Correlation of Chemical Shifts with Substituent Parameters in *N*-Benzyl Derivatives of Pyrrole, 3a,7a-Dihydroindole, and Indole Esters[†]

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Series of *m*- and *p*-substituted benzyl derivatives of pyrrole, tetramethyl 1-benzyl-3a,7a-dihydroindole-2,3,3a,4-tetracarboxylate, and trimethyl 1-benzylindole-2,3,4-tricarboxylate were prepared and their ^{13}C NMR spectra were obtained in 0.1 M solutions of chloroform-*d*. Both single substituent parameter and dual substituent parameter analyses were carried out to correlate the substituent chemical shifts. The β carbon of the indole series showed the most profound substituent effect dependence as well as the best correlation. The results are explained by the hyperconjugation of the benzyl methylene group.

Key Words : Single substituent parameter, Dual substituent parameter, Chemical shift, Hyperconjugation

Introduction

Correlation of the chemical shift with substituent constant (*e.g.*, Hammett σ) has been widely used to investigate the nature of the effect of the substituent on the physical properties of compounds. Electron density around the nucleus of interest (H, C) is mostly affected by the electron-donating and electron-withdrawing ability of the substituent.

Therefore, a correlation between the observed chemical shift and any parameter representing such ability seems to be well-founded, and there are numerous reports on the subject.[1]

The single substituent parameter (SSP) approach which is represented by Eq. (1) has been used to correlate the chemical shift of *m*- and *p*-substituted compound to unsubstituted compound using the Hammett σ_m and σ_p values. Values of $^{13}\sigma$ were reported for the system of *m*- and *p*-substituted cinnamic acids in order to have a better correlation of ^{13}C chemical shift.[2] The dual substituent parameter (DSP) approach, on the other hand, divides the effect of substituent effect into inductive (σ_I) and resonance (σ_R) parameters as represented in Eq. (2).

$$\delta = \rho\sigma + \delta_o \qquad (1)$$

$$\delta = \rho_I\sigma_I + \rho_R\sigma_R + \delta_o \qquad (2)$$

The magnitude as well as the sign of ρ should have a profound meaning on the mechanism of the transmission of the substituent effect. For example, correlations of the chemical shift of carbonyl carbon with the Hammett σ for the system of benzanilides, X-C_6H_4-CO-NH-C_6H_4-Y show normal correlation when Y is varied, but reverse correlation is observed when X is varied. π Polarization has been attributed for such observation.[3,4] The magnitude of ρ_X (-2.838 ppm, r = 0.940) is larger than that of ρ_Y (0.853 ppm, r = 0.975) in DMSO-d_6. The carbonyl carbon is directly bonded to the phenyl ring of X-C_6H_4, but it is separated by

the nitrogen atom from C_6H_4-Y and therefore, the ρ_X should be larger than ρ_Y. The estimation of sign and magnitude of the substituent chemical shift, however, seems to be complicated by many factors which affect the chemical shift.

In the course of exploring of the possibility of using NMR spectroscopy for quantification of aromaticity of heterocyclic compounds[5] we observed a striking contrast in the correlation of the chemical shifts of α- and β-protons and carbons in 1-benzylpyrroles.[6] For example, the β-Hs show excellent correlation (ρ = 35.2 Hz, r = 0.995) with the Hammett σ whereas the α-Hs show poor correlation (ρ = 16.8 Hz, r = 0.779). In case of carbon $\rho_{\beta\text{-C}}$ is 117.9 Hz (r = 0.973) which is more than five times larger than that of $\rho_{\alpha\text{-C}}$ of 21.7 Hz (r = 0.651). The correlation is much worse for the α-C. The benzylic protons show a fair correlation with ρ 85.4 Hz (r = 0.942), but the benzylic carbons show negative slope with ρ -55.9 Hz with very poor correlation coefficient (r = 0.599). This can hardly be considered a trend. Apparently, the electronic effect of the pyrrole ring and that of the substituent in the phenyl ring collide at the benzylic center to cause such abnormality in correlation. However, it is not certain what the exact cause of such abnormality is.

In order to have a better understanding on the nature of the substituent chemical shift it seems desirable to have a system in which the five-membered nitrogen-containing heterocycle is not fully aromatic so that the ring current effect of the heterocycle does not collide with the electronic effect of the substituent in the phenyl ring at the benzylic center. A system like 3,4-dihydro-1-benzylpyrrole should be a reasonable choice for such purpose. Although 2,5-dihydropyrrole (3-pyrroline) is commercially available, 3,4-dihydropyrrole (or 2-pyrroline) is not known to date. However, one closely related system to 2-pyrroline is the skeleton of 3a,7a-dihydroindole, which is a known compound.[7]

In this paper we report the synthesis of eleven *N*-(*m*- and *p*-substituted)benzyl derivatives of pyrrole **1**, tetramethyl 3a,7a-dihydroindole-2,3,3a,4-tetracarboxylates **2** and trimethyl indole-2,3,4-tricarboxylates **3**, and their substituent chemical shift properties.

Results and Discussion

The 3a,7a-dihydroindole esters **2** were prepared by the known method from 1-(*m*- and *p*-substituted)benzylpyrroles and dimethyl acetylenedicarboxylate (DMAD).[7] The di-hydroindoles (**2**) were converted to indoles (**3**) by treatment with bromine in methanol. The aromatization went well for all the cases except *p*-nitro (**2f**) and *p*-bromo (**2g**) compounds. Analytical purity is essential to make 0.1 M solution in chloroform-*d* for each compound so that the error originated from the concentration is minimized. Therefore, the products were isolated using column chromatography and then purified by recrystallization. The chemical shift values of protons and carbons for **2** and **3** are listed in Tables 5-12.

Z: **a**, *m*-NO₂; **b**, *m*-Br; **c**, *m*-Cl; **d**, *m*-OCH₃; **e**, *m*-CH₃,

f, *p*-NO₂; **g**, *p*-Br; **h**, *p*-Cl; **i**, *p*-OCH₃; **j**, *p*-CH₃, **k**, H
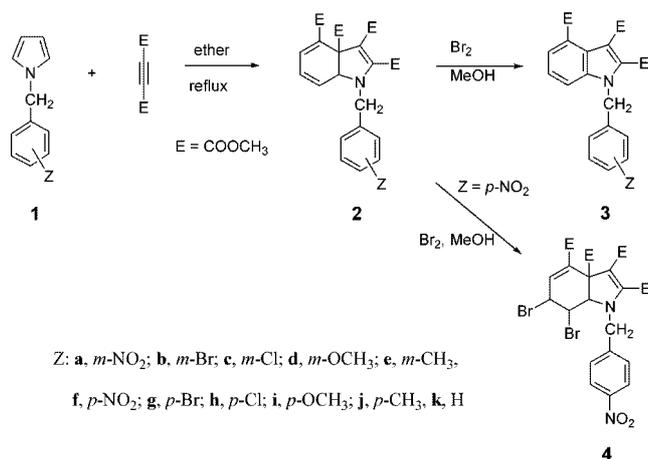
Attempted aromatization of **2f** (*p*-NO₂) with bromine gave **4** of which bromine was added to 6-C–7-C double bond in 60% yield. No signal corresponding to **3f** was detected in the NMR spectrum of the reaction mixture. The structure of **4** was confirmed by spectroscopic method as well as elemental analysis. An attempt to aromatize **2g** (*p*-Br) was most troublesome, resulting in many components present in the reaction mixture including **3g** and a compound similar to **4**.

The NMR assignments were made with the aid of ^{1}H-^{1}H COSY and ^{1}H-^{13}C HETCOR analyses. The assignments for carbons bearing a proton were quite obvious, but the carbons and the protons of the ester groups were assigned by examination of HMBC spectra. The 3a-COOCH₃ of **2** is bonded to an sp^3-hybridized carbon atom and its ^{13}C chemical shift of the carbonyl carbon is downfield by about 10 ppm compared to those of 2-, 3- and 4-COOCH₃ which are bonded to an sp^2-hybridized carbons. The methoxy carbon of 3a-COOCH₃ group is also further downfield than other ester groups.

The assignments of 2-, 3-, 3a-, and 7a-C of **3** which are based on the reported chemical shift of various indole derivatives[8] are consistent with the analysis of HMBC spectra. Among them, in general, 7a-C appears in most downfield (*ca.* 136-138 ppm) and 3-C appears in most upfield (*ca.* 100-110 ppm). The observed chemical shift for 3-C (*ca.* 116.55 ppm) seems to be influenced by the presence of 4-COOCH₃ group. In fact, the chemical shift of 3-C

Table 1. Best Fit of the Single Substituent Parameter Equation for ^{13}C Chemical Shifts of 1-Benzylpyrrole **1**, Dihydroindoles **2**, and Indoles **3** in Chloroform-*d* (0.1 M) in Hz

	1		**2**		**3**	
	ρ	r	ρ	r	ρ	r
CH₂	-64.3	0.648	-49.7	0.646	-60.6	0.642
2	21.6	0.610	-96.0	0.983	-104.2	0.977
3	124.6	0.985	216.8	0.981	126.7	0.991
3a			12.7	0.776	15.8	0.911
4			12.6	0.843	28.5	0.927
5			11.5	0.836	56.3	0.993
6			99.0	0.956	80.3	0.990
7			-77.1	0.973	-73.8	0.968
7a			71.2	0.952	-11.9	0.628
2-C=O			-31.2	0.983	-23.6	0.958
3-C=O			-31.8	0.989	-20.5	0.906
3a-C=O			-51.2	0.986		
4-C=O			-25.9	0.986	-39.6	0.982
2-OCH₃			12.7	0.980	15.9	0.969
3-OCH₃			25.6	0.978	13.8	0.969
3a-OCH₃			28.2	0.935		
4-OCH₃			10.2	0.975	20.1	0.975

of indole-2-carboxylic acid and indole-3-carboxylic acid is about same (107.28 *vs* 107.26 ppm) in chloroform-*d*, but that of indole-4-carboxylic acid is 102.18 ppm.

The C-2 and C-3 portion of **2** may be considered an amino-maleate system. The assignments can be made by comparison to similar aminomaleate compounds.[9] The signal for 7a-C of **2** is readily assigned (*ca.* 67-68 ppm) by the ^{1}H-^{13}C HETCOR spectrum. The assignment of 3a-C which is an sp^3 hybridized carbon, then becomes obvious (*ca.* 55 ppm).

The results of the correlation with the SSP are listed in Table 1. In our previous report[6] with **1**, a σ_p value of -0.268 was used for the methoxy substituent.[10] A value of -0.12 is used for the same substituent[11] in the present report because it gives better correlations for all series examined for the present study.

1-Benzylpyrrole (**1**) and 1-benzylindole (**3**) are systems in which the aryl and heteroaryl groups are connected to the same methylene carbon. Therefore, it is expected that the chemical shift of CH₂, 2-C and 3-C are influenced similarly by the substituted phenyl group. However, to our surprise, the methylene carbons, which are directly bonded to the substituted phenyl ring, show no correlation (r = 0.642-0.646). The 2-C of **1** show no correlation (r = 0.610) whereas that of **3** show negative correlation (ρ = -104.2 Hz) with a moderate correlation coefficient (r = 0.977). In contrast, the 3-Cs of **1** and **3** show strong dependency to the effect of substituent with good to excellent linear relationship (ρ = 124.6 Hz, r = 0.985 for **1**; and ρ = 126.7 Hz, r = 0.991 for **3**). Furthermore, the bridge-head carbons, 3a-C and 7a-C of **3** show quite contrasting trends. For 3a-C, which should correspond to 3-C of **1** show a moderate trend with a normal relationship (ρ = 15.8, r = 0.911). On the other hand, 7a-C, which corresponds to 2-C of **1**, show a reverse trend of

correlation (ρ = -11.9 Hz, r = 0.628), but the difference in absolute magnitude of $\rho_{7a\text{-}C}$ and $\rho_{3a\text{-}C}$ may be considered negligible.

The two rings in **1** may be rotating freely along C-C and C-N bonds. Similar free rotation is not feasible in **3** due to the bulkiness of the indole skeleton. The presence of the ester groups at 2-C may make the free rotation even more difficult. The consequence of restricted rotation is that the overlapping of the back lobe of one of the sp^3 orbitals (which forms a C-H bond of the methylene group) and the lone pair orbital on the N atom is feasible. The result of such overlapping may be hyperconjugation like **I**.
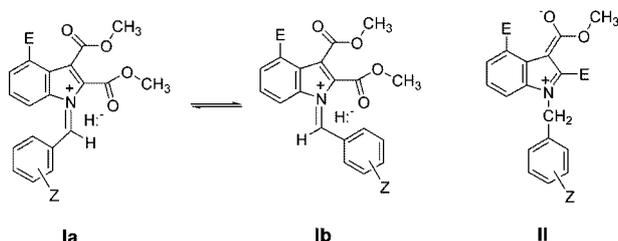
The structure like **I** may be considered an extended conjugated double bond system similar to an extended cinnamate ester.[12] It is known that a normal and inverse effect alternate in such systems. The correlation of the substituent chemical shift of each carbon atom along the conjugated chain is usually good. This is the case with **3** as shown in Table 1. The contribution of structure **II** also seems significant because the averaged chemical shift of the carbonyl carbons at 3-C is 161.26 ppm which is shifted to upfield by more than 5 ppm compared to other two carbonyl carbons (166.74 for 2-C and 166.90 ppm for 4-C in average).

Both 2-C and 7a-C are bonded to the nitrogen atom and both show inversed effect of the substituent. This is understandable because π polarization of a conjugate system induces an alternating partial positive and negative charge at each end of the π unit.[1,13] The magnitude of $\rho_{2\text{-}C}$, however, is about nine times larger than that of $\rho_{7a\text{-}C}$. This may be evidence of the conformation **Ia** being more favorable than **Ib**. The effect of a substituent should transmit like a dipole and the atoms which lie on the direction of the dipole moment should be more influenced by the electronic nature of the substituent than other atoms are. This may be one of the reasons that ^{1}H chemical shifts are rather poorly correlated to the Hammett σ, although we have not included such analysis in the present report.

Transmission of the effect of a substituent, however, occurs not only through bonds but also through space. The latter type of transmission becomes significant in **Ia** in which the indole and the phenyl rings are in close proximity. The two rings are not coplanar and 7-C is closest to the top of the phenyl ring. Therefore, 7-C may show inverse correlation.

Analysis of 6-C shows the largest ρ value among the carbons in the benzene ring. It is at the meta position from the nitrogen atom to which the through-space transmission is minimal but the induced π polarization is greatly enhanced.

An excellent correlation coefficient (r = 0.990) may also reflect the presence of such polarization.

The SSP correlation of **2** with the Hammett σ is also interesting. As mentioned in the section of the assignments of the chemical shift, the dihydroindole skeleton consists of two parts: an aminomaleate and an extended α,β-unsaturated ester. The 5- and 6-membered rings are cis-fused. Also, 6-C, 7-C, and 7a-C are in the vicinity of the phenyl ring, while 4-C and 5-C are away from the phenyl ring. One of the striking observation is the exceptionally large ρ value for 3-C (216.8 Hz) with good correlation coefficient (r = 0.981). Unlike **3** which is fully aromatic, neither ring in **2** is aromatic. Furthermore, the conjugation is disrupted and the lone-pair electrons on the nitrogen atom can only be delocalized through resonance to the α,β-unsaturated ester. The unusually large ρ value cannot be explained by the through-bond transmission of the effect of the substituent only. If that is the case, $\rho_{2\text{-}C}$ should be larger than $\rho_{3\text{-}C}$ because 2-C is closer to the substituent. The 3-C lies in the region where the effect can be transmitted through space, like in structure **III**.
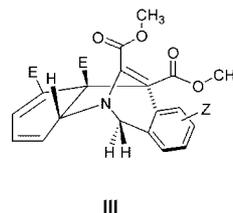
The results of DSP analysis are listed in Tables 2, 3, and 4 for **1**, **2**, and **3**, respectively. The best fit was obtained using $\sigma_{R(BA)}$ values.[14] Other values such as σ_{Ro}, σ_{R+}, and σ_{R-} did not give good correlation. The fitness of $\sigma_{R(BA)}$ is understandable because the methylene group should act as an insulator for the transmission of the effect of substituents. Furthermore, the hyperconjugate nature in which the methylene carbon bears some sp^2 hybrid character is in consistent with the use of $\sigma_{R(BA)}$. The "goodness of fit" of a DSP correlation is usually judged by the parameter f (= SD/RMS; where SD stands for the standard deviation of the fit, and RMS is the root-mean-square size of the experimental data). The smaller the f value, the better the fit. Therefore, f values of 0.0-0.1 represent excellent correlation, and f value of 0.1-0.2 represent moderately good correlation. Also, f values greater than 0.3 may be considered to represent only a crude trend.[14]

The DSP analysis shows that, in general, λ (= ρ_R/ρ_I) values are smaller than 1, indicating that the inductive effect is more important than the resonance effect in most cases,

Table 2. Best Fit of the Dual Substituent Parameter Equation with $\sigma_{R(BA)}$ for ^{13}C Chemical Shifts of 1-Benzylpyrole **1** in Chloroform-*d* (0.1 M)

	ρ_I	ρ_R	δ_0, ppm	SD	f	λ
CH$_2$	1.48	0.20	53.06	0.19	0.38	0.14
2,5	0.12	0.70	120.97	0.15	1.32	5.83
3,4	1.40	0.60	108.49	0.10	0.22	0.43

Table 3. Best Fit of the Dual Substituent Parameter Equation with $\sigma_{R(BA)}$ for ^{13}C Chemical Shifts of Dihydroindoles **2** in Chloroform-*d* (0.1 M)

	ρ_I	ρ_R	δ_0, ppm	SD	f	λ
CH$_2$	-1.16	0.05	49.44	0.16	0.34	-0.04
2	-1.10	-0.40	152.47	0.06	0.14	0.36
3	2.33	1.27	102.65	0.11	0.13	0.57
3a	0.30	0.06	55.43	0.06	1.15	0.20
4	0.21	0.06	126.74	0.03	0.68	0.28
5	0.18	0.06	130.96	0.03	0.58	0.33
6	1.05	0.60	124.83	0.05	0.13	0.57
7	-0.85	-0.40	124.17	0.04	0.13	0.47
7a	0.85	0.40	67.95	0.10	0.41	0.47
2-C=O	-0.33	-0.16	164.25	0.01	0.07	0.48
3-C=O	-0.34	-0.18	163.44	0.02	0.20	0.53
3a-C=O	-0.55	-0.45	174.54	0.08	0.37	0.82
4-C=O	-0.28	-0.13	166.34	0.01	0.08	0.46
2-OCH$_3$	0.16	0.03	55.03	0.01	0.22	0.19
3-OCH$_3$	0.28	0.13	51.09	0.01	0.15	0.46
3a-OCH$_3$	0.34	0.14	55.10	0.003	0.25	0.41
4-OCH$_3$	0.10	0.07	51.97	0.005	0.14	0.70

except 2-C=O and 3-C=O of **3** and 2,5-C of **1**. The latter case is very unusual because *f* value is 1.32 indicating no correlation. The λ value of 5.83 is also unrealistic and these values represent that the chemical shift of 2,5-C of **1** does not correlate at all with any substituent constants.

In most cases where *f* values are less than 0.2, the value of λ varies from 0.36 to 0.70 with an average of 0.52. This means ρ_R is about half of ρ_I: that is, the inductive effect is more significant than the resonance effect. However, if one considers the prevention of the transmission of the substituent effect by CH$_2$ group, the magnitude of ρ_R is quite significant.

The magnitudes of ρ_R and ρ_I of 2-C and 3-C of **2** and **3** are

Table 4. Best Fit of the Dual Substituent Parameter Equation with $\sigma_{R(BA)}$ for ^{13}C Chemical Shifts of Indoles **3** in Chloroform-*d* (0.1 M)

	ρ_I	ρ_R	δ_0, ppm	SD	f	λ
CH$_2$	-1.26	0.41	48.27	0.18	0.43	-0.33
2	-1.05	-0.55	128.06	0.03	0.11	0.52
3	1.25	0.82	116.50	0.06	0.16	0.66
3a	0.19	0.08	121.58	0.02	0.31	0.42
4	0.29	0.21	124.37	0.03	0.27	0.72
5	0.60	0.25	125.33	0.03	0.18	0.42
6	0.70	0.60	124.86	0.05	0.20	0.86
7	0.75	0.40	115.44	0.01	0.06	0.53
7a	-0.30	-0.003	138.40	0.04	0.67	0.01
2-C=O	-0.20	-0.25	166.81	0.04	0.51	1.25
3-C=O	-0.20	-0.21	161.30	0.03	0.50	1.05
4-C=O	-0.40	-0.21	166.95	0.01	0.11	0.53
2-OCH$_3$	0.19	0.06	52.33	0.02	0.32	0.32
3-OCH$_3$	0.25	0.03	52.61	0.02	0.31	0.12
4-OCH$_3$	0.16	0.05	52.06	0.01	0.26	0.31

significantly larger than any other carbons in the series. The exceptionally large λ value of 2,5-C of **1** and close values of 2-C and 3-C of **2** and **3** may be considered evidence of the hyperconjugation described earlier. The methylene proton of **1** is not acidic enough to form a structure like **IV**.
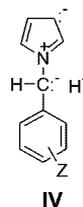
On the other hand, the presence of the ester groups at 2-C and 3-C of **2** and **3** should enhance the probability of the hyperconjugative structure like **Ia** or **Ib**. Such hyperconjugation should make the transmission of the effect through resonance more effective.

Experimental Section

Melting points were determined on a Fischer MEL-TEMP apparatus and are uncorrected. Nuclear magnetic resonance

Table 5. ^{1}H Chemical Shift Values (δ) of Substituted Dihydroindoles **2** in Chloroform-*d* (0.1 M)

	CH$_2$	J$_{CH2}$[a]	5-H	6-H	7-H	7a-H	2-OMe	3-OMe	3a-OMe	4-OMe
2a	4.37	16.09	7.04	6.24	5.82	4.84	3.81	3.65	3.75	3.76
2b	4.24	15.83	7.01	6.21	5.80	4.83	3.82	3.63	3.76	3.76
2c	4.24	15.79	7.01	6.20	5.80	4.83	3.82	3.63	3.75	3.76
2d	4.24	15.66	6.99	6.19	5.80	4.83	3.81	3.63	3.71	3.75
2e	4.23	15.55	6.99	6.18	5.80	4.83	3.83	3.63	3.72	3.75
2f	4.37	16.43	7.04	6.23	5.79	4.83	3.81	3.65	3.75	3.77
2g	4.21	15.78	7.00	6.20	5.78	4.80	3.82	3.63	3.73	3.76
2h	4.23	15.71	7.01	6.20	5.78	4.80	3.82	3.63	3.73	3.76
2i	4.21	15.33	6.99	6.18	5.79	4.79	3.84	3.62	3.71	3.75
2j	4.23	15.49	6.99	6.18	5.79	4.81	3.83	3.63	3.72	3.75
2k	4.27	15.58	6.99	6.19	5.80	4.82	3.82	3.63	3.71	3.75

[a]Hz.

Table 6. ^{13}C Chemical Shift Values (δ) of Substituted Dihydroindoles **2** in Chloroform-*d* (0.1 M)

	CH$_2$	2-C	3-C	3a-C	4-C	5-C	6-C	7-C	7a-C
2a	48.75	151.71	104.33	55.48	126.79	131.05	125.57	123.66	68.39
2b	48.75	152.07	103.31	55.44	126.70	130.98	125.06	123.95	68.13
2c	48.81	152.08	103.27	55.45	126.70	130.97	125.04	123.97	68.11
2d	49.31	152.47	102.62	55.40	126.69	130.90	124.70	124.26	67.78
2e	49.30	152.56	102.39	55.38	126.68	130.91	124.67	124.26	67.81
2f	48.88	151.77	104.37	55.42	126.83	130.99	125.62	123.57	68.28
2g	48.88	152.19	103.32	55.36	126.74	130.93	125.12	123.94	67.90
2h	48.81	152.22	103.25	55.35	126.72	130.95	125.10	123.96	67.89
2i	48.92	152.53	102.50	55.31	126.70	130.93	124.76	124.30	67.65
2j	49.15	152.57	102.44	55.33	126.70	130.93	124.74	124.26	67.71
2k	49.41	152.50	102.64	55.37	126.71	130.93	124.81	124.20	67.85

Table 7. ^{13}C Chemical Shift Values (δ) of the Ester Groups in Substituted Dihydroindoles **2** in Chloroform-*d* (0.1 M)

	2-CO	3-CO	3a-CO	4-CO	2-OMe	3-OMe	3a-OMe	4-OMe
2a	164.00	163.22	174.20	166.13	53.12	51.27	53.32	52.04
2b	164.12	163.31	174.46	166.24	53.06	51.15	53.22	52.00
2c	164.24	163.43	174.57	166.33	53.05	51.06	53.06	51.96
2d	164.26	163.46	174.63	166.36	53.01	51.05	53.05	51.96
2e	164.00	163.19	174.04	166.14	53.14	51.29	53.29	52.05
2f	164.12	163.30	174.45	166.24	53.07	51.15	53.26	52.00
2g	164.12	163.35	174.29	166.24	53.06	51.15	53.17	51.99
2h	164.14	163.36	174.32	166.26	53.06	51.15	53.17	52.00
2i	164.26	163.50	174.54	166.35	53.03	51.06	53.09	51.96
2j	164.27	163.46	174.58	166.36	53.01	51.05	53.08	51.96
2k	164.24	163.44	174.53	166.34	53.02	51.08	53.09	51.97

Table 8. ^{1}H Chemical Shift Values (δ) of Substituted Indoles **3** in Chloroform-*d* (0.1 M)

	CH$_2$	5-H	6-H	7-H	2-OMe	3-OMe	4-OMe
3a	5.87	7.92	7.41	7.52	3.90	3.94	4.00
3b	5.75	7.89	7.38	7.51	3.89	3.93	3.99
3c	5.76	7.89	7.38	7.51	3.89	3.93	3.99
3d	5.76	7.87	7.35	7.54	3.89	3.92	3.98
3e	5.75	7.87	7.35	7.54	3.89	3.93	3.99
3h	5.75	7.89	7.37	7.51	3.88	3.93	3.99
3i	5.72	7.86	7.36	7.57	3.89	3.92	3.98
3j	5.75	7.86	7.35	7.55	3.88	3.92	3.98
3k	5.79	7.87	7.35	7.54	3.88	3.93	3.98

Table 9. ^{13}C Chemical Shift Values (δ) of Substituted Indoles **3** in Chloroform-*d* (0.1 M)

	CH$_2$	2-C	3-C	3a-C	4-C	5-C	6-C	7-C	7a-C
3a	47.78	127.30	117.41	121.72	124.63	125.72	125.53	114.97	138.33
3b	47.81	127.64	116.92	121.62	124.47	125.51	125.22	115.29	138.38
3c	47.88	127.64	116.92	121.62	124.47	125.51	125.21	115.30	138.38
3d	48.32	128.07	116.53	121.57	124.38	124.94	125.32	115.56	138.48
3e	48.40	128.12	116.36	121.57	124.36	125.28	124.89	115.62	138.48
3h	47.78	127.69	116.84	121.61	124.47	125.46	125.14	115.30	138.35
3i	47.88	128.14	116.33	121.59	124.42	125.23	124.84	115.57	138.37
3j	48.17	128.11	116.36	121.55	124.34	125.26	124.86	115.59	138.42
3k	48.37	128.05	116.52	121.57	124.39	125.31	124.93	115.54	138.44

Table 10. ^{13}C Chemical Shift Values (δ) of the Ester Groups in Substituted Indoles **3** in Chloroform-*d* (0.1 M)

	2-CO	3-CO	4-CO	2-OMe	3-OMe	4-OMe
3a	166.60	161.18	166.68	52.43	52.76	52.16
3b	166.70	161.19	166.82	52.37	52.67	52.10
3c	166.71	161.19	166.82	52.37	52.67	52.10
3d	166.77	161.29	166.96	52.31	52.60	52.05
3e	166.82	161.31	167.01	52.32	52.59	52.06
3h	166.70	161.21	166.84	52.36	52.65	52.10
3i	166.77	161.36	167.01	52.29	52.60	52.04
3j	166.81	161.30	167.00	52.30	52.59	52.04
3k	166.77	161.28	166.96	52.31	52.59	52.05

Table 11. ^{1}H Chemical Shift Values (δ) of Phenyl Protons in Substituted Dihydroindoles **2** and Indoles **3** in Chloroform-*d* (0.1 M)

	2'-H	3'-H	4'-H	5'-H	6'-H	Me
2a	8.10		8.17	7.54	7.63	
3a	8.08		8.10	7.43	7.28	
2b	7.37		7.43	7.22	7.21	
3b	7.26		6.90	7.12	7.37	
2c	7.22		7.26	7.14	7.26	
3c	7.08		7.17	7.20	6.88	
2d	6.80		6.83	7.24	6.83	3.63
3d	6.60		6.59	7.17	6.76	3.71
2e	7.04		7.10	7.23	7.03	2.34
3e	6.87		7.03	7.14	6.81	2.26
2f	7.44	8.20				
3f	*a*					
2g	7.13	7.47				
3g	*a*					
2h	7.31	7.18				
3h	7.23	6.97				
2i	7.16	6.86				3.62
3i	7.00	6.79				3.74
2j	7.12	7.14				2.33
3j	7.06	6.93				2.28
2k	7.26	7.33	7.33			
3k	7.03	7.24	7.25			

^{a}Not prepared (see text).

Table 12. ^{13}C Chemical Shift Values (δ) of the Carbons in Substituted Benzyl Groups in Dihydroindoles **2** and Indoles **3** in Chloroform-*d* (0.1 M)

	1'-C	2'-C	3'-C	4'-C	5'-C	6'-C	CH$_3$
2a	138.39	122.50	148.49	123.20	129.93	133.60	
3a	139.11	121.52	148.50	122.78	129.95	132.26	
2b	138.16	131.32	122.90	130.41	130.66	126.25	
3b	139.17	130.39	122.91	129.31	130.84	124.80	
2c	137.90	128.38	134.77	127.73	130.13	125.78	
3c	138.93	127.89	134.75	126.41	130.11	124.47	
2d	137.14	113.93	160.08	112.94	129.83	119.88	55.26
3d	138.47	112.64	159.93	112.24	129.86	118.44	55.17
2e	135.43	128.39	138.58	128.91	128.73	124.78	21.40
3e	136.77	128.65	138.52	126.80	128.40	123.26	21.42
2f	147.76	128.39	123.57	143.54			
3f	*a*						
2g	134.73	129.41	131.95	122.14			
3g	*a*						
2h	134.19	129.00	129.10	134.04			
3h	135.38	128.95	127.60	133.45			
2i	129.13	127.34	114.20	159.48			55.31
3i	128.90	127.64	114.14	159.04			55.25
2j	137.95	127.72	129.51	132.35			21.13
3j	137.29	126.15	129.42	133.81			21.04
2k	135.53	127.76	128.84	128.18			
3k	136.85	126.18	128.77	127.59			

^{a}Not prepared (see text).

(NMR) spectra were recorded on a Bruker DPX-400 FT NMR spectrometer in the Central Lab of Kangwon National University with chloroform-d as the solvent at 400 MHz for ^{1}H and 100 MHz for ^{13}C and were referenced to tetramethyl-silane. The concentration of the solution was 0.10 M. Electron-impact mass spectra (MS) were obtained using an Automass M363 mass spectrometer.

Starting Materials. 1-Benzylpyrroles (**1**) were prepared by the reaction of 2,5-dimethoxytetrahydrofuran and the corresponding benzylamines as reported.[6]

An Illustrative Procedure for Preparation of 2. A mixture of **1** (10 mmoles) and DMAD (22 mmoles) was placed in a v-vial (5 mL) and stirred at 50 °C for 48 h. The mixture was chromatographed on a column of silica gel with hexane-ethyl acetate (4 : 1). The eluents were evaporated and the residue was recrystallized from methanol. The yields and mp: **2a**: 63%, 65 °C (dec.); **2b**: 20%, 107 °C; **2c**: 42%, 100-101 °C; **2d**: 78%, 79 °C (dec); **2e**: 20%, 107 °C; **2f**: 63%, 177-178 °C; **2g**: 57%, 137 °C; **2h**: 42%, 157-158 °C; **2i**: 13%, 114 °C; **2j**: 72%, 143-144 °C; **2k**: 49%, 137 °C.

An Illustrative Procedure for Preparation of 3. A solution of **2** (2 mmoles) in methanol (25 mL) was cooled in an ice-water bath and bromine (0.16 mL, 3 mmoles) was added. The solution was gradually brought to room temperature and stirred for 2 h. The solvent was removed by evaporation and the residue was recrystallized from methanol. The yield and mp: **3a**: 54%, 185-187 °C; **3b**: 5%, 115 °C; **3c**: 68%, 103 °C; **3d**: 23%, 67 °C; **3e**: 31%, 97 °C; **3h**: 51%, 147-148 °C; **3i**: 26%, semi-solid; **3j**: 31%, 109 °C; **3k**: 61%, 117 °C.

Tetramethyl 6,7-Dibromo-3a,7a-dihydro-1-(*p*-nitrobenzyl)indole-2,3,3a,4-tetracarboxylate (4). The dihydroindole **2f** (0.1584 g, 0.33 mmole) was dissolved in dried methanol (20 mL) by stirring for 2 h. The solution was cooled in an ice-water bath and bromine (0.026 mL, 0.51 mmole) was added. The solution was stirred in the bath for 1 h and then at room temperature for an additional hour. After the solvent was evaporated the residue was recrystallized from methanol to give **4** (60%): mp 175 °C: ^{1}H-NMR δ 3.49, 3.62, 3.76, 3.88 all s, 3H, COOCH$_3$; 4.31 d, 1H, 7a-H, J = 9.51 Hz; an AB pattern centered at 4.48 and 4.80 2H, J = 15.85 Hz; 4.63 dd, 1H, 7-H, J = 9.50 and 3.50 Hz; 4.84 dd, 1H, 6-H, J = 5.72 and 3.60 Hz; 6.98 d, 1H, 5-H, J = 5.72 Hz; 7.49 d, 2H, 2'- and 6'-H J = 8.55 Hz; 8.23 d, 2H, 3'- and 5'-H, J = 8.55 Hz: ^{13}C-NMR ppm 47.67 (6-C), 49.52 (7-C), 51.50 (OCH$_3$), 51.80 (CH$_2$), 52.53 (OCH$_3$), 53.28 (OCH$_3$), 53.35 (OCH$_3$),

59.08 (3a-C), 68.68 (7a-C), 103.55 (3-C), 124.01 (3',5'-C), 129.46 (2',6'-C), 129.89 (4-C), 135.95 (5-C), 143.04 (1'-C), 147.87 (4'-C), 151.64 (2-C), 162.64 (CO), 163.38 (CO), 165.91 (CO), 172.15 (3a-CO): MS, m/z (%) 648 (6, M$^+$ + 4), 646 (12, M$^+$ + 2), 644 (6, M$^+$), 617 (4) 615 (8) and 613 (4, all M$^+$ - OCH$_3$), 589 (52) 587 (100) and 585 (51, all M$^+$ - COOCH$_3$), 567 (11) and 565 (11, all M$^+$ - Br), 557 (26) 555 (51) and 553 (26, all M$^+$ - COOCH$_3$ - HOCH$_3$), 535 (18) and 533 (17, all M$^+$ - OCH$_3$ - HBr), 486 (65, M$^+$ - 2 Br), 475 (72) and 473 (72, all M$^+$ - HBr - COOCH$_3$, HOCH$_3$), 455 (56, M$^+$ - 2 Br - OCH$_3$), 427 (22), 426 (24), 260 (26), 228 (22), 136 (37), 106 (100). Anal. Calcd for C$_{27}$H$_{22}$Br$_2$N$_2$O$_{10}$ (646.25): C, 42.75; H, 3.43; Br, 24.73; N, 4.33. Obs: C, 42.66; H, 3.54; Br,24.52; N, 4.35.

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