KBr) cm^{-1}: 1730 and 1710 (CO); ^1H NMR ($CDCl_3$) δ=3.4 (4H, m, 6- and 7-H), 3.79, 4.00 (3H each, 2s, $-CH_3$), 7.30 (1H, br s, 4-H), 7.4—7.6 (5H, m, phenyl protons), 7.65 (1H, d, J=8 Hz, 8-H), and 8.29 (1H, d, J=8 Hz, 9-H); MS m/z (rel intensity): 465, 463 (M^+, base peak), 434, 432 (M^+-OCH_3), 384 (M^+-Br, 23), 267 (29), 266 (48), and 265 (53).

Found: C, 62.33; H, 4.02; N, 3.23%. Calcd for $C_{24}H_{18}BrNO_4$: C, 62.08; H, 3.90; N, 3.03%.

4a-d_5: ^1H NMR ($CDCl_3$) δ=3.4 (4H, br s, 6- and 7-H), 3.85, 4.05 (3H each, 2s, $-CH_3$), 7.36 (2H, br s, 4-H), 7.68 (1H, d, J=8 Hz, 8-H), and 8.22 (1H, d, J=8 Hz, 9-H).

5a: Deep red needles (ethanol); mp 195.5—197 °C; IR (KBr) cm^{-1}: 1730 and 1710 (CO); ^1H NMR ($CDCl_3$) δ=3.76, 4.04 (3H each, 2s, $-CH_3$), 6.7 (2H, br s, 6- and 7-H), 7.4—7.7 (6H, m, 8-H and phenyl protons), 7.79 (1H, s, 4-H), and 8.28 (1H, d, J=8 Hz, 9-H); MS m/z (rel intensity): 463, 461 (M^+, base peak), 432, 430 (M^+-OCH_3, 17), 282 (M^+-Br, 14), 265, 264, and 263.

Found: C, 62.62; H, 3.54; N, 3.24%. Calcd for $C_{24}H_{16}BrNO_4$: C, 62.35; H, 3.49; N, 3.03%.

5a-d_5: ^1H NMR ($CDCl_3$) δ=3.88, 4.12 (3H each, 2s, $-CH_3$), 6.65 (2H, br s, 6- and 7-H), 7.38 (1H, d, J=8 Hz, 8-H), 7.83 (1H, br s, 4-H), and 8.10 (1H, d, J=8 Hz, 9-H).

A solution of **4a** (100 mg, 0.22 mmol) and NBS (40 mg, 0.22 mmol) in dry carbon tetrachloride (10 mL) was similarly refluxed for 5 h. After a similar work-up, **5a** was obtained in 64% yield together with the unreacted **4a** (22%).

The reaction of **1b**, **1c**, and **1d** with NBS gave the corresponding 6-bromo-6,7-dihydro-**4** and 6-bromo derivatives **5**, respectively. These results are presented in Table 1.

4b: Yellow needles (ethanol); mp 157—159 °C; IR (KBr) cm^{-1}: 1685 (CO), ^1H NMR ($CDCl_3$) δ=3.4 (4H, m, 6- and 7-H), 4.02 (3H, s, $-CH_3$), 7.43 (1H, br s, 4-H), 7.4—7.8 (6H, m, 8-H and phenyl protons), 8.08 (1H, s, 2-H), and 8.25 (1H, d, J=8 Hz, 6-H); MS m/z (rel intensity): 407, 405 (M^+, base peak), 376, 374 (M^+-OCH_3, 12), 326 (M^+-Br, 48), and 267 ($M^+-Br-CO_2CH_3$, 71).

Found: C, 65.11; H, 4.11; N, 3.57%. Calcd for $C_{22}H_{16}BrNO_2$: C, 65.04; H, 3.97; N, 3.45%.

5c: Deep brown needles (ethanol); mp 205—206 °C; IR (KBr) cm^{-1}: 1700 (CO); ^1H NMR ($CDCl_3$) δ=4.05 (3H, s, $-CH_3$), 6.64, 6.75 (1H each, 2d, J=11 Hz each, 6- and 7-H), 7.4—7.7, 7.7—7.8 (7H total, m, 4- and 8-H and phenyl protons), 8.19 (1H, s, 2-H), and 8.31 (1H, d, J=8 Hz, 9-H); MS m/z (rel intensity): 405, 403 (M^+, base peak), 374, 372 (M^+-OCH_3, 9), 346, 344 ($M^+-CO_2CH_3$, 36), and 267 (78).

Found: C, 65.15; H, 3.51; N, 3.78%. Calcd for $C_{22}H_{14}BrNO_2$: C, 65.36; H, 3,49; N, 3.47%.

4c: Orange plates (ethanol); mp 221—222 °C; IR (KBr) cm^{-1}: 1720 and 1700 (CO); ^1H NMR ($CDCl_3$) δ=3.4 (4H, br s, 6- and 7-H), 3.84, 3.90, 4.00 (3H each, s, $-CH_3$), 7.04 (2H, br d, J=8.5 Hz, phenyl protons), 7.27 (1H, s, 4-H), 7.53 (2H, br d, J=8.5 Hz, phenyl protons), 7.62 (1H, d, J=8 Hz, 8-H), and 8.23 (1H, d, J=8 Hz, 9-H); MS m/z (rel intensity): 493, 491(M^+, base peak), 478, 476 (M^+-CH_3, 12), and 417 (66).

Found: C, 60.59; H, 4.04; N, 2.74%. Calcd for $C_{25}H_{20}BrNO_5$: C, 60.37; H, 4.07; N, 2.83%.

The recrystallization of **5c** from benzene gave deep red needles, which consisted as 2:1 molecular complex of **5c** and benzene. Mp 204—205 °C; IR (KBr) cm^{-1}: 1730 and 1710 (CO); ^1H NMR ($CDCl_3$) δ=3.82, 3.91, 4.04 (3H each, 3s, $-CH_3$), 6.73 (2H, br s, 6- and 7-H), 7.08 (2H, br d, J=8 Hz, protons), 7.37 (3H, s, benzene), 7.52 (1H, d, J=7.5 Hz, 8-H), 7.58 (2H, br d, J=8 Hz, phenyl protons), 7.76 (1H, br s, 4-H), and 8.33 (1H, d, J=7.5 Hz, 9-H); MS m/z (rel intensity): 493, 491 (M^+, base peak), 478, 476 (M^+-CH_3, 7), 462, 460 (M^+-OCH_3, 12), and 252.

Found: C, 63.31; H, 4.07; N, 2.69%. Calcd for $C_{25}H_{18}BrNO_5 \cdot 1/2\ C_6H_6$: C, 63.31; H, 4.07; N, 2.63%.

4d: Yellow needles (ethanol); mp 191—192 °C; IR (KBr) cm^{-1}: 1740 and 1700 (CO); ^1H NMR ($CDCl_3$) δ=3.4 (4H, m, 6- and 7-H), 3.82, 4.00 (3H each, 2s, $-CH_3$), 7.21 (1H, s, 4-H), 7.4—7.7 (5H, m, 8-H and phenyl protons); MS m/z (rel intensity): 545, 543, 541 (M^+, base peak), 514, 512, 510 (M^+-OCH_3, 14), and 265 (26).

Found: C, 53.29; H, 3.15; N, 2.80%. Calcd for $C_{24}H_{17}Br_2NO_4$: C, 53.06; H, 3.16; N, 2.58%.

5d: Deep brown needles (benzene); mp 177—178 °C; IR (KBr) cm^{-1}: 1730 and 1705 (CO); ^1H NMR ($CDCl_3$) δ=3.81, 4.04 (3H each, 2s, $-CH_3$), 6.8 (2H, br s, 6- and 7-H), 7.4—7.6 (3H, m, 8-H and phenyl protons), 7.68 (2H, br d, J=8.5 Hz, phenyl protons), 7.71 (1H, br s, 4-H), and 8.36 (1H, d, J=8.5 Hz, 9-H); MS m/z (rel intensity): 543, 541, 539 (M^+, 22), 512, 510, 508 (M^+-OCH_3, 5), 463, 461(M^+-Br, base peak), 432, and 430(16).

Found: C, 53.31; H, 3.07; N, 2.70%. Calcd for $C_{24}H_{15}Br_2NO_4$: C, 53.26; H, 2.79; N, 2.59%.

Preparation of 3 by Dehydrobromination of 4 with DBU. Typical Procedure: A solution of **4a** (200 mg, 0.43 mmol) and DBU (300 mg, 2.0 mmol) in dry toluene (30 mL) was heated under reflux for 24 h. The resultant precipitate was filtered off and the filtrate was washed with water (20 mL×3). The toluene layer was dried and evaporated to give a residue. The residue was subjected to column chromatography on silica gel using benzene to afford

159 mg (64%) of **3a**.

Analogously, the dehydrobromination of **4a**-d_5, **4b**, **4c**, and **4d** with DBU gave the corresponding cyclohepta[*hi*]-pyrrolo[2,1,5-*cd*]indolizines **3a**-d_5, **3b**, **3c**, and **3d** in good yields. These results are presented in Table 2.

3a-d_5: Deep brown needles (ethanol); mp 184—186 °C; ^{1}H NMR ($CDCl_3$) δ=3.73, 4.01 (3H each, 2s $-CH_3$), 6.25 (1H, dd, J=11 and 8 Hz, 5-H), 6.52(1H, dd, J=10 and 8 Hz, 6-H), 6.95 (1H, d, J=10 Hz, 7-H), 7.44(1H, d, J=10 Hz, 4-H), 7.47(1H, d, J=8 Hz, 8-H), and 8.30 (1H, d, J=8 Hz, 9-H).

3b: Red needles (ethanol); mp 170—171.5 °C; IR (KBr) cm^{-1}: 1690 (CO); ^{1}H NMR ($CDCl_3$) δ=4.00 (3H, s, $-CH_3$), 6.29 (1H, dd, J=11 and 8 Hz, 5-H), 6.44 (1H, dd, J=11 and 8 Hz, 6-H), 6.91 (1H, d, J=11 and 7-H), 7.4—7.6 (5H, m, 4- and 8-H and phenyl protons), 7.85 (2H, m, phenyl protons), 8.13 (1H, s, 2-H), and 8.28 (1H, d, J=8.5 Hz, 9-H); MS m/z (rel intensity): 325 (M^+, base peak), 294 (M^+-OCH_3, 24), and 162.5 (M^+/2, 5).

Found: C, 81.44; H, 4.71; N, 4.45%. Calcd for $C_{22}H_{15}NO_2$: C, 81.21; H, 4.65; N, 4.31%.

3c: Deep red needles (benzene); mp 177—178 °C; IR (KBr) cm^{-1}: 1730 and 1710 (CO); ^{1}H NMR ($CDCl_3$) δ=3.82, 3.91, 4.04 (3H each, 3s, $-CH_3$), 6.27 (1H, dd, J=11 and 8.5 Hz, 5-H), 6.52 (1H, dd, J=11.5 and 8.5 Hz, 6-H), 6.96 (1H, d, J=11.5 Hz, 7-H), 7.02 (2H, br d, J=9 Hz, phenyl protons), 7.41 (1H, d, J=11 Hz, 4-H), 7.54 (1H, d, J=8.5 Hz, 8-H), 7.61 (2H, br d, J=9 Hz, phenyl protons), and 8.33 (1H, d, J=8.5 Hz, 9-H); MS m/z (rel intensity): 413 (M^+, base peak), 398 (M^+-CH_3, 9), 382 (M^+-OCH_3, 11), and 251(15).

Found: C, 72.44; H, 4.68; N, 3.42%. Calcd for $C_{25}H_{19}NO_5$: C, 72.63; H, 4.63; N, 3.39%.

3d: Deep red needles (ethanol); mp 189—190 °C; IR (KBr) cm^{-1}: 1710 and 1690 (CO); ^{1}H NMR ($CDCl_3$) δ=3.81, 4.02 (3H each, 2s, $-CH_3$), 6.33 (1H, dd, J=11 and 8.5 Hz, 5-H), 6.59 (1H, dd, J=11.5 and 8.5 Hz, 6-H), 7.02 (1H, d, J=11.5 Hz, 7-H), 7.38 (1H, d, J=11 Hz, 4-H), 7.52 (2H, br d, J=9 Hz, phenyl protons), and 8.37 (1H, d, J=8.5 Hz, 9-H); MS m/z (rel intensity): 463, 461 (M^+, base peak), 432, 430 (M^+-OCH_3, 14), 403, 402 ($M^+-CO_2CH_3$, 7), 265, 264, and 263.

Found: C, 62.40; H, 3.51; N, 3.07%. Cacld for $C_{24}H_{16}BrNO_4$: C, 62.35; H, 3.49; N, 3.03%.

Preparation of 1,2-Unsubstituted Cyclohepta[*hi*]pyrolo-[2,1,5-*cd*]indolizines 6 from 3. Typical Procedure: 3a (120 mg, 0.31 mmol) was heated under reflux in 5% methanolic potassium hydroxide (40 mL) for 20 h and the methanol was removed to give a residue. The residue was made acidic with 6 M hydrochloric acid (50 mL). The resultant diacid was filtered, dried and subjected to the next decarboxylation without further purification. A solution of the diacid in quinoline (15 mL) in the presence of copper dust (50 mg) was refluxed for 1 h. The copper dust was filtered off and the filtrate was evaporated to give a residue. The residue was dissolved in dichloromethane and washed with 0.5 M hydrochloric acid (50 mL×3) in order to remove the quinoline completely. The organic layer was evaporated to dryness. The residue was subjected to chromatography on silica gel using hexane–benzene (3:1) to afford 70 mg (84% from **3a**) of the desired **6a**.

6a: Deep red needles (ethanol); mp 79.5—81 °C; IR (KBr) cm^{-1}: 800, 760, and 680; ^{1}H NMR ($CDCl_3$) δ=6.11 (1H, ddd, J=11.2, 8.4, and 1.2 Hz, 5-H), 6.35 (1H, ddd, J=11.8, 8.4, and 1.2 Hz, 6-H), 6.91 (1H, dd, J=11.8 and 1.2 Hz, 7-H), 7.23 (1H, d, J=8.4 Hz, 8-H), 7.4—7.8 (8H, m, 1-, 2-, and 4-H and phenyl protons), and 7.89 (1H, d, J=8.4 Hz, 9-H); MS m/z (rel intensity): 267 (M^+, base peak), 265 (M^+-H_2, 28), 133.5 (M^+/2, 10), 132.5 (M^+-H_2/2, 17), and 77(7).

Found: C, 89.99; H, 5.04; N, 5.17%. Calcd for $C_{20}H_{13}N$: C, 89.86; H, 4.90; N, 5.24%.

6d: Yield 90% from **3d**; deep brown needles (ethanol); mp 151—153 °C; IR (KBr) cm^{-1}: 1310, 1020, and 800; ^{1}H NMR ($CDCl_3$) δ=6.06 (1H, ddd, J=12, 8, and 1 Hz, 5-H), 6.32 (1H, ddd, J=12, 8, and 1 Hz, 6-H), 6.84 (1H, dd, J=12 and 1 Hz, 7-H), 7.18 (1H, d, J=8 Hz, 8-H), and 7.3—8.0 (9H, m, 1-, 2-, 4-, and 9-H and phenyl protons); MS m/z (rel intensity): 347, 345 (M^+, base peak), 267 (33), 266 (M^+-Br, 31), 265 (M^+-HBr, 88), 173.5, and 172.5 (M^+/2, 9).

Found: C, 69.58; H, 3.70; N, 4.24%. Calcd for $C_{20}H_{12}BrN$: C, 69.38; H, 3.49; N, 4.05%.

As referential compounds, **7a** and **7a**-d_5 were obtained similarly from **1a** and **1a**-d_5, respectively.

7a: Yield 78%; orange prisms (ethanol); mp 102—104 °C; IR (KBr) cm^{-1}; 1280, 1020, 790, and 690; ^{1}H NMR ($CDCl_3$) δ=1.7—2.1 (4H, m, 5- and 6-H), 3.1-3.3 (4H, m, 4- and 7-H), and 7.2—8.0 (9H, m, 1-, 2-, 8-, and 9-H and phenyl protons).

Found: C, 88.32; H, 6.36; N, 5.31%. Calcd for $C_{20}H_{17}N$: C, 88.52; H, 6.32; N, 5.16%.

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Table 4. Electronic Spectral Data of Cyclohepta[*hi*]-pyrrolo[2,1,5-*cd*]indolizines and Their Dihydro and Tetrahydro Derivatives

Compd	λ_{nm}^{max} (log ε) in $CHCl_3$
1a	205(4.46), 269(4.45), 319(4.27), 412(3.68), 424(3.71)
2	245(4.42), 271(4.56), 342(4.28), 438(4.12), 450(4.12)
4a	243(4.40), 274(4.40), 344(4.27), 442(4.20), 455(4.21)
4b	246(4.36), 263(4.39), 286(4.46), 343(4.29), 441(4.17), 458(4.17)
3a	241(4.52), 265(4.74), 322(4.25), 345(4.30), 357(4.33), 390(3.75), 412(4.02), 438(4.19), 489(3.40), 524(3.28), 568(2.97), 620(2.33)
5a	246(4.52), 265(4.77), 304(4.42), 324(4.27), 345(4.35), 358(4.37), 392(3.78), 417(4.08), 443(4.21), 537(3.12), 585(2.74), 640(2.07)
5b	245(4.53), 267(4.76), 324(4.28), 349(4.39), 358(4.39), 393(3.76), 417(4.03), 442(4.16), 500(3.03), 539(2.80), 584(2.41), 640(1.81)
6d	249(4.56), 284(4.34), 297(4.32), 356(4.26), 410(3.72), 431(3.72), 467(2.96), 501(2.95), 538(2.83), 582(2.54), 640(1.97)

Shigeki Nagai, Yoshiaki Ishida, and Keiji Saito and Mr. Tsuyoshi Arai, Ube Research Laboratory, Ube Industries LTD, for the measurement of ^{1}H NMR spectra at 200 MHz.

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4) The syntheses and properties of 2-aza and 2,3-diaza analogs of this system were reported.[9]

5) The 4,5-dihydro derivative as another structure for **2** was ruled out from the similarity of its electronic spectrum to those of **4**. Also, the dark-green solution at the initial stage of the DDQ oxidation suggested the formation of the CT complex between benzene ring of **1a** and DDQ similarly to the regioselective oxidation of 5,6-dihydro-4*H*-benzo[*hi*]-pyrrolo[2,1,5-*cd*]indolizines.[3]

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7) π-Electron density (a) and bond order (b) for cyclohepa[*hi*]pyrrolo[2,1,5-*cd*]indolizine (**B**) by Hückel method are shown.

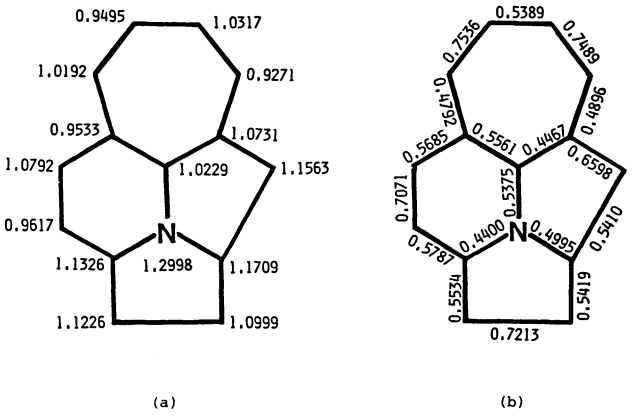

Fig. 3

8) The chemical shifts were almost constant at concentrations below 0.1 M, e.g., the difference of the chemical shifts between 0.12 and 0.06 M deuteriochloroform solution of **6a** was within 0.03 ppm.

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