A Convenient Synthesis of Indolotropones and 6-Substituted 5-Azabenz[*b*]azulenes*

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Several substituted indolo[2,3-*b*]tropones were prepared by the dehydrobromination of 7,7-dibromo-7,8,9,10-tetrahydrocyclohept[*b*]indole-6(5*H*)-ones (**2a**—**h**), which had been obtained by the bromination of 7,8,9,10-tetrahydrocyclohept[*b*]indol-6(5*H*)-ones (**1a**—**h**) with phenyltrimethylammonium tribromide (PTAB). 6,7,8,9-Tetrahydrocyclohept[*b*]indole-10(5*H*)-one (**5a**) and 6,7,8,9-tetrahydro-5-methylcyclohept[*b*]indol-10(5*H*)-one (**5b**) were obtained by the oxidation of hexahydrocyclohept[*b*]indole (**4a**) and the 5-methyl derivative (**4b**) with dichlorodicyanobenzoquinone (DDQ). Indolo[3,2-*b*]tropones (**6a** and **6b**) were derived from **5a** and **5b** respectively. The reactions of 6-chloro-5-azabenz[*b*]azulene (**8**) with nucleophilic reagents gave the corresponding substituted products (**9a**—**j**).

In a previous paper,[1] it has been reported that cyclohept[*b*]indol-6(5*H*)-ones (indolo[2,3-*b*]tropones) were obtained by using 2-hydrazinotropones as the starting material.

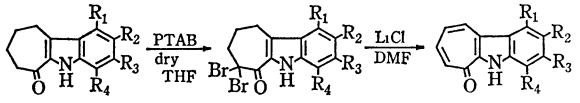
We will outline here a convenient method for the synthesis of cyclohept[*b*]indol-6(5*H*)-ones and cyclohept[*b*]indol-10(5*H*)-ones (indolo[3,2-*b*]tropones) by a modification of the synthetic method of G. Jones and his co-workers for heterocyclic tropones.[2] It will also be described for substitution reactions of 6-chloro-5-azabenz[*b*]azulene, obtained from **3a**, with several nucleophilic reagents.

Results and Discussion

Cyclohept[b]*indol-6(5*H*)-ones.* 7,8,9,10-Tetrahydrocyclohept[*b*]indol-6(5*H*)-one (**1a**) was brominated with phenyltrimethylammonium tribromide (PTAB) in dry tetrahydrofuran to give 7,7-dibromo-7,8,9,10-tetrahydrocyclohept[*b*]indol-6(5*H*)-one (**2a**). The dehydrobromination of the dibromo compound (**2a**) with lithium chloride in boiling *N*,*N*-dimethylformamide (DMF) gave yellow micro needles (mp 245—246 °C).

The IR spectrum was identical with that of the cyclohept[*b*]indol-6(5*H*)-one prepared by the dehydrogenation of 1,2,3,4-tetrahydrocyclohept[*b*]indol-6(5*H*)-one with chloranil or 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ).[1]

Further, several substituted cyclohept[*b*]indol-6(5*H*)-ones (**3b**—**h**) were obtained from the corresponding 7,8,9,10-tetrahydrocyclohept[*b*]indol-6(5*H*)-ones (**1b**—**h**) in the same way. The results are shown in Tables 1, 2, and 3.



1 **2** **3**

a: $R_1=R_2=R_3=R_4=H$
b: $R_2=CH_3$, $R_1=R_3=R_4=H$
c: $R_4=CH_3$, $R_1=R_2=R_3=H$
d: $R_2=NO_2$, $R_1=R_3=R_4=H$
e: $R_4=NO_2$, $R_1=R_2=R_3=H$
f: $R_2=R_4=CH_3$, $R_1=R_3=H$
g: $R_3=R_4=CH_3$, $R_1=R_2=H$
h: $R_2=Cl$, $R_1=R_3=R_4=H$

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Cyclohept[b]*indol-10(5*H*)-ones.* 5,6,7,8,9,10-Hexahydrocyclohept[*b*]indole (**4a**) reacts rapidly with DDQ at room temperature in wet dioxane to give colorless micro prisms (mp 224—225 °C).

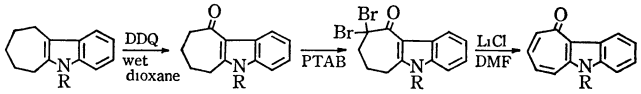
The analytical data revealed a composition with the formula of $C_{13}N_{13}ON$. The IR spectrum does not agree with that of **1a**.

The structure of this product was confirmed by a direct comparison with an authentic sample of 6,7,8,9-tetrahydrocyclohept[*b*]indol-10(5*H*)-one (**5a**) prepared[4] from the phenylhydrazone of 5-acetylvaleric acid.

Compound **5a** has also been prepared[4] by the hydrolysis of 5,6,7,8,9,10-hexahydro-10-*p*-tolylsulphonyliminocyclohept[*b*]indole or by the irradiation of acridine *N*-oxide, followed by hydrogenation.

6,7,8,9-Tetrahydro-5-methylcyclohept[*b*]indol-10-(5*H*)-one (**5b**) was also obtained by the reaction of hexahydro-5-methylcyclohept[*b*]indole (**4b**) with DDQ by a similar method. It was identical with the material obtained by the methylation of **5a** with dimethyl sulfate.

The bromination of **5a** and **5b** with PTAB afforded α,α-dibromo ketones **6a** and **6b**, which were then converted to cyclohept[*b*]indol-10(5*H*)-ones **7a**[4b] and **7b** respectively by dehydrobromination with lithium chloride.



4 **5** **6** **7**

a R=H
b $R=CH_3$

Nucleophilic Substitution Reactions of 6-Chloro-5-azabenz[b]*azulene.* In the previous paper,[1] we have reported that 6-chloro-5-azabenz[*b*]azulene (8-chlorobenz[*b*]-1-azaazulene) (**8**) was obtained when cyclohept[*b*]indol-6(5*H*)-one (**3a**) was heated with phosphoryl chloride or thionyl chloride.

The treatment of Compound **8** with sodium methoxide, sodium hydrosulfide, dimethylamine, aniline, *etc.* in ethanol or dimethyl sulfoxide gave the corresponding substituted products (**9a**—**j**). The results are shown

TABLE 1. 7,7-DIBROMO-7,8,9,10-TETRAHYDROCYCLOHEPT[*b*]INDOL-6(5*H*)-ONES (**2**)

Compound	Mp (°C)	Yield (%)	Formula	Elemental analysis Found (Calcd) (%)				IR (KBr) (cm^{-1})	
				C	H	N	Br	NH	C=O
2a	154—155	91	$C_{13}H_{11}ONBr_2$	43.87 (43.73	3.15 3.11	3.98 3.92	44.14 44.76)	3363	1618
2b	180 (dec)	87	$C_{14}H_{13}ONBr_2$	45.24 (45.31	3.52 3.53	3.64 3.78	42.98 43.07)	3358	1623
2c	158—159	93	$C_{14}H_{13}ONBr_2$	44.99 (45.31	3.46 3.53	3.82 3.78	42.67 43.07)	3378	1625
2d	>250	78	$C_{13}H_{10}O_3N_2Br_2$	39.00 (38.83	2.81 2.51	7.00 6.97	40.00 39.75)	3385	1626
2e	173—174	87	$C_{13}H_{10}O_3N_2Br_2$	38.98 (38.83	2.64 2.51	7.20 6.97	39.99 39.75)	3463	1626
2f	182 (dec)	84	$C_{15}H_{15}ONBr_2$	46.77 (46.78	3.82 3.93	3.66 3.64	41.50 41.50)	3370	1615
2g	177—178	92	$C_{15}H_{15}ONBr_2$	47.00 (46.78	3.95 3.93	3.75 3.64	41.50 41.50)	3336	1630
2h	183 (dec)	79	$C_{13}H_{10}ONClBr_2$	39.15 (39.88	2.40 2.51	3.85 3.53	40.43 40.82)	3378	1625

TABLE 2. CYCLOHEPT[*b*]INDOL-6(5*H*)-ONES (**3**)

Compound	Mp (°C)	Yield (%)	Formula	Elemental analysis Found (Calcd) (%)			IR (KBr) (cm^{-1})	
				C	H	N	NH	C=O
3a[1]	245—246	82	$C_{13}H_9ON$				3195	1614
3b	242—244	100	$C_{14}H_{11}ON$	79.92 (80.36	5.26 5.30	6.70 6.70)	3183	1610
3c	135—136	92	$C_{14}H_{11}ON$	80.22 (80.36	5.32 5.30	6.77 6.70)	3190	1605
3d	>300	100	$C_{13}H_8O_3N_2$	64.60 (65.00	3.26 3.36	11.56 11.66)	3165	1616
3e	287—288	100	$C_{13}H_8O_3N_2$	65.17 (65.00	3.31 3.36	11.52 11.66)	3310	1611
3f	245—247	100	$C_{15}H_{13}ON$	80.85 (80.69	5.75 5.87	6.29 6.27)	3200	1615
3g	245—246	100	$C_{15}H_{13}ON$	80.62 (80.69	5.75 5.87	6.20 6.27)	3190	1610
3h	292—293	100	$C_{13}H_8ONCl$	67.58 (67.99	3.41 3.51	6.43 6.10)	3203	1608

TABLE 3. ULTRAVIOLET AND VISIBLE ABSORPTION MAXIMA OF CYCLOHEPT[*b*]INDOL-6(5*H*)-ONE (**3**)

Compound	λ_{max} nm (log ε) (in CH_3OH)
3b	278(4.34), 313(4.24), 326(4.23), 338(4.19), 392(3.68) (sh), 409(3.82)
3c	281(4.32), 309(4.13), 323(4.11), 337(4.02), 390(3.72) (sh), 407(3.83)
3d	255(4.34), 296(4.32), 305(4.27) (sh), 320(4.27), 376(4.01), 397(4.02)
3e	254(4.45), 338(4.09), 366(4.13), 386(4.15)
3f	282(4.35), 316(4.21), 326(4.22), 338(4.14), 396(3.81) (sh), 409(3.88)
3g	286(4.36), 310(4.30), 326(4.21) (sh), 337(4.11) (sh), 390(3.80) (sh), 408(3.90)
3h	275(4.32), 317(4.19) (sh), 324(4.22), 338(4.16), 384(3.72), 402(3.84)

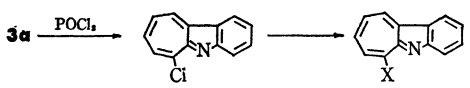
Table 4. Nucleophilic substitution reaction products (**9**) from 6-chloro-5-azabenz[*b*]azulene (**8**)

Compound	Mp (°C) Apearance (color, crystal form)	Yield (%)	Formula	Elemental analysis Found (Calcd) (%) C	H	N	IR (KBr) (cm^{-1})
9b	(Picrate) 203—204 (yellow micro needles)	26[a)]	$C_{20}H_{14}O_8N_4$	54.64 (54.80	3.44 3.22	12.81 12.78)	
9c	(Picrate) 219—220 (yellow micro needles)	10[a)]	$C_{21}H_{16}O_8N_4$	55.55 (55.75	3.60 3.57	12.30 12.39)	
9d	215 (dec) (orange micro needles)	85[a)]	$C_{13}H_9NS$	73.47 (73.92	4.20 4.30	6.81 6.63)	3226, 1616, 1601, 1498, 1478, 1433
9e	96— 98 (a) (red prisms) (b)	70[a)] 94[b)]	$C_{15}H_{14}N_2$	81.37 (81.37	6.34 6.25	12.43 12.61)	1599, 1561, 1504
9f	112—114 (a) (red prisms) (b)	49[a)] 85[b)]	$C_{19}H_{14}N_2$	84.54 (84.41	5.14 5.22	10.35 10.37)	1611, 1586, 1526, 1474
9g	86— 87 (orange prisms)	59[a)]	$C_{20}H_{16}N_2$	84.75 (84.47	5.70 5.67	9.93 9.85)	3413, 1614, 1599, 1539
9h	231—233 (yellow plates)	54[a)]	$C_{19}H_{13}N_3O_2$	72.09 (72.37	4.18 4.15	12.89 13.33)	3391, 1616, 1591, 1541, 1519, 1499
9i	138—139 (red needles)	50[a)]	$C_{17}H_{16}N_2O$	77.38 (77.25	6.09 6.10	10.76 10.60)	2957, 2857, 1601, 1567, 1498
9j	136—137 (red prisms)	43[a)]	$C_{20}H_{17}N_3$	80.20 (80.24	5.89 5.73	13.86 14.04)	3394, 1521, 1496, 1481

a) General procedure (a). b) General procedure (b).

Table 5. Ultraviolet and visible absorption maxima of substituted 5-Azabenz[*b*]azulenes (**9**)

Compound	λ_{max} nm (log ε)
9d	234(4.30), 300(4.41), 403(3.94), 461(4.17) (in MeOH)
9e	236(4.20), 268(4.16), 301(4.45), 311(4.49), 363(4.13), 382(4.22), 400(3.95)(sh), 507(3.68) (in cyclohexane)
9f	277(4.22), 305(4.32), 372(4.18) (in MeOH)
9g	281(4.20), 304(4.36), 473(4.20) (in MeOH)
9h	277(4.31), 323(4.20), 421(4.31) (in MeOH)
9i	237(4.29), 279(4.27), 305(4.48), 315(4.50), 370(4.11), 389(4.22), 408(4.03), 513(3.55) (in cyclohexane)
9j	249(4.44), 303(4.25), 363(4.07) (in MeOH)



8 **9**

a: X=$NHNH_2$[1)]
b: X=OCH_3
c: X=OCH_2CH_3
d: X=SH
e: X=$N(CH_3)_2$
f: X=NHC_6H_5
g: X=$NHC_6H_4CH_3$
h: X=$NHC_6H_4NO_2$
i: X= 
j: X=$NHNC_6H_5$ (CH_3)

in Tables 4 and 5.

Compound **9d** can exist in two tautomeric forms, such as **A** and **B**:

A **B**

The IR spectrum contained a band at 3226 cm^{-1} due to NH, but no band due to SH between 2600—2550 cm^{-1}. On the UV and visible absorption spectra, the absorption maxima of the visible portion was shifted to shorter wavelengths than those of **8**, **9e**, and **9i**, which could take only the type-B tautomeric form. Therefore, it is assumed that Compound **9d** takes the type-A tautomeric form.

Also, we can consider a similar tautomerism on Compounds **9a**, **9f**, **9g**, **9h**, and **9j**. However, it is difficult to decide on the basis of only the UV and IR spectra toward which form the equilibria of these compounds tend.

Experimental**

All the melting points are uncorrected.

Bromination of 7,8,9,10-Tetrahydrocyclohept[b]*indole-6(5H)-ones (**1a—h**) with PTAB.* *7,7-Dibromo-7,8,9,10-tetra-*

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hydrocyclohept[b]*indol-6(5H)-one (**2a**)*: To a solution of **1a** (0.3 g) in dry tetrahydrofuran (15 ml), we added phenyltrimethylammonium tribromide (PTAB) (1.1 g) at room temperature. The mixture was stirred for 15 h. The precipitate was filtered and washed with tetrahydrofuran. The combined tetrahydrofuran solutions were evaporated, and the residue was recrystallized from methanol to give **2a** as yellow micro needles (0.49 g, 91%); mp 154—155 °C.

Dibromo compounds (**2b—h**) were also prepared from the corresponding cyclic ketones (**1b—h**) by a method similar to that described above. The results are given in Table 1.

Dehydrobromination of 7,7-Dibromo-7,8,9,10-tetrahydrocyclohept-[b]*indol-6(5H)-ones (**2a—h**).* *Cyclohept*[b]*indol-6(5H)-one (**3a**)*: A mixture of **2a** (0.6 g) and lithium chloride (0.2 g) in DMF (20 ml) was refluxed under nitrogen for 3 h. The solvent was then removed under reduced pressure, after which the residue was diluted with water to give a precipitate. The separated material was collected and dried. Recrystallization from benzene gave **3a** as yellow micro needles, (0.27 g, 82%); mp 245—246 °C.

Cyclohept[*b*]indol-6(5*H*)-ones (**3b—h**) were also prepared from the dibromo compounds (**2b—h**) by a method similar to that described above. The results are given in Table 2.

6,7,8,9-Tetrahydrocyclohept[b]*indol-10(5H)-one (**5a**).* Into a solution of 5,6,7,8,9,10-hexahydrocyclohept[*b*]indole (**4a**) (1.0 g) in dioxane (100 ml) and water (10 ml), we stirred DDQ (2.4 g) at 5 °C. After 10 min, the precipitate was filtered off, and the filtrate was evaporated. The residue was extracted with chloroform. The chloroform layer was washed with a dilute sodium hydrogencarbonate solution, dried over anhydrous sodium sulfate, and evaporated to leave a residue. It recrystallized from benzene–ethanol to give **5a** as colorless micro prisms (0.73 g, 68%); mp 224—225 °C.

9,9-Dibromo-6,7,8,9-tetrahydrocyclohept[b]*indol-10(5H)-one (**6a**).* To a solution of **5a** (0.3 g) in dry tetrahydrofuran (30 ml) we added PTAB (1.1 g). The mixture was then treated by a method similar to that used for the preparation of **2a—h**. Yellow prisms (0.48 g, 89%); mp 182—184 °C (dec). IR(KBr): 3238, 2925, 1610, 1595, and 1445 cm^{-1}. Found: C, 43.92; H, 3.15; N, 3.79; Br, 44.68%. Calcd for $C_{13}H_{11}ONBr_2$: C, 43.73; H, 3.11, N, 3.92; Br, 44.76%.

Cyclohept[b]*indole-10(5H)-one (**7a**).* A mixture of **6a** (0.3 g) and lithium chloride (0.11 g) in DMF (10 ml) was refluxed under nitrogen for 3 h. The reaction mixture was treated by a method similar to that used for the preparation of **3a—h**. Yellow micro prisms (0.27 g, *ca.* 100%); mp 285—286 °C.

6,7,8,9-Tetrahydro-5-methylcyclohept[b]*indol-10(5H)-one (**5b**).* (*a*): To a solution of hexahydro-5-methylcyclohept[*b*]indole (**4b**) (1.0 g) in dioxane (50 ml) and water (5 ml), we added DDQ (2.28 g). The mixture was treated by a method similar to that used for the preparation of **5a**. Colorless scales (0.47 g, 44%), were recrystallized from cyclohexane; mp 136—137 °C.

(*b*): A mixture of **5a** (0.2 g) and dimethyl sulfate (0.24 g) in acetone (10 ml) and 1 M sodium hydroxide (3 ml) was heated at 90 °C for 30 min. The reaction mixture was then diluted with water and extracted with chloroform. The chloroform layer was dried over anhydrous sodium sulfate and evaporated to leave a oily residue. It was recrystallized from cyclohexane to give colorless scales (0.08 g, 38%); mp 135—136 °C.

The IR spectrum was identical with that of a sample prepared by Method (a), and the mixed melting point was not depressed.

9,9-Dibromo-6,7,8,9-tetrahydro-5-methylcyclohept[b]*indol-10(5H)-one (**6b**).* To a solution of **5b** (0.3 g) in dry tetrahydrofuran (30 ml), we added PTAB (1.1 g). The mixture was then treated by a method similar to that used for the preparation of **2a—h**. Pale yellow prisms (0.41 g, 79%); mp 173 °C (dec). IR(KBr): 2962, 2939, 1624, 1511, 1471, 1406, and 1414 cm^{-1}. Found: C, 45.00; H, 3.47; N, 3.72; Br, 42.83%. Calcd for $C_{14}H_{11}ONBr_2$: C, 45.31; H, 3.53; N, 3.78; Br, 43.07%.

5-Methylcyclohept[b]*indol-10(5H)-one (**7b**).* A mixture of **6b** (0.1 g) and lithium chloride (0.04 g) in DMF (5 ml) was refluxed under nitrogen for 3 h. The reaction mixture was then treated by a method similar to that used for the preparation of **3a—h**. Yellow micro needles (0.05 g, 89%); mp 169—170 °C. IR(KBr): 1628, 1556, and 1478 cm^{-1}. Found: C, 79.84; H, 5.28; N, 6.64%. Calcd for $C_{14}H_{11}ON$: C, 80.36, H, 5.30; N, 6.69%.

The Reaction of 6-Chloro-5-azabenz[b]*azulene with Nucleophilic Reagents.* *General Procedure*: (*a*); A solution of **8** (0.0005 mol) and a nucleophilic reagent (0.0007 mol) in ethanol (6 ml) was refluxed for 30 min on a water bath. The solvent was then removed. The resdiue was diluted with water, made slightly alkaline by adding aqueous sodium hydrogencarbonate, and extracted with benzene. The benzene layer was concentrated and passed through a silica gel column. The product obtained from the main effluent was recrystallized from cyclohexane, hexane, or cyclohexane–benzene.

(*b*); A mixture of **8** (0.0005 mol) and a nucleophilic reagent (0.0007 mol) in dimethyl sulfoxide (5 ml) was stirred for 15 min at room temperature. The reaction mixture was then diluted with water to separate the precipitate. The solid was collected, dried under reduced pressure, and recrystallized from cyclohexane. The results are given in Tables 4 and 5.

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