CHEMICAL PECULIARITIES AND STRUCTURE OF 2-(INDANE-1', 3'-DIONID-2'-YL)PYRIDINIUM (α-PYROPHTHALONE)

A. A. Kemme, M. F. Bundule,
Ya. Ya. Bleidelis, É. É. Liepin'sh,
É. S. Lavrinovich, and Yu. É. Fridmanis

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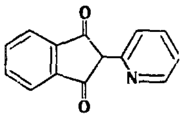
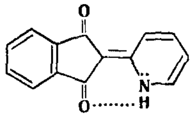
The fine structure of 2-(indane-1',3'-dionid-2'-yl)pyridinium (α-pyrophthalone) was determined by PMR spectroscopy and x-ray diffraction analysis. The α-pyrophthalone molecule is almost planar; the dihedral angle between the pyridine ring and the indanedione ring is 5°. The structure is stabilized by an intramolecular hydrogen bond with a length of 2.73 Å. The molecules are packed in the crystal at van der Waals distances similar to those in molecular self-complexes. The data obtained for α-pyrophthalone confirm a dipolar ion structure.

In contrast to the isomeric 2-(N-pyridinia)indane-1,3-dione, which is readily reduced by sodium borohydride [1], α-pyrophthalone (I) is absolutely inert with respect to reduction by complex metal hydrides. Compound I was reduced to the monoketone only by the action of zinc dust in an alkaline medium.

The lack of an unambiguous concept regarding the fine structure of I hinders the interpretation of the reactions of I. Of the set of possible structures for α-pyrophthalone, preference has been expressed for pyridine enol [2-4], intraionic [5, 6], or dihydropyridine (Ia) structures; in the opinion of Kuhn and Bär [7], and Amiel and co-workers [8], the latter is in equilibrium with the intraionic structure (Ib).


I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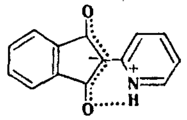
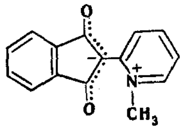

Ib

On the basis of a study of the electronic absorption spectra and theoretical calculations by the Hückel MO LCAO method it has been concluded [6] that the only structure that explains the chemical peculiarities of I (the markedly reduced reactivity of the carbonyl groups, the high dipole moment of the molecule, the low solubility, and the high melting point) is dipolar ion structure Ib.

To establish the fine structure of α-pyrophthalone more precisely we recorded the PMR spectra of I and its methyl derivatives (III and IV) and subjected I to x-ray diffraction analysis.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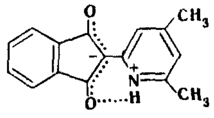
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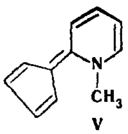
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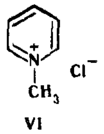
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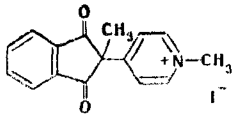
VII

Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga 226006.
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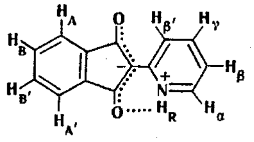
TABLE 1. Parameters of the PMR Spectra of α-Pyrophthalone and Its Methyl Derivatives



Compound	Chemical shifts, δ, ppm							SSCC, J, Hz					
	H_A	H_B	H_α	H_β	H_γ	H_β	H_R	α—β	α—γ	α—β′	β—γ	β—β′	γ—β′
I	7,59	7,47	7,82	6,89	7,72	8,56	9,4	6,4	1,2	0,6	6,4	1,2	9,0
III	7,67	7,50	7,94	7,11	7,82	8,01	4,19	6,7	1,5	0,5	6,9	1,5	8,5
IV	7,48	7,48	2,52	6,31	2,38	8,06	14,4	—	—	—	—	1,5	—

The data from the PMR spectra are presented in Table 1.

It is apparent from the data in Table 1 that the spin—spin coupling constants (SSCC) of I and III differ little from the values in the spectra of 1-methyl-2-(1'-cyclopentadienylidene)-1,2-dihydropyridine (V) ($J_{\alpha\beta}$ = 6.74 Hz, $J_{\alpha\gamma}$ = 1.47 Hz, $J_{\alpha\beta'}$ = 0.76 Hz, $J_{\beta\gamma}$ = 6.61, $J_{\beta\beta'}$ = 1.43, and $J_{\gamma\beta'}$ = 9.27 Hz) [9], which is a model compound for structure Ia. On the other hand, the $J_{\alpha\beta}$ values for I, III, and V are extremely close to the values of methylpyridinium chloride (VI) ($J_{\alpha\beta}$ = 6.4 Hz), which is an analog of structure Ib. The phthaloyl protons in I, III, and IV are considerably more shielded than those in the model compound, 4-(2'-methylindane-1',3'-dionid-2'-yl)pyridine methiodide (VII) (δ_A and δ_B = 8.11 ppm). This constitutes evidence for localization of the negative charge in the indanedione fragments of the I, III, and IV molecules, i.e., for a substantial contribution by the Ib form.

The shift of the resonance of the $H_{\beta'}$ protons to a weaker field as compared with the chemical shift of the resonance of the H_β protons in I, III, and IV is due to coupling of the $H_{\beta'}$ protons with the oxygen atoms of the carbonyl group in direct proximity. The introduction of a CH_3 group at the nitrogen atom (III) gives rise to a considerable diamagnetic shift of the resonance of the $H_{\beta'}$ protons and a paramagnetic shift of the H_β protons. This is explained by disruption of the coplanarity of the III molecule; the effect of the anisotropy of the carbonyl group on $H_{\beta'}$ is weakened in this case, and this causes the observed strong-field shift. Disruption of the coplanarity of the molecule leads to a decrease in the contribution of the indanedione substituent to the shielding of all of the protons of the pyridine ring; this is in agreement with their weak-field shift in the PMR spectra. The difference in the chemical shifts for the H_R proton in I and IV is evidently due to the great strength of the intramolecular $\overset{\oplus}{N}$—H...O=C hydrogen bond in IV. The protons of the benzene ring (H_A, $H_{A'}$, H_B, and $H_{B'}$) form a singlet that is affiliated with a symmetrical AA'BB' system; this excludes structure Ia for α-pyrophthalone. Thus from the PMR data, formula Ib is in better agreement with the real state of α-pyrophthalone in solution.

It was established by x-ray diffraction analysis that 2-(indane-1',3'-dionid-2'-yl)-pyridinium crystallizes in monoclinic syngony. The principal crystallographic data for $C_{14}H_9NO_2$ are as follows: a = 6.918(1) Å, b = 14.004(2) Å, c = 10.755(1) Å, β = 91.43(1)°, V = 1041.6(3) Å^3, M = 223.23, Z = 4, and d_{calc} = 1.42 g·cm^{-3}, and symmetry space group $P2_1/a$.

The coordinates of the atoms and the temperature factors are presented in Table 2. The bond lengths and valence angles are given in Fig. 1. The accuracy in the determination of the interatomic distances and the valence angles does not exceed ±0.008 Å and ±0.5°.

The six-membered fragment of the indane ring of the molecule and the pyridine ring are strictly planar, since the deviations of the individual atoms that form them from the average planes do not exceed 0.005 and 0.009 Å, respectively. The deviations of the atoms from the average plane of the five-membered ring are an order of magnitude larger (the reach 0.02 Å). The planarity of the molecule as a whole is disrupted by slight bending of the indane ring of the molecule along the C(8')—C(9') bond (the dihedral angle is ∿2°) and the small degree of deflection of the pyridine ring along the C(2)—C(2') bond with respect to the indane ring (the angle between them is on the order of 5°).

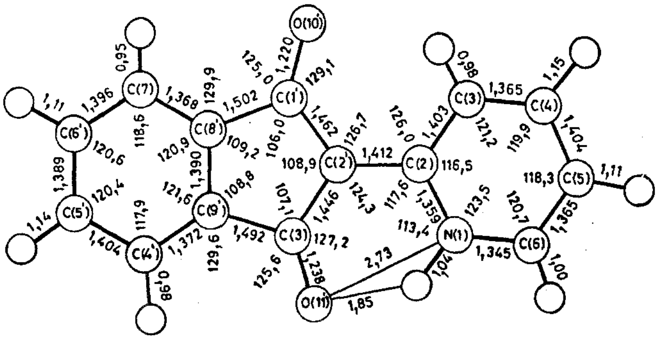


Fig. 1. Bond lengths and valence angles in the 2-(indane-1',3'-dionid-2'-yl)pyridinium molecule.

TABLE 2. Coordinates of the Atoms and Temperature Factors*

Atom	X	Y	Z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
010′	1,2054(5)	0,0937(3)	0,2424(4)	3,0(2)	4,5(2)	2,3(2)	−0,4(2)	1,1(2)	−0,5(2)
011′	0,6813(5)	0,0737(3)	0,5145(3)	2,6(2)	3,7(2)	2,3(2)	−0,6(2)	0,8(2)	−0,8(2)
N1	0,6211(6)	−0,0233(3)	0,2973(4)	2,6(2)	2,7(2)	1,8(2)	−0,2(2)	0,2(2)	−0,6(2)
C2	0,8017(7)	0,0036(4)	0,2648(5)	2,7(3)	1,7(2)	1,9(3)	0,2(2)	0,1(2)	0,1(2)
C3	0,8620(8)	−0,0260(4)	0,1473(5)	3,1(3)	3,2(3)	2,1(3)	−0,5(2)	0,6(2)	−0,5(2)
C4	0,7429(9)	−0,0776(4)	0,0697(5)	4,6(3)	3,5(3)	2,1(3)	−0,4(3)	0,3(3)	−0,5(3)
C5	0,5572(8)	−0,1031(4)	0,1079(5)	4,0(3)	3,5(3)	2,5(3)	−0,9(3)	−0,5(3)	−0,4(3)
C6	0,5009(8)	−0,0742(4)	0,2227(6)	3,2(3)	3,2(3)	3,0(3)	−0,5(2)	0,2(3)	−0,4(3)
C1′	1,1005(8)	0,1017(4)	0,3313(5)	2,6(3)	2,2(3)	2,3(3)	0,4(2)	−0,0(2)	0,2(2)
C2′	0,9088(7)	0,0609(4)	0,3497(5)	2,4(3)	2,3(2)	1,6(3)	0,3(2)	0,0(2)	−0,0(2)
C3′	0,8382(8)	0,0934(4)	0,4678(5)	2,7(3)	2,1(3)	1,9(3)	0,3(2)	−0,1(2)	0,1(2)
C4′	0,9899(8)	0,2070(4)	0,6338(5)	3,4(3)	2,7(3)	2,5(3)	−0,5(2)	0,4(2)	−0,3(2)
C5′	1,1551(9)	0,2606(4)	0,6660(5)	4,8(3)	3,1(3)	2,3(3)	−0,7(3)	0,0(3)	−0,4(2)
C6′	1,3132(8)	0,2615(4)	0,5890(6)	3,7(3)	2,9(3)	3,5(3)	−0,8(2)	−1,1(3)	0,0(3)
C7′	1,3088(7)	0,2110(4)	0,4769(5)	2,4(3)	2,9(3)	2,9(3)	−0,0(2)	0,2(2)	0,3(3)
C8′	1,1468(7)	0,1594(4)	0,4459(5)	2,5(3)	1,9(3)	2,0(3)	0,2(2)	−0,1(2)	0,3(2)
C9′	0,9902(7)	0,1566(4)	0,5243(5)	2,8(3)	1,8(2)	2,0(3)	−0,1(2)	−0,2(2)	0,0(2)
HN	0,587	−0,003	0,387	2,4					
HC3	0,999	−0,014	0,134	2,8					
HC4	0,784	−0,106	−0,027	3,4					
HC5	0,444	−0,131	0,042	3,3					
HC6	0,373	−0,092	0,256	3,1					
HC4′	0,868	0,212	0,678	2,8					
HC5′	1,146	0,308	0,752	3,5					
HC6′	1,447	0,299	0,618	3,4					
HC7′	1,420	0,207	0,426	2,9					

*The isotropic temperature factors are presented for the hydrogen atoms.

The structure is stabilized by an N(1)—H...O(11') intramolecular hydrogen bond with a length of 2.73 Å, which forms a six-membered ring with an extremely planar structure; the deviation of the individual atoms that form it from the average plane does not exceed 0.02 Å. The N(1)—H...O(11') bond is not linear; the valence angle with the hydrogen atom is 140°. The increase in the O(11')—C(3')—C(2') and C(1')—C(2')—C(2) valence angles to 127° and the decrease in the NH(1)—C(2) angle to 113° are evidently a consequence of the formation of an intramolecular hydrogen bond.

The geometry of the indane ring basically corresponds to the geometry in indane-1,3-dione [10], 2-(p-bromophenyl)indane-1,3-dione [11], bindone [12], and 2-pivaloylindane-1,3-dione [13]. The interatomic distances in the pyridine ring are very small (0.02 Å), and the valence angles differ, within the limits of 5°, from the angles in the pyridine [14] and pyridine hydrochloride [15] molecules.

A comparison of the structure of the I molecule with the structure of the identically composed 2-(N-pyridinia)indane-1,3-dione betaine molecule [16] shows that the corresponding interatomic distances in these molecules coincide within the limits of 0.02 Å. With respect to the angles, only the endocyclic valence angles at the nitrogen atoms (123.5 and 119.3°), which have a planar coordination in both molecules, differ (by 4°).

In the indane fragment of the I molecule the endocyclic valence angles at the C(4') and C(7') atoms are reduced (117.9 and 118.6°); this is similar to the decrease observed in molecules that contain an indane fragment [10,13, 16-18].

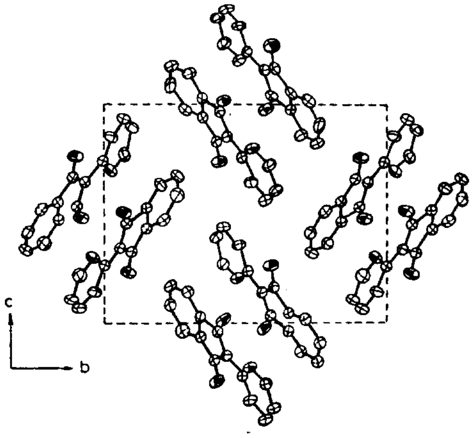


Fig. 2. Distance between the molecules in the unit cell of the crystal.

The C(1')—C(2') and C(2')—C(3') valence bonds have sesqui character; this indicates delocalization of the charge along the O⩦C⩦C⩦C⩦O atoms.

The interatomic C—H distances obtained from differential synthesis were not refined and range from 0.95 to 1.15 Å.

As shown in Fig. 2, the molecules are packed in the crystal at van der Waals distances similar to those in molecular self-complexes in which the donor fragment of one molecule is located above (under) the acceptor fragment of another molecule [19].

The data obtained in this study completely exclude the dihydropyridine structure Ia proposed in [8] for I and confirm the calculated structure of dipolar ion Ib, which is also in agreement with the chemical peculiarities of I.

EXPERIMENTAL

The PMR spectra of solutions of I, III, and IV in $CDCl_3$ were recorded with Bruker WH-90 and Perkin—Elmer R-12A spectrometers with tetramethylsilane as the internal standard.

α-Pyrophthalone (I) and 4,6-dimethyl-2-(indane-1',3'-dionid-2'-yl)pyridinium (IV) were obtained by the methods in [20, 21]. 1-Methyl-2-(indane-1',3'-dionid-2'-yl)pyridinium, with mp 224-225°C, was obtained by the method in [7].

The x-ray diffraction study was made with a $P2_1$ automatic diffractometer with a system for the determination of the XTL structure. A 0.15 ×0.17 × 0.25 mm crystal was used to measure the intensities of 1139 independent nonzero reflections by the θ/2θ scanning method with monochromatic copper emission (graphite monochromator) up to $\theta_{max} = 50°$. A total of 975 reflections with $1 \geqslant 1.96\sigma$ was used in the calculation.

A model of the molecule was found by a direct method from a MULTAN program [22]. A variant of the E synthesis that revealed the positions of all of the nonhydrogen atoms of the molecule gave R = 0.214. The model was refined by the method of least squares within a complete matrix anisotropic approximation for the nonhydrogen atoms with utilization of the coordinates of the hydrogen atoms determined from differential synthesis of the electron density distribution in the unit cell of the crystal. The B values for the hydrogen atoms were assumed to be equal to the B_{isotr} values of the nonhydrogen atoms bonded to them. The final R value was 0.059.

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THE STEREOCHEMISTRY OF THE PROTONATED FORMS OF HETEROCYCLIC BASES.

I. 1,2,3,4-TETRAHYDROBENZOFURO[3,2-c]PYRIDINES

S. G. Rozenberg, V. A. Zagorevskii,
L. M. Sharkova, and N. F. Kucherova

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The configurational and conformational ratios of protonated 2,4-dimethyl- and 1,2,4-trimethyl-1,2,3,4-tetrahydrobenzofuro[3,2-c]pyridines and their conjugate bases were studied by PMR spectroscopy. The trimethyl derivatives have a 1,4-trans configuration. The equilibrium concentrations of the epimeric salts in solution were determined. In the crystalline state the salts exist in the form of the energetically more favorable epimer, which in solution has a completely equatorial conformation.

Protonation of a basic nitrogen atom has a substantial effect on the electronic properties and three-dimensional structure of both the amino group itself and the entire molecule; this should be particularly reflected in the specific character of the biological activity of the compounds (penetration through physiological membranes, distribution in organs and tissues, reaction with bioreceptors, etc.).

The epimers that develop in the case of protonation of cyclic amines with substituents attached to the ring nitrogen and carbon atoms [1-18] in substituted pyrrolidines [1, 12], piperidines [3-9], tetrahydropyridines [2, 18], condensed azacycloalkanes [1], and tetrahydroisoquinolines [10] can be detected by means of ^{1}H and ^{13}C NMR spectroscopy. The ability of cyclic amines to form geometrical isomers on protonation can be used for the study of the rates of exchange of the proton attached to the amino group and inversion of the ring or amino group, for the establishment of the conformational equilibrium of the protonated and unprotonated forms, and, in some cases, for the establishment of the con-

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