CONFORMATIONAL ANALYSIS OF CARBONYL DERIVATIVES OF 1,3,3-TRIMETHYL-2-METHYLENEINDOLINE

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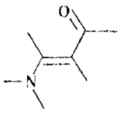
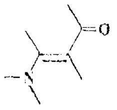
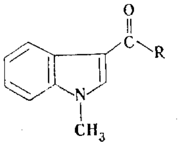
The preferred conformations of a number of carbonyl derivatives of 1,3,3-trimethyl-2-methyleneindoline were determined by PMR spectroscopy with the use of lanthanide shift reagents. It was established that the COR group is trans-oriented relative to the heteroring nitrogen atom, and the aldehyde exists primarily in the s-trans conformation, and the ketones exist primarily in the s-cis conformation. The conclusions regarding the structures of the preferred conformations of the investigated compounds were confirmed by data from the IR spectra.

It is known that α,β-unsaturated carbonyl compounds, including vinylogs of amides, can exist in the form of two conformers:


s-cis


s-trans

Infrared spectroscopy has often been used to establish which of these conformers is preferred [1]. It was later supplemented by PMR spectroscopy, particularly with the use of lanthanide shift reagents [2]. Among the cyclic compounds of this sort investigated by this method one should point out the acyl derivatives of heterocycles such as indoles I [3]. The C=C bond of the enamino carbonyl fragment in them is included in an aromatic ring, and the C—CO bond is therefore primarily a single bond. As a consequence of this, these compounds do not form stable conformers, whereas this cannot be said of acyclic vinylogs of amides [4].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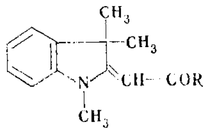
II–V

II R=H; III R=CH_3; IV R=C_6H_5; V R=2-thienyl

In this connection it seemed of interest to carry out the conformational analysis of enamino carbonyl compounds with an exocyclic C=C bond of the enamino carbonyl fragment. Acylmethylene bases of nitrogen heterocycles can be classified as cyclic compounds of this type. They have been known for a long time [5], but they have not been subjected to conformational analysis.

The aim of the present research was to determine the preferred conformations in a number of carbonyl derivatives (II-V) of 1,3,3-trimethyl-2-methyleneindoline as a function of the character of substituent R.

Compounds II-V can exist in two conformations, viz., s-cis and s-trans, and, with allowance for geometrical isomerism relative to the exocyclic C=C bond, there are four possible conformations. In V rotation about the bond connecting the CO group to the unsymmetrical thiophene residue is retarded, and the total number of possible conformations is therefore eight in this case.

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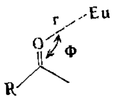
TABLE 1. Chemical Shifts and Specific Lanthanide Induced Shifts (in Parentheses) in the PMR Spectra of II-V (ppm)

Compound	R	1-CH_3	=CH—	3-CH_3	4-H	5-H	6-H	7-H	CHO	$COCH_3$	2′-H	3′-H	4′-H
II	H	3,21 (2,48)	5,37 (12,06)	1,64 (1,92)	7,25	7,04	7,23	6,83	9,99 (3,58)				
III	CH_3	3,16 (2,48)	5,30 (2,70)	1,73 (5,68)	7,19	6,96	7,17	6,73		2,18 (9,49)			
IV	C_6H_5	3,28 (2,70)	5,98 (3,43)	1,84 (7,68)	7,23	7,00	7,20	6,78			7,93	7,41	7,45
V	2-Thienyl	3,29 (1,54)	5,91 (1,38)	1,83 (4,40)	7,24	7,09	7,19	6,79			7,63 (5,35)	7,41	7,45

TABLE 2. Geometric Parameters of Adducts of $Eu(POD)_3$ with Acyl Derivatives of 1,3,3-Trimethyl-2-methyleneindoline



Conformation	r, nm	Φ, deg
2a	0,52	145
	0,16	147
	0,19	136
2b	0,27	124
3	0,28	218

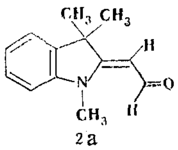
The PMR spectra of II-V in the presence of a lanthanide shift reagent and without one were measured, and the lanthanide-induced shifts of the most easily identifiable signals were also found (Table 1).

It follows from the data in Table 1 that for protons in similar environments (1-CH_3, 3-CH_3, =C—) the lanthanide-induced shifts of II differ from those of III-V, which have close values. It might therefore be assumed that the preferred conformation of II should differ from those for III-V, which evidently exist primarily in the same conformation.

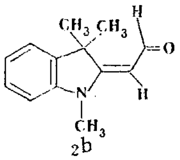
In order to confirm these assumptions and determine the structures of the preferred conformations of II and III we calculated the sites of coordination of the shift reagent from the measured lanthanide-induced shifts with allowance for all of the possible planar structures of the substrate. The most probable site of coordination of the lanthanide shift reagent is the oxygen atom of the carbonyl group.

In the calculations by the method in [6] the structure for which the smallest mean square deviations of the lanthanide-induced shifts found experimentally from the values calculated from the McConnell—Robertson formula [7] were observed was considered to be the most probable structure.

Dreiding models, the orthogonal projections of which were found by the shadow method, were used to calculate the cartesian coordinates. The centers of the orbits of rotation of the protons of the methyl groups were taken as the positions of these protons. The results of calculations with a computer by means of the LINIYa program [6] are presented in Table 2.



2a



2b

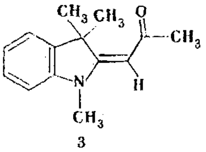


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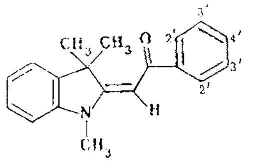
TABLE 3. Data from the IR Spectra of Acyl Derivatives of 1,3,3-Trimetyl-2-methyleneindoline

Frequency, cm^{-1}	Compound			
	II	III	IV	V
νC=O	1630 (s)	1615 (w) 1650 (w)	1615 (w) 1630 (w)	1615 (w)
νC=C	1575 (s)	1535 (s)	1530 (s)	1535 (s)



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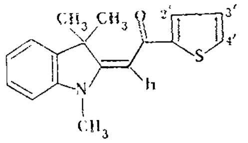

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For the 2a conformation of II the calculations give somewhat local minima of the mean square deviations, none of which is in agreement with the results of calculations for the adducts of other carbonyl derivatives with the lanthanide shift reagent.

The most probable conformation is the 2b structure. In this case the orientation of the europium ion relative to the coordination center best satisfies the chemical requirements [8].

In the case of III the best solution corresponds to structure 3. Here in the adduct with the shift reagent the 3-CH_3 groups, which have the greatest induced shift, are located closer than the others to the europium ion. The induced shifts of the 3-CH_3 groups are also greatest in the case of IV and V, on the basis of which the conformation shown by structures 4 and 5 was assigned to these compounds.

To find the preferred conformation of the thiophene ring in V relative to the remainder of the molecule we made calculations for two structures with different orientations of the thiophene ring. It follows from the results of the calculations that the S,O-trans conformation shown by structure 5 is the more probable conformation.

To confirm the results we recorded the IR spectra of II-V (Table 3). It is known that α,β-unsaturated carbonyl compounds have a more intense νC=O band in the s-trans form than in the s-cis form [1]. Data from the IR spectra of II-V confirm the conclusions regarding the structures of the preferred conformations drawn on the basis of the PMR spectra. In the spectra of III-V the peak intensity of the bands of the vibrations of the C=C bond is greater by a factor of three on the average than in the case of the bands of the vibrations of the C=O bond, which indicates the s-cis conformer. For II the peak intensities of the corresponding bands are almost identical with a slight preponderance for the νC=O band. This confirms that II exists in the s-trans form. The positions of the νC=O and νC=C bands do not contradict the literature data for other enamino carbonyl compounds [9].

Thus in the series of carbonyl derivatives (II-V) of 1,3,3-trimethyl-2-methyleneindoline the COR group is trans-oriented relative to the nitrogen atom; aldehyde II exists primarily in the s-trans conformation, while ketones III-V exist primarily in the s-cis conformation, which is in agreement with the literature data for other α,β-unsaturated carbonyl compounds [10].

EXPERIMENTAL

The PMR spectra of solutions of the compounds in deuterochloroform were recorded with a Brucker WP-200 spectrometer (200 MHz) with tetramethylsilane as the internal standard and $Eu(FOD)_3$ as the lanthanide shift reagent. The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The lanthanide induced shifts were found by the method described in [8]. The location of europium in the shift reagent—substrate adducts was calculated with an SM-1 computer.

Compounds III-V were obtained via the scheme in [11]; aldehyde II was prepared by the method in [12].

1,3,3-Trimethyl-2-(2-thienyl)methyleneindoline (V). A solution of 1.1 g (7.5 mmole) of thiophene-2-carboxylic acid chloride in 7.5 ml of benzene was added to a solution of 2.6 g (15 mmole) of 1,3,3-trimethyl-2-methyleneindoline in 7.5 ml of benzene, and the mixture was refluxed for 1 h. The precipitated 1,2,3,3-tetramethyl-3H-indolium chloride was removed by filtration and washed with benzene, and the filtrate was passed through a column packed with aluminum oxide and evaporated *in vacuo*. The crystalline residue was washed with hexane and removed by filtration to give 0.98 g (46%) of a product with mp 136-137°C (from methanol). Found: C 71.7; H 5.9; N 4.7; S 11.6%. $C_{17}H_{17}NOS$. Calculated: C 72.0; H 6.0; N 4.9; S 11.3%.

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BISINDOLES.

15.* ACIDIC CONDENSATION OF BIS(2-ETHOXYCARBONYL-5-INDOLYL) OXIDE AND BIS(2-ETHOXYCARBONYL-5-INDOLYL)METHANE WITH AROMATIC ALDEHYDES

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and N. N. Suvorov

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The acidic condensation of bis(2-ethoxycarbonyl-5-indolyl) oxide and bis(2-ethoxycarbonyl-5-indolyl)methane with aromatic aldehydes was studied. Bis(3-chloro) compounds with labile chlorine atoms, by nucleophilic substitution of which the corresponding dimethylamino, hydroxy, methoxy, acetoxy, cyano, and mercapto derivatives were obtained, were isolated.

In connection with the accessibility of bisindoles with various structures [2, 3] it seemed of interest to subject them to acidic condensation with aromatic aldehydes and to ob-

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*See [1] for communication 14.

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