90. A. V. Moskvin, V. A. Ostrovskii, I. Yu. Shirobokov, G. I. Koldobskii, and B. V. Gidaspov, Zh. Org. Khim., 14, 2440 (1978).
91. R. H. Erlich and A. L. Popov, J. Phys. Chem., 74, 338 (1970).
92. O. Mo, J. L. G. de Paz, and M. Yanez, J. Phys. Chem., 80, 5597 (1986).
93. A. F. Pozharskii, Theoretical Foundations of the Chemistry of Heterocycles [in Russian], Khimiya, Moscow (1985), p. 278.
94. É. S. Petrov, Usp. Khim., 52, 1974 (1983).
95. L. I. Belen'kii, Khim. Geterotsikl. Soedin., No. 6, 749 (1986).
96. V. N. Babin and E. B. Zavelovich, Khim. Geterotsikl. Soedin., No. 6, 781 (1977).
97. R. L. Baxter and A. I. Scott, Comprehensive Heterocyclic Chemistry, Vol. 1, ed. A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford–New York (1984), p. 83.
98. R. L. Benoit, D. Boulet, L. Seguin, and M. Frechette, Can. J. Chem., 63, 1226 (1985).
99. N. C. Marziano, P. G. Traverso, A. Tomasin, and R. C. Passerini, J. Chem. Soc., Perkin Trans. 2, No. 3, 309 (1977).
100. R. A. Cox and K. Yates, J. Am. Chem. Soc., 100, 3861 (1978).
101. Yu. L. Khaldna, Reakts. Sposobn. Org. Soedin., 17, 235 (1980).
102. Thermodynamic Properties of Individual Substances [in Russian], Vol. 1, Book 2, Nauka, Moscow (1978), p. 27.
103. P. Vogel, Carbocation Chemistry, Elsevier, Amsterdam–Oxford–New York (1985), p. 569.

---

^1H AND ^{13}C NMR SPECTRA, STEREOISOMERISM, AND CONFORMATIONAL STATES OF 3-PHENYL-5-ISOPROPOXYTETRAHYDRO-2-FURANONES

A. A. Panasenko, A. A. Fatykhov,
L. V. Spirikhin, and G. A. Tolstikov

UDC 547.722.3:541.63:543.
422.25:681.3.06

The ^1H and ^{13}C NMR spectra of the diastereomers of 3-phenyl-5-isopropoxytetrahydro-2-furanone were obtained. The stereoisomerism and preferred conformational states of these diastereomers were established by means of the spectroscopic criteria found for 3,4-disubstituted sulfolanes and 1,1,3,4-tetrasubstituted silacyclopentanes. It is shown that for the cis isomer the equilibrium is shifted to favor pseudoequatorial conformers, whereas for the trans isomer it shifted to favor ae conformers with a preferred pseudoequatorial orientation of phenyl substituent.

The diastereomeric pair of 3-phenyl-5-isopropoxytetrahydro-2-furanone, in which the substituents are attached to carbon atoms separated by one CH_2 group, is a convenient subject for testing the efficiency of the spectroscopic criteria for the determination of the stereoisomerism of disubstituted five-membered heterocycles developed primarily in the investigation of the ^1H and ^{13}C NMR spectra of vicinally substituted five-membered cyclic compounds [1-3].

The ^1H NMR spectra of the ring protons of diastereomers I and II correspond to a four-spin ABKX system (Tables 1 and 2).

As analysis of the chemical shifts (CS) of the ring carbon atoms shown that the chemical shifts of the $C_{(2)}$ and $C_{(4)}$ nuclei, i.e., the carbon nuclei coupled with one substituent, of I are greater than the CS of the corresponding carbon nuclei of II. It is known that in disubstituted derivatives of cyclopentane and cyclohexane the carbon nuclei coupled with one substituent are more strongly shielded in the trans isomers if the substituted carbon atoms are separated by one methylene fragment [5, 6] as compared with the CS of the analogous atoms in the cis isomers. Consequently, II is the trans isomer, and I is the cis isomer. Since

---

Institute of Chemistry, Bashkir Branch, Academy of Sciences of the USSR, Ufa 450054.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 593-597, May, 1988. Original article submitted July 8, 1986; revision submitted May 25, 1987.

0009-3122/88/2405-0480$12.50

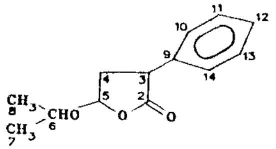
TABLE 1. Parameters of the ^1H NMR Spectra (δ, ppm; J_{HH}, Hz)* of the Diastereoisomers of 3-Phenyl-5-isopropoxytetrahydro-2-furanone (in $CDCl_3$)

Compound	δ_A	δ_B	δ_K	δ_X	J_{AB}	J_{AX}	J_{AK}	J_{BX}	J_{BK}	J_{KX}
cis-I	2.27±0.04	2,86±0,04	3.81±0,04	5,70±0,04	−13,69±0,06	5,15±0.06	8,52±0.06	5,65±0.06	10,11±0.06	−0,02±0,06
trans-II	2,49±0.08	2.58±0,08	4,05±0,04	5,70±0,04	−15,09±0,05	5.70±0,09	10,86±0.08	1,13±0,09	8.99±0,09	−0.01±0.05

---

*Obtained as a result of iteration analysis.

TABLE 2. Chemical Shifts (δ) and Constants of Direct Carbon-Proton Spin-Spin Coupling ($^1J_{^{13}C}$) from the ^{13}C NMR Spectra of the Stereoisomers of 3-Phenyl-5-isopropoxytetrahydro-2-furanone (in $CDCl_3$)



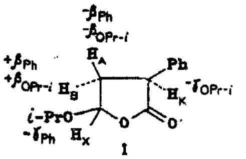
Atom	δ, ppm, ($^1J_{^{13}C-H}$, Hz)		Atom	δ, ppm ($^1J_{^{13}C-H}$, Hz)	
	cis isomer	trans isomer		cis isomer	trans isomer
$C_{(2)}$	175,84	177,0	$C_{(8)}$	21,70	21,59
$C_{(3)}$	45,97 (128,2)	44,29 (128,8)	$C_{(9)}$*	136,97	136,61
$C_{(4)}$	37,38	38,52	$C_{(10)}$, $C_{(14)}$	128,16	127,98
$C_{(5)}$	101,40 (172.7)	100,18 (178,0)	$C_{(11)}$, $C_{(13)}$	128,73	128,84
$C_{(6)}$	72,68	71,65	$C_{(12)}$	127,49	127,57
$C_{(7)}$	23,22	23,32			

---

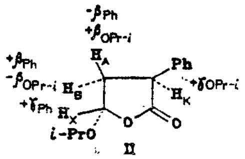
*Calculations of the chemical shifts via additive schemes [4] were used for the assignment of the signals of the carbon atoms of the aromatic substituent.

$^1J_{^{13}C-H}$ for $C_{(4)}$ of II is greater than the corresponding constant for I, while the constants for $C_{(2)}$ of the two compounds are approximately the same, the equilibrium in solution at room temperature for I, according to [1, 3], is shifted to favor the pseudoequatorial conformers, whereas for II it is shifted to favor the ae conformers with a primarily pseudoaxial isopropoxy group.

The parameters of the ^1H NMR spectra (primarily the CS of the geminal protons) presented in Table 1 confirm the assignments of the stereoisomers made on the basis of the ^{13}C NMR spectra. It is known that β substituents shield cis-vicinal protons and deshield trans-vicinal protons [7], and the CS of the geminal protons attached to the $C_{(4)}$ atom of the cis compound therefore should differ significantly from one another, while this difference should be insignificant for trans isomer II. In fact, $\nu_0\delta_{AB}$ = ~59.0 Hz in the ^1H NMR spectrum, while $\nu_0\delta_{AB}$ is on the order of 9.0 Hz for II. Moreover, taking into account the effect of γ substituents on the CS of the 3- and 5-H protons in accordance with [3] also confirms the correctness of the establishment of the configurations of I and II.



I



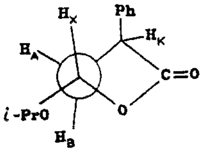
II

According to the scheme presented above for taking into account the effect of the β and γ substituents on the CS, the signals of the 3- and 5-H protons of I should be found at stronger field as compared with the signals of the corresponding protons of II; this is completely confirmed experimentally.

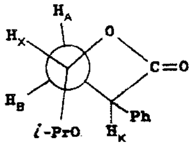
It has been shown that γ-lactones in the crystalline state exist in the "envelope" form with the $C_{(3)}$ atom outside of the $C_{(2)}$—O—$C_{(5)}$ plane [8]. On the basis of this it might be assumed that an "envelope" conformation with the $C_{(4)}$ atom outside of the plane of the ring is also the most likely conformation in solution for the two diastereomers of 3-phenyl-5-isopropoxytetrahydro-2-furanones. For the analysis of the angular dependence of the vicinal constants we used a modified Karplus equation (1) with the constants found for cyclic α-acetoxy ketones [9]:

$$^3J_{HH}=\begin{cases}10\cos^2\theta, & 0°\leqslant\theta\leqslant 90°;\\ 16\cos^2\theta, & 90°\leqslant\theta\leqslant 180°.\end{cases} \qquad (1)$$

An analysis of the vicinal constants for trans isomer II shows that of the two possible conformations, conformation B is preferred:



A



B

In fact, according to Eq. (1), when $^3J_{H_BH_X}$ = 1.13 Hz dihedral angle $H_XC_{(5)}C_{(4)}H_B$ = 90°, which corresponds to conformation B, in which the isopropoxy group is pseudoaxially oriented in conformity with the ^{13}C NMR data.

The $^3J_{H_BH_X}$ and $^3J_{H_AH_K}$ coupling constants are the trans-vicinal values, and the corresponding torsion angles can therefore be determined most accurately from them. The other two coupling constants $^3J_{H_BH_K}$ and $^3J_{H_AH_X}$ are cis-vicinal values, and their values show only the degree of puckering of the ring [10]. Thus according to expression (1), in the trans compound dihedral angle $\angle H_KC_{(3)}C_{(4)}H_A \approx 146°$, and $\angle H_XC_{(5)}C_{(4)}H_B \approx 72°$.

In the cis isomer the trans-vicinal constants are $^3J_{H_BH_X}$ and $^3J_{H_BH_K}$, and the two substituents are oriented either pseudoaxially or pseudoequatorially.

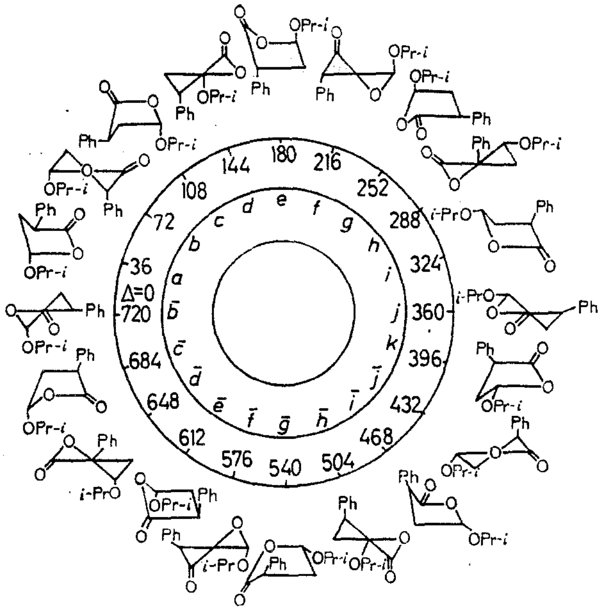
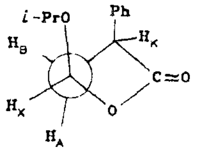
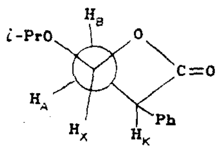


Fig. 1. Scheme of the pseudorotations of the trans-2-phenyl-4-isopropoxy-γ-lactone molecule (Δ is the phase angle of pseudorotation).



C



D

Vicinal constant $^3J_{H_BH_X}$ = 5.65 Hz was obtained experimentally. According to Eq. (1), for this value of the constant dihedral angle $\angle H_XC_{(5)}C_{(4)}H_B$ can be found both over the 0-90° range and over the 90-180° range. This is also valid for the other trans-vicinal constant $^3J_{H_BH_K}$. Thus in the cis isomer it is impossible to unambiguously determine the preferred orientation of the substituents and choose between conformations C and D only on the basis of ^{1}H NMR data. However, according to the ^{13}C NMR data, in the cis isomer the substituents are oriented primarily pseudoequatorially, and of the two possible conformations, the D conformation is consequently preferred. Then, according to (1), the dihedral angles in the cis compound are $\angle H_KC_{(3)}C_{(4)}H_B \approx 143°$ and $\angle H_XC_{(5)}C_{(4)}H_B \approx 126°$.

The values of the dihedral angles obtained in an analysis of the angular dependence of the vicinal constants taking into account the electronegativities of the substituents [11] are close to the values found from expression (1). Thus $\angle H_KC_{(3)}C_{(4)}H_A \approx 158°$ and $\angle H_XC_{(5)}C_{(4)}H_B \approx 74°$ for the trans isomer; $\angle H_KC_{(3)}C_{(4)}H_B \approx 154°$ and $\angle H_XC_{(5)}C_{(4)}H_B \approx 135°$ for the cis isomer. Twenty of the most probable conformations for the trans-3-phenyl-5-isopropoxytetrahydro-2-furanone molecule [12, 13], the analysis of which taking into account the NMR spectroscopic data shows that trans isomer II exists in equilibrium between the $\bar{c}$, $\bar{b}$, a, b, and c forms (Dreiding models were used in the analysis), are presented in Fig. 1. Here there are three "envelope" conformations, viz., $\bar{c}$, a, and c, in which the terminal atoms [$C_{(3)}$, $C_{(4)}$, and $C_{(5)}$, respectively] are situated outside of the plane of the ring. The other two conformations, viz., $\bar{b}$ and b, are "half-chair" conformations. Pseudoequatorial character of the phenyl substituent and pseudoaxial character of the isopropoxy group are characteristic for all five states. The same most probable conformations were similarly found in cis isomer I.

Thus an investigation of the ^{1}H and ^{13}C NMR spectra of the diastereomers of 3-phenyl-5-isopropoxytetrahydro-2-furanone shows that, first, the spectroscopic criteria that we previously found in an investigation of substituted sulfolanes are also valid for γ-lactones and, second, only the combined analysis of the vicinal proton-proton and direct carbon-proton SSCC makes it possible to most fully investigate the conformational states of five-membered saturated heterocyclic compounds.

EXPERIMENTAL

The ^{13}C NMR spectra of 5-10% solutions of the compounds in $CDCl_3$ were recorded with a Jeol FX-90Q pulse spectrometer (22.5 MHz). The radiation-pulse duration was 45-90° and was consistent with a time between pulses from 3 to 6 sec: the buildup of the spectrum was carried out for 16K points with a spectral sweep width of 2000-6000 Hz, which made it possible to obtain a digital resolution of 0.24 Hz. The ^1H NMR spectra of 1.0-1.5% solutions of the compounds in $CDCl_3$ were recorded with a Tesla BS-567 Fourier spectrometer (100 MHz). The buildup was carried out for the maximum number of points – 16K – with a minimal sweep width of 760 Hz and a digital resolution of 0.095 Hz. Tetramethylsilane (TMS) was used as the internal standard in both cases.

Iteration analysis of the ^1H and ^{13}C NMR spectra was carried out by means of the LAOCOON-3 program described in [14] and adapted with an SM-4 minicomputer. Test parameters ν_A, ν_B, ν_K, ν_X, J_{AK}, J_{AX}, J_{BK}, and J_{BX} were determined from data from the experimental spectra. It was assumed that J = 14.0 Hz [15] for the geminal constants. The J_{KX} value was assumed to be equal to zero.

In conclusion, the authors thank master's candidate A. Spivak for the compounds provided for investigation.

LITERATURE CITED

1. A. A. Panasenko, L. V. Spirikhin, V. S. Sultanova, R. A. Sadykov, and G. A. Tolstikov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 12, 2723 (1983).
2. A. A. Panasenko, L. V. Spirikhin, and G. A. Tolstikov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 4, 818 (1986).
3. A. A. Panasenko, L. V. Spirikhin, I. A. Gailyunas, and G. A. Tolstikov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 8, 1769 (1986).
4. A. A. Fatykhov, L. M. Khalilov, R. A. Sadykov, and A. A. Panasenko, Summaries of Papers Presented at the All-Union Conference on the Use of Computers in the Spectroscopy of Molecules and in Chemical Research [in Russian], Novosibirsk (1983), p. 158.
5. J. B. Stothers and C. T. Tan, Can. J. Chem., 52, 308 (1974).
6. M. Christl, H. J. Reich, and J. D. Roberts, J. Am. Chem. Soc., 93, 3463 (1971).
7. L. M. Jackman and S. Sternhell, Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry, Pergamon Press, Oxford (1969), p. 236.
8. A. McL. Mathieson and J. C. Taylor, Tetrahedron Lett., No. 17, 590 (1961).
9. K. L. Williamson and W. S. Johnson, J. Am. Chem. Soc., 83, 4623 (1961).
10. R. L. Lipnick, J. Am. Chem. Soc., 96, 2941 (1974).
11. C. A. G. Haasnoot, A. A. M. de Leeuw, and C. Altona, Tetrahedron, 33, 2783 (1980).
12. H. J. Geise, C. Altona, and C. Romers, Tetrahedron Lett., No. 30, 1383 (1967).
13. C. Altona and A. P. M. van der Veek, Tetrahedron, 24, 4377 (1968).
14. J. W. Cooper, Spectroscopic Techniques for Organic Chemists, Wiley Interscience, New York–Chichester (1980), p. 376.
15. D. Savostianoff and M. Pfau, Bull. Soc. Chim. France, No. 10, 4162 (1967).