Synthesis of 5*H*-Cyclohepta[4,5]pyrrolo[2,3-*b*]indoles[1]

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Synopsis. The title compounds (indolo[2,3-*b*][1]azaazulenes) were synthesized from 2-hydrazino-1-azaazulene and cyclohexanone utilizing Fischer's indole synthesis, followed by dehydrogenation of the *N*-acetylated tetrahydro precursor with DDQ. Structures of the neutral and cationic species of these compounds were discussed on the basis of the spectral data.

We have prepared several troponoid compounds fused with an indole ring.[2] We now wish to report herein the synthesis of the first examples of 1-azaazulene[3] fused with a pyrrole or an indole ring.

Condensation of 2-hydrazino-1-azaazulene (**1**)[4] with various ketones and an aldehyde readily gave the corresponding hydrazones: i.e. **2** (with cyclohexanone), **3** (with cycloheptanone), **4** (with acetone), **5** (with ethyl methyl ketone), and **6** (with phenylacetaldehyde). Among these hydrazones, only **2** was managed to be led to the pyrrolo[2,3-*b*][1]azaazulene derivative (**7**) by the application of Fischer's indole synthesis, whereas on employing the similar procedures the conversion of other hydrazones **3**—**6** into the corresponding pyrrolo-[2,3-*b*][1]azaazulenes has remained unsuccessful because of the profound decomposition of the starting materials accompanied by the formation of many complex products.

Attempts of dehydrogenation of **7** with chloranil or DDQ (2,3-dichloro-5,6-dicyano-*p*-benzoquinone) failed mainly due to the exclusive precipitation of an unidentified, dark blue solid, from which no desired product was liberated. However, treatment of its *N*-acetyl derivative **8** with DDQ yielded the dehydrogenated *N*-acetyl compound (**9**), which in turn was led to the parent title compound (indolo[2,3-*b*][1]-azaazulene, **10**) on acid or alkaline hydrolysis.

Physical data for the structural proof for all these compounds are given in the Experimental section. Usful ^{1}H NMR parameters of the pryyolo- and indolo-1-azaazulenes **7**—**10** are summarized in Table 1. The position (N-5) of the acetyl group of **8** and **9** are derived from the evidence of the considerable down-field shifts (0.5 and 1.2 ppm) of H-4 signals of these compounds (compared with those of **7** and **10**, respectively) apparently due to an anisotropic effect of the *N*-acetyl group.[5] Moreover, since the UV spectra of **7** and **10** closely resemble those of **8** and **9**, respectively, these compounds are considered to exist predominantly in 5*H*-cyclohepta[4,5]pyrrolo[2,3-*b*]indole forms (**7** and **10**) rather than in their tautomeric 6*H*-forms. An appreciable down-field shift (0.6 ppm) observed for H-1 signal of **10** (in $CDCl_3$, when compared with that of H-4) can be explained by an anisotropic effect caused by the ring current of the 1-azaazulene moiety that is situated in the vicinity.[6] The divergences of the vicinal coupling constants suggests some degree of bond alternation in the seven-membered ring of **7**—**10**, as was observed in the case of azuleno[1,2-*b*]thiophene.[7]

The signals of the seven-membered ring protons of **7**

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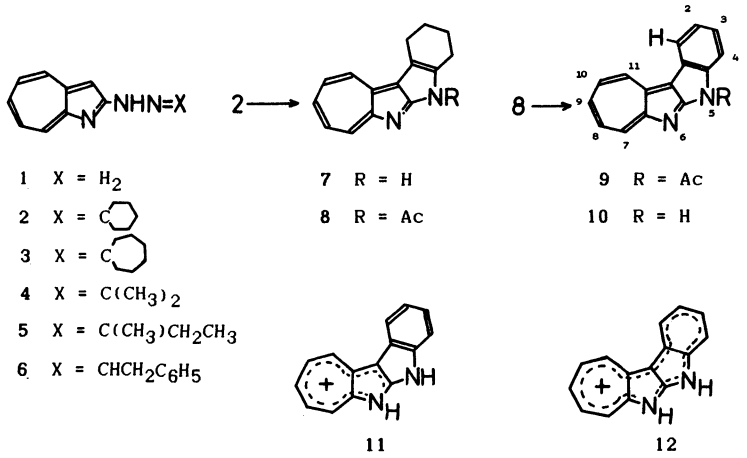
Table 1. ^{1}H NMR Parameters for Cyclohepta[4,5]pyrrolo[2,3-*b*]indoles in $CDCl_3$

Compd	Chemical shifts, δ									
	H-1	H-2	H-3	H-4	R-5	H-7	H-8	H-9	H-10	H-11
7[a]	2.97[b]	1.98[b]	1.98[b]	2.97[b]	9.5[c]	8.55	7.60	7.74	7.68	8.61
7[a,d]	3.02[b]	2.07[b]	2.07[b]	2.89[b]	11.0[c]	8.66	8.11	8.23	8.15	8.92
8[a]	3.21[b]	2.22[b]	2.22[b]	3.51[b]	3.44[e]	8.62	7.67	7.88	7.79	8.74
9[f]	8.01	7.45	7.44	8.73	3.23[e]	8.71	7.84	7.90	7.79	8.82
10[f]	8.14	7.36	7.41	7.57	9.44[c]	8.64	7.85	7.83	7.79	8.84
10[d,f]	8.05	7.47	7.51	7.56	11.65[c]	8.65	8.15	8.23	8.24	8.95

	Coupling constants/Hz[g]												
	$J_{1,2}$	$J_{1,3}$	$J_{1,4}$	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{7,8}$	$J_{7,9}$	$J_{8,9}$	$J_{8,10}$	$J_{8,11}$	$J_{9,10}$	$J_{9,11}$	$J_{10,11}$
7							9.5	1.0	10.2	1.0	0.5	9.4	1.0	10.0
7[d]							9.5	1.0	10.3	1.0	0.5	9.4	1.0	10.2
8							9.5	1.0	10.3	1.0	0.5	9.4	1.0	10.2
9	8.0	1.2	0.5	7.5	1.2	7.6	9.5	1.0	10.2	1.0	0.5	9.4	1.0	10.0
10	8.0	1.2	0.5	7.5	1.0	7.6	9.5	1.0	10.0	1.0	0.5	9.4	1.0	10.0
10[d]	8.0	1.2	0.5	7.5	1.0	8.0	9.5	1.0	10.3	1.0	0.5	9.4	1.0	10.2

a) At 100 MHz. b) A multiplet (2H) centered at this value. c) R=H, broad singlet. d) In CF_3COOD. e) R=$COCH_3$, singlet. f) At 400 MHz. g) Values confirmed by double resonance and simulation analysis.



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and **10** in trifluoroacetic acid-*d* show a down-field shift of 0.2—0.55 ppm (when compared with the corresponding compounds measured in $CDCl_3$, whereas those of the benzene ring protons of **10** show an almost negligible shift (ca. 0.1 ppm) in the acid (see Table 1). This suggests that the positive charge of the cation derived from **10** in trifluoroacetic acid is delocalized mostly over the 1-azaazulene ring (as in **11**) rather than over the 18π peripheral tetracyclic ring system **12**.

Experimental†

Melting points were determined with a Yanagimoto MP-S3 and are uncorrected. Column chromatography was performed with Wako C-200 silica gel. UV and IR spectra were taken on Hitachi 345 and Shimadzu Multipurpose MPL 50L spectrophotometers, respectively. NMR spectra were recorded with a JEOL JNM-4H-100 (100 NHz at 30°C) or JEOL GX400 (400 MHz, for **9** and **10**) with TMS as an internal standard. The assignments of all signals were made by employing a first-order analysis with the aid of decoupling technique and the parameters were confirmed by a computer-assisted simulation analysis using an NEC 9801F Personal Computer[8]; those values are summarized in Table 1. Mass spectra were taken on a Hitachi RMS-4 low-resolution instrument at 70 eV, and are given in terms of *m/z* (rel intensity).

Cyclohexanone Cyclohepta[*b*]pyrrol-2-ylhydrazone (2). A solution of 4.5 g (27 mmol) of **1**[4] and 3.9 g (40 mmol) of cyclohexanone in 86 cm^3 of ethanol was refluxed for 15 min. The solvent and excess cyclohexanone was evaporated in vacuo and the residue was recrystallized from acetonitrile to give **2** as dark brown plates (4.9 g, 76%): mp 152—153°C; UV (MeOH) 279, 288, 316, 435, and 490 sh nm (log ε 4.43, 4.40, 4.22, 4.07, and 3.52); IR (KBr) 3185 (NH), 1620 sh, and 1600 cm^{-1} (C=N, C=C); ^1H NMR ($CDCl_3$) δ=1.5—2.0 (6H, m, 2H-3′,4′,5′), 2.3—2.6 (4H, m, 2H-2′,6′), 6.85 (1H, brs, H-3), 7.1—7.5 (3H, m, H-5,6,7), and 7.7—8.0 (3H, m, H-4,8, NH); MS *m/z* 239 (M^+, 100), 196 (76), 144 (90), 116 (40), and 41 (79).

Found: C, 75.47; H, 7.26; N, 17.32%. Calcd for $C_{15}H_{17}N_3$: C, 75.28; H, 7.16; N, 17.56%.

Cycloheptanone Cyclohepta[*b*]pyrrol-2-ylhydrazone (3). Similar procedures for **2** were followed. Thus 3.7 g (23 mmol) of **1** and 2.6 g (23 mmol) of cycloheptanone in refluxing ethanol (75 cm^3, for 45 min) gave **3** as dark brown plates (4.3 g, 74%): mp 121—122°C (from hexane); UV (EtOH) 280, 288, 324, 385, 398, 444, 463 sh, and 495 sh nm (log ε 4.43 4.40, 4.18, 4.03, 4.01, 3.83, 3.75, and 3.33); IR (KBr) 3165 (NH), 1620 sh, and 1600 cm^{-1} (C=N, C=C); ^1H NMR ($CDCl_3$) δ=1.4—2.1 (8H, m, 2H-3′,4′,5′,6′), 2.4—2.8 (4H, m, 2H-2′,7′), 7.00 (1H, brs, H-3), 7.2—7.6 (3H, m, H-5,6,7), and 7.8—8.3 (3H, m, H-4,8, NH); MS *m/z* 253 (M^+, 100), 252 (47), 196 (55), 144 (81), and 116 (27).

Found: C, 75.74; H, 7.51; N, 16.57%. Calcd for $C_{16}H_{19}N_3$: C, 75.85; H, 7.56; N, 16.59%.

Acetone Cyclohepta[*b*]pyrrol-2-ylhydrazone (4). Similar procedures for **2** were followed. Thus 100 mg of **1** and 30.4 mg of acetone in refluxing ethanol (20 cm^3, for 60 min) gave **4** as dark amber plated (86 mg, 69%): mp 147—147.5°C (from hexane); UV (EtOH) 280, 288, 325, 386, 400, 444, and 495 sh nm (log ε 4.51, 4.46, 4.18, 4.02, 4.01, 3.84, and 3.32); IR (KBr) 3170 (NH), 1608, and 1600 cm^{-1} (C=N, C=C); ^1H NMR ($CDCl_3$) δ=1.93 (3H, s, Me), 2.09 (3H, s, Me), 7.00 (1H, brs, H-3), 7.2—7.6 (3H, m, H-5,6,7), 7.8—8.1 (2H, m, H-4,8), and 8.85 (1H, m, NH); MS *m/z* 199 (M^+, 73), 184 (100), 143 (40), 116 (51), and 89 (30).

Found: C, 72.45; H, 6.64; N, 21.14%. Calcd for $C_{12}H_{13}N_3$: C, 72.34; H, 6.58; N, 21.09%.

Ethyl Methyl Ketone Cyclohepta[*b*]pyrrol-2-ylhydrazone (5). Similar procedures for **2** were followed. Thus 100 mg of **1** and 38 mg of ethyl methyl ketone gave **5** as dark amber needles (90 mg, 67%) after purification by chromatography in a column of alumina with CH_2Cl_2 as an eluant: mp* 113.5—114°C (from hexane); UV* (EtOH) 280, 288, 322, 332, 382, 400, 447, 464 sh, and 496 sh nm (log ε 4.48, 4.44, 4.18, 4.17, 4.02, 4.00 3.81, 3.73, and 3.31); IR* (KBr) 3160 (NH), 1605, and 1595 cm^{-1} (C=N, C=C); ^1H NMR* ($CDCl_3$) δ=1.17 (3H, t, J=6.5 Hz, CH_3-CH_2-), 1.89 (3H, s, Me), 2.38 (2H, q, J=6.5 Hz, CH_2), 7.03 (1H, brs, H-3), 7.2—7.6 (3H, m, H-5,6,7), 7.8—8.1 (2H, m, H-4,8), and 8.95 (1H, m, NH), besides these, there exist signals due to a small proportion (ca. 15%) of **5** (presumably in the Z-form) at δ=1.08 (t). 2.06 (s), and 2.30 (q); MS* *m/z* 213 (M^+, 35), 184 (100), 144 (27). 143 (27), and 116 (36).

Found*: C, 73.10; H, 6.85; N, 19.60%. Calcd for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70%.

Phenylacetaldehyde Cyclohepta[*b*]pyrrol-2-ylhydrazone (6). Similar procedures for **2** were followed. Thus 120 mg of **1** and 75.5 mg of phenylacetaldehyde in refluxing ethanol (25 cm^3, for 30 min) gave **6** as dark brown needles (125 mg,

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*For specimen consisting of a ca. 85:15 mixture of E- and Z-form (by NMR), because their separation could not be achieved by recrystallization or chromatography.

63%): mp 143.5—144°C (from benzene–hexane); UV (EtOH) 278, 287, 317, 380, 398, 440, 462 sh, and 495 sh nm (log ε 4.47, 4.47, 4.22, 4.01. 3.95, 3.83, 3.76, and 3.31); IR (KBr) 3170 (NH) and 1610 cm^{-1} (C=N, C=C); ^1H NMR ($CDCl_3$) δ= 3.80 (2H, d, *J*=4.5 Hz, CH_2), 6.80 (1H. brs, H-3), 7.1—7.9 (12H, m, H-4,5,6,7,8, CH, C_6H_5, NH); MS *m/z* 261 (M^+, 18), 170 (100), 144 (22), 116 (18), and 91 (17).

Found C, 78.09; H, 5.73; N, 15.96%. Calcd for $C_{17}H_{15}N_3$: C, 78.13; H, 5.79; N, 16.08%.

1,2,3,4-Tetrahydro-5*H*-cyclohepta[4,5]pyrrolo[2,3-*b*]indole (7). A solution of 4.9 g of **2** in 247 cm^3 of 1 M sulfuric acid (1 M=1 mol dm^{-3}) was refluxed for 5 h. After cooling, the mixture was diluted with cold water, brought to pH 9—10 with 2 M NaOH, and extracted with benzene. The organic layer was dried (Na_2SO_4), treated with active carbon, and evaporated in vacuo. The residue was recrystallized from ethanol to give **7** as dark red needles (1.64 g, 36%): mp 243—244°C; UV (MeOH) 233, 258, 312, 340, 417, 522, and 560 sh nm (log ε 4.16, 4.34, 4.63, 4.22, 3.75, 2.69, and 263), (MeOH+0.1 M HCl) 230, 259, 265, 322, and 350 sh nm (log ε 4.31, 4.38, 4.35, 4.19, and 4.35); IR (KBr) 3100 (NH), 2930, 2840 (CH_2), and 1605 cm^{-1} (C=N and C=C); ^1H NMR, see Table 1.

Found: C, 80.67; H, 6.07; N, 11.92%. Calcd. for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35; N, 11.60%.

5-Acetyl-1,2,3,4-tetrahydro-5*H*-cyclohepta[4,5]pyrrolo[2,3-*b*]indole (8). A mixture of 1.0 g of **7** and 10 g of acetic anhydride was gently refluxed for 2 h. After cooling, it was diluted with water and brought to pH 8—9 with a saturated aqueous $NaHCO_3$. The ppt was filtered off and the filtrate was extracted with $CHCl_3$. The organic layer was evaporated in vacuo. The residue combined with the above ppt was chromatographed in a column of silica gel with chloroform as an eluant, giving **8** as red-violet needles (1.2 g, 70%): mp 133—135°C. (from cyclohexane): UV (MeOH) 232, 258, 313, 341, 417, 510, and 550 sh nm (log ε 4.14, 4.32, 4.59, 4.17, 3.71, 2.61, and 2.55); IR (KBr) 2930, 2850 (CH_2) and 1700 cm^{-1} (C=O); ^1H NMR, see Table 1.

Found: C, 77.03; H, 6.02; H, 10.74%. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60%.

5-Acetyl-5*H*-cyclohepta[4,5]pyrrolo[2,3-*b*]indole (9). A solution of 0.5 g (1.9 mmol) of **8** and 0.9 g (4 mmol) of DDQ in 80 cm^3 of dry benzene was refluxed for 5 h. After cooling, the ppt was filtered off and the filtrate was evaporated in vacuo. The residue and the above ppt were combined and triturated with $CHCl_3$. The combined $CHCl_3$ solution was washed with saturated aqueous $NaHCO_3$ and concentrated in vacuo. The residue was chromatographed over silica gel with $CHCl_3$ as an eluant, giving **9** as red-violet needles (0.34 g, 69%): mp 200—202°C (from benzene); UV (MeOH) 241, 284, 297, 325, 480, 500, and 545 sh nm (log ε 4.27, 4.28, 4.29, 4.56, 3.12, 3.11, and 2.83); IR (KBr) 1695 cm^{-1} (C=O); ^1H NMR, see Table 1; MS *m/z* 260 (M^+, 39), 218 (100), 190 (14), and 164 (5).

Found: C, 78.22; H, 4.44; N, 10.79%. Calcd for $C_{17}H_{12}N_2O$: C, 78.44; H, 4.65; N, 10.76%.

5*H*-Cyclohepta[4,5]pyrrolo[2,3-*b*]indole (10). A solution of 0.1 g of **9** in 10 cm^3 of 6 M HCl was refluxed for 5 h and then, after cooling, diluted with 10 cm^3 of water. The ppt was filtered off and recrystallized from ethanol, giving **10** as red-brown needles (0.084 g, 100%): mp>300°C (decomp); UV (MeOH) 240, 284, 296, 325, 472, 495, and 545 sh nm (log ε 4.30, 4.33, 4.32, 4.57, 3.17, 3.16, and 2.84), (MeOH+0.1 M HCl) 263, 282, 335, and 415 sh, nm (log ε 4.30, 4.31, 4.25, and 3.94); IR (KBr) 3050 (NH), 1620, and 1605 cm^{-1} (C=N, C=C); ^1H NMR, see Table 1; MS *m/z* 218 (M^+, 100), 190 (16), 164 (5), and 109 (4).

Found: C, 82.73; H, 4.65; N, 12.87%. Calcd for $C_{15}H_{10}N_2$: C, 82.54; H, 4.62; N, 12.84%.

Hydrolysis of **9** with 2 M NaOH similarly gave **10** in a quantitative yield.

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