[Chem. Pharm. Bull.
15(7)1010~1014(1967)]

UDC 547.756.07

125. Takayuki Shioiri, Kikuo Ishizumi, and Shun-ichi Yamada: Studies in the Indole Series. III.[*1] Steric Inhibition of Resonance in Cycloalkan[*b*]indolones.

(*Faculty of Pharmaceutical Sciences, University of Tokyo*[*2])

The ultraviolet, infrared and nuclear magnetic resonance spectra of cycloalkan[*b*]indolones have been investigated.

Steric inhibition of resonance is accompanied by a bathochromic and hypochromic shift in the ultraviolet spectra. It was found that the carbonyl stretching frequency of cycloalkan[*b*]indolones increased as increasing ring size. The nuclear magnetic resonance spectra also showed ring size effect.

(Received October 24, 1966)

Recent developments of organic chemistry have clarified two important factors, polar and steric factors, of which the latter often play a conspicuous role in physical properties of organic compounds. The influence of steric factors on the resonance contribution is generally called "steric inhibition of resonance." There are many studies[1] where steric inhibition of resonance has been proposed to explain the reduction in ultraviolet spectral absorption, changes in dipole moment, and various physical properties. However, most of the studies have dealt with aromatic compounds. Less attention has been paid to steric inhibition of resonance in heteroaromatic compounds.

In the preceding paper,[*1] a general synthetic method of cycloalkan[*b*]indolones (I and II) has been established from 3-indolealkanoic acids. Now we wish to investigate the steric inhibition of resonance in various cycloalkan[*b*]indolones (I and II) obtained by us.

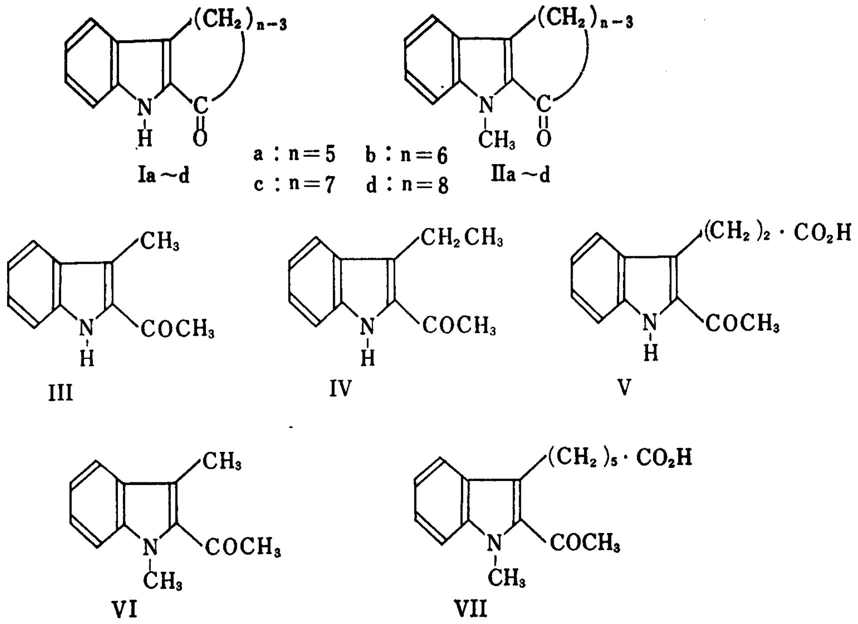


Chart 1.

[*1] Part II. This Bulletin, 15, 863 (1967).

[*2] Hongo, Tokyo (塩入孝之, 石墨紀久夫, 山田俊一).

1) *a*) B.M. Wepster: "Progress in Stereochemistry," Ed. by W. Klyne, P. de la Mare, Vol. 2, 99 (1958), Butterworth Scientific Pub., London. *b*) L.L. Ingraham: "Steric Effects in Organic Chemistry," Ed. by M.S. Newman, 479 (1956), John Wiley & Sons, Inc., New York.

I. Discussion on Ultraviolet Spectra

The ultraviolet spectra of some cyclic compounds[2] provide considerable information of steric inhibition of resonance as a function of the ring size of the cyclic portions. In cyclic aromatic ketones, steric inhibition of resonance is caused by non-planarity between the aromatic nucleus and the carbonyl group, and in normal and medium-sized rings it increases as the ring size becomes larger. The forces keeping the oxygen atom out of the plane of the aromatic ring are of the same nature as those causing strain in medium-sized rings, viz. bond-opposition forces and *cis*-butane interactions. Non-planarity generally reduces the intensities of ultraviolet absorption and changes the wavelength of absorption depending on variation of the double bond character (bond order) of an essential[*3] single bond on excitation.

Cycloalkan[*b*]indolones (I and Ⅱ) have two transition bands of high intensities ($\varepsilon >$ 10,000) near 237 and 310 mμ as shown in Table I.

Table I. Ultraviolet Spectra of Cycloalkan[*b*]indolones

	Ring size	Compound	Primary band			Secondary band			
			λ_{max} (mμ)	$\varepsilon \times 10^{-3}$	f	λ_{max} (mμ)	$\varepsilon \times 10^{-3}$	f	θ (deg.)
N-H Series	5	Ia	233	22.4	0.507	300.5	29.9	0.406	0°
	6	Ib	237	16.5	0.222	309	23.0	0.374	29°
	7	Ic	238	12.8	0.221	312.5	19.0	0.329	37°
	8	Id	238	9.97	0.207	314.5	16.7	0.271	42°
		Ⅲ	237	17.5		312	23.6		27°
		Ⅳ[*1]	238	15.9		314	20.0		35°
		Ⅴ	236	13.6		313	17.3		40°
N-Me Series	5	Ⅱa	236	28.0	0.603	301.5	31.9	0.416	0°
	6	Ⅱb	238	20.6	0.385	310	23.8	0.326	30°
	7	Ⅱc	239	16.7	0.264	310.5	19.9	0.307	38°
	8	Ⅱd	239	13.6	0.215	313	17.1	0.258	43°
		Ⅵ	239	16.5		309	19.6		38°
		Ⅶ	238	15.4		311	16.9		43°

[*1] Measured in 95% aq. EtOH by E. Leete (J. Am. Chem. Soc., **83**, 3645 (1961)).

Both absorption bands are displaced to slightly longer wavelengths with increasing ring size. A reasonable explanation of the shift might be as follows : In cycloalkan[*b*]-indolones, the bond order of the essential single bond in the ground state decreases on excitation. As steric strain is relieved by twisting around this essential single bond, the sterically more hindered compound such as an eight-membered one shows a more bathochromic shift relative to the less hindered one such as a five-membered one. Heilbronner, *et al.*[3] have discussed the similar spectral properties of 1-acylazulene derivatives on the basis of the molecular orbital calculations.

The usual decrease in the absorption intensity was observed with increasing the steric hindrance. It is possible to estimate the angle by which the carbonyl oxygen is forced out of coplanarity with the indole ring, assuming the usual $\cos^2\theta$ relationship.[4]

[*3] A single bond is called "essential" if it is single in all principal resonance structures which do not involve long bonds or formal charges. A single bond between the aromatic nucleus and the carbonyl group is essential. cf. H.C. Longuet-Higgins : J. Chem. Phys., **18**, 265 (1950).

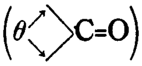
2) *a*) H.H. Jaffe, M. Orchin : "Theory and Applications of Ultraviolet Spectroscopy," 384 (1962), John Wiley & Sons., Inc., New York. *b*) R. Huisgen : Angew. Chem., **69**, 341 (1957).

3) E. Heilbronner, R. Gerdil : Helv. Chim. Acta, **39**, 1996 (1956).

4) E.A. Braude : Experientia, **11**, 457 (1955).

Although there are some criticisms[5] against the $\cos^2\theta$ relationship, it has been widely used to calculate angles of twist. The common procedure is to employ the main band in the ultraviolet spectrum and to calculate the angle of twist θ from the expression, $\varepsilon/\varepsilon_0=\cos^2\theta$, where ε is the molar extinction coefficient of the partially twisted compound, and ε_0 is the corresponding value for the unhindered homolog and hence assumed to be planar ($\theta=0°$). In this case Ia and IIa are supposed to be planar. The results are summarized in Table I accompanied with values of the oscillator strength f.[*4] It is very interesting to note that the carbonyl group of acyclic 2-acylindole derivatives (III~VII) is also twisted out of the plane.

II. Discussion on Infrared Spectra

It is well known that the carbonyl stretching absorption band for cyclic ketones varies with ring size.[6] This observation has been used extensively especially for the differentiation between carbonyl groups associated with five and six-membered ring systems. Such ring strain effects depend on the change in the carbonyl force constant as a result of rehybridization in the orbitals of the carbonyl carbon. The higher stretching frequency (higher force constant) of the carbonyl group in cyclopentanone than in cyclohexanone is attributed to a larger amount of s-character in the σ-bonds of the carbonyl group of cyclopentanone resulting from the constraining of the angle θ  to a value less than 120°.

Besides this, in cyclic aromatic ketones, steric inhibition of resonance between the aromatic nucleus and the carbonyl group affects the carbonyl stretching vibration. Steric inhibition of aryl-carbonyl conjugation, which increases with increasing ring size, results in a displacement toward higher frequency.

Of these two opposing features of ring effects, the former predominates in most benzocyclanones,[7,8] and as the size of the ring is larger, the frequency of the carbonyl

Table II. Infrared Spectra of Cycloalkan[*b*]indolones

	Ring size	Compound	ν_{N-H} (cm^{-1})		$\nu_{C=O}$ (cm^{-1})		$\delta_{arom.}$ (cm^{-1}) in Nujol
			in $CHCl_3$	in Nujol	in $CHCl_3$	in Nujol	
N-H Series	5	Ia	3460	3186	1679	1658	744
	6	Ib	3456	3320	1656, 1651	1641	748, 733
	7	Ic	3453	3284	1630	1640	741, 728
	8	Id	3451	3260	1637	1630	739
		III	3453	3343	1642	1633	739
		IV[*1]		3330		1632	
		V	3446	3273	1730, 1643	1724	747
N-Me Series	5	IIa			1675	1669	740
	6	IIb			1655, 1650	1670, 1640	738
	7	IIc			1643.5	1659	737
	8	IId			1642.5	1644	735
		VI			1650	1643	735
		VII			1713, 1648	1695, 1645	744

[*1] Measured in KBr by E. Leete (J. Am. Chem. Soc., **83**, 3645 (1961)).

[*4] The oscillator strength f was calculated from the equation, $f=4.32\times10^{-9}\int\varepsilon(\nu)\,d\nu$. cf. H. Baba: "Jikken Kagaku Koza," Vol. 3, 386 (1957), Maruzen & Co., Tokyo.

5) For example; N.L. Allinger, E.S. Jones: J. Org. Chem., **30**, 2165 (1965).

6) R.N. Jones, C. Sandorfy: "Chemical Applications of Spectroscopy," Ed. by W. West, 443 (1956), Interscience, New York.

7) W.M. Schubert, W.A. Sweeny: J. Am. Chem. Soc., **77**, 4172 (1955).

8) R. Huisgen, G. Seidl, I. Wimmer: Ann., **677**, 21 (1964).

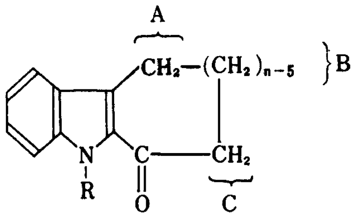
group is lower. The dependence of the carbonyl bands in I and II on the ring size is parallel to that of benzocyclanones as shown in Table II. The lower carbonyl frequency of 2-acylindole derivatives (*ca.* 1650 cm^{-1}) than that of alkyl aryl ketones (*ca.* 1690 cm^{-1})[9] strongly suggests that the former are a kind of vinylogous amides similar to 3-acylindoles.[10] This contributed to the assignment of the two carbonyl band in 2,5-diacetylindole derivatives.*1

A doubling of the carbonyl peak has been noted in the spectra of six-membered ketones (Ib in chloroform, IIb in chloroform and nujol). The nature of the lower frequency band could be attributed to a vibrational coupling of the normal carbonyl stretching vibration with an overtone of a low lying vibration; the effect is occasionally observed in the spectra of five-membered carbonyl compounds.[6]

III. Discussion on Nuclear Magnetic Resonance Spectra

The nuclear magnetic resonance spectra of cycloalkan[*b*]indolones (I and II) also exhibit ring size effect. The spectra of N-unsubstituted series (I) and N-methyl series (II) are quite similar to each other as shown in Table III.

Table III. Nuclear Magnetic Resonance Spectra of Cycloalkan[*b*]indolones



	Ring size	Compound	N-CH_3 (3H, singlet) τ	A-protons (2H, triplet) τ	A-protons (2H, triplet) J (c.p.s.)	B-protons (multiplet) τ	C-protons (2H, triplet) τ	C-protons (2H, triplet) J (c.p.s.)
N-H Series	5	Ia				6.94		
	6	Ib		6.98	6.0	7.74	7.32	6.0
	7	Ic		6.86	6.2	7.97	7.16	6.2
	8	Id		6.70	7.0	8.24, 8.48	6.98	7.0
N-Me Series	5	IIa	6.13			7.03		
	6	IIb	5.94	6.98	6.0	7.79	7.35	6.0
	7	IIc	5.98	6.91	6.2	8.09	7.19	6.2
	8	IId	5.93	6.67	7.0	8.16, 8.50	6.98	7.0

Ring protons on cyclanone portions may be divided into three parts A, B and C from their spectra. The five-membered ketones (Ia and IIa), which were presumed to be maximum delocalization of electrons from ultraviolet spectral data, show abnormal patterns in comparison with the other cyclic ketones. In the other ketones, A and C part methylene protons shift to lower field with increasing ring size. This change is parallel to that of simple cyclic ketones; cyclopentanone (7.98τ)→cyclohexanone (7.75τ) →cycloheptanone (7.58τ).[11] On the other hand, it is of interest that B part methylene protons shift higher with increasing ring size. Since A and C part protons show two-proton triplets ($J=6\sim7$ c.p.s.), the two geminal protons on the carbon of A or C part seem to be equivalent owing to rapid inversion of alicyclic portions.

---

9) L. J. Bellamy : "The Infra-red Spectra of Complex Molecules," 132 (1958), Methuen & Co., Ltd. (London).

10) D. R. Liliegren, K. T. Potts : J. Org. Chem., **27**, 377 (1962).

11) L. M. Jackman : "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 57 (1959), Pergamon Press, Ltd., London.

The N-methyl group of II except IIa shows three-proton singlet about 0.3 p.p.m. lower than that of the N-methylindole derivatives which have not a 2-acyl group. This fact could be used to differentiate 2-acylindoles from 2-unsubstituted or 2-alkylindoles.

A comprehensive analysis of the nuclear magnetic resonance spectra in cyclic ketones would be accomplished after the more accumulated data about them.

Experimental

Materials——All materials examined were prepared by methods in the preceding paper.[*1]

Ultraviolet Spectra——The UV Spectra were taken in 90% aq. EtOH solution on a Cary Model 11 spectrophotometer. The wavelengths are expressed in mμ.

Infrared Spectra——The IR spectra were taken in $CHCl_3$ or nujol on a Koken Model DS-402G spectrophotometer. To obtain an accurate value for the carbonyl frequency, dilute $CHCl_3$ solution was used so that the intensity of the carbonyl band was about 50 to 80%. The curve was calibrated for each sample by tracing a polystyrene spectrum on the same paper, both curves being traced at a very slow speed.

Nuclear Magnetic Resonance Spectra——The NMR spectra were taken at 100 Mc. on a Varian HR-100 high resolution NMR spectrometer. The spectra were observed in 2.5~3.8 w/v% $CDCl_3$ solution containing tetramethylsilane as an internal reference at room temperature.

The authors are grateful to Dr. T. Hino and Miss Y. Shibanuma of the Institute of Radiological Sciences for NMR spectra. They are also indebted to the members of the Central Analysis Room of this Faculty for infrared and ultraviolet spectral data.