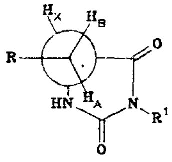
STUDY OF THE ROTATIONAL ISOMERISM OF THE SIDE CHAIN OF 3,5-DISUBSTITUTED HYDANTOINS

K.-A. V. Klimavichyus, G. V. Mikul'skene,
and V. V. Lutsenko

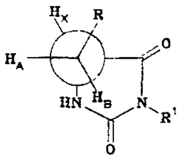
UDC 547.783.04:541.
63:543.422.25

The rotational isomerism of 3-alkyl(aryl)-5-alkyl(aralkyl)hydantoins in which the methylene group of the side chain, together with the methylidyne group in the 5 position of the ring, forms the structure of a substituted ethane was investigated by means of PMR spectroscopy.

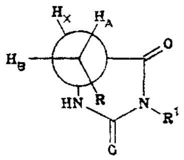
A number of 3,5-disubstituted hydantoins have been previously synthesized, and the structures of these compounds have been studied by PMR spectroscopy [1]. The literature contains data on the conformational analysis of the side chain of hydantoins of only some aromatic amino acids [2, 3]. It has been shown that rotational isomerism of the side chain occurred in the molecules of these compounds. As a result of calculations, it was established that, of the three possible rotamers, the most preferable was the so-called "locked" rotamer **C**, in which the aromatic ring is situated directly above the hydantoin ring. In the opinion of Bose and co-workers and Attia and Siemion [2, 3], this is explained by its stabilization as a consequence of intramolecular interaction between the π electrons of the aromatic ring and the dipole of the ring system of hydantoin.



A

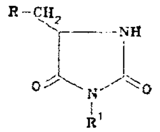


B



C

In the present research we used PMR spectroscopy to investigate the rotational isomerism of the side chain in the 5 position of the ring of 3-alkyl(aryl)-5-alkyl(aralkyl)hydantoins I-XI.



I-XI

I R=C_6H_5, R^1=C_6H_{13}; II R=R^1=C_5H_5; III R=C_5H_5, R^1=α-$C_{10}H_7$; IV R=C_5H_5, R^1=β-$C_{10}H_7$; V R=$(CH_3)_2CH$, R^1=C_6H_{13}; VI R=$(CH_3)_2CH$, R^1=C_6H_5; VII R=CH_3SCH_2, R^1=C_6H_{13}; VIII R=CH_3SCH_2, R^1=C_6H_5; IX R=$CH_3SO_2CH_2$, R^1=C_6H_{13}; X R=$CH_3SO_2CH_2$, R^1=C_6H_5; XI R=OH, R^1=C_6H_{13}

On the basis of the experimental J_{AX} and J_{BX} spin–spin coupling constants (SSCC) of the observed ABX system (Table 1) we calculated the **A**:**B**:**C** rotamer ratios by the Pachler method [4]. Thus it was established that in the case of β-phenyl-α-alanine hydantoins I-IV rotamers **C** predominate in amounts that are comparable with the data indicated above [2, 3].

In contrast to I-IV, the hydantoins of nonaromatic amino acids, viz., those of leucine (V, VI), methionine (VII, VIII), and sulfomethionine (IX, X), preferably contain **A** conformations in which the side chain in the 5 position is most remote with respect to the carbonyl groups. Nevertheless, the percentages of rotamers **C** are high in the case of methionine hydantoins VII and VIII, and preponderance of rotamer **C** is again observed for serine hydan-

---

Institute of Biochemistry, Academy of Sciences of the Lithuanian SSR, Vilnius 232021.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 337-338, March, 1987. Original article submitted August 22, 1985.

0009-3122/87/2303-0282$12.50

TABLE 1. Spin–Spin Coupling Constants (SSCC) and Ratios of the Rotamers of Hydantoins I-XI

Compound*	J_{AX}	J_{BX}	A : B : C rotamer ratios
I	5,0	4,5	0,22 : 0,17 : 0,61
II	5,0	4,5	0,22 : 0,17 : 0,61
III	5,0	4,5	0,22 : 0,17 : 0,61
IV	5,5	4,0	0,22 : 0,13 : 0,65
V	8.0	4,5	0,49 : 0,17 : 0,34
VI	7,5	5,0	0,46 : 0,22 : 0,32
VII	7,0	5,0	0,40 : 0,22 : 0,38
VIII	7,0	5,0	0,40 : 0,22 : 0,38
IX	7,5	5,5	0,46 : 0,26 : 0,28
X	7,5	5.5	0,46 : 0.26 : 0.28
XI	5.0	4.0	0.22 : 0.13 : 0.65

---

*The PMR spectra of I-IV and IX-XI were recorded from solutions in a mixture of d_6-acetone with d_6-DMSO, while the PMR spectra of V-VIII were recorded from solutions in d_6-acetone.

toin XI. The literature contains similar data for cyclic serine-containing dipeptides, in which the hydroxy group also occupies the preferred position above the diketopiperazine ring [5]. The character of the substituents in the 3 position of the hydantoin did not have a substantial effect on the ratios of the rotational isomers. However, in the case of hydantoins I, II, and XI, which contain primarily C conformations as a result of the shielding effect of the phenyl or hydroxy group, there was a shift of the signals of these substituents to the strong-field side. It is characteristic for the investigated hydantoins that the B conformations, in which bulky substituents were gauche-oriented relative to the carbonyl group, were the least preferable in all cases.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in d_6-acetone or a mixture of the latter with d_6-DMSO were recorded with a Hitachi R-22 spectrometer (90 MHz) with hexamethyldisiloxane (HMDS) as the internal standard at 35°C. The SSCC were measured with an accuracy of 0.5 Hz. 3-Phenyl-5-benzylhydantoin (II) and 3-phenyl-5-isobutylhydantoin (VI) were previously synthesized [6]. The remaining hydantoins were obtained from the corresponding α-ureido acids by the method in [1].

LITERATURE CITED

1. K.-A. Klimavichyus, V. V. Lutsenko, G. V. Paulauskaite, P. P. Mikul skis, G. A. Bal'chitis, and S. L. Ionushauskas, Khim. Geterotsikl. Soedin., No. 10, 1404 (1984).
2. A. K. Bose, M. S. Manhas, R. F. Tavares, J. M. van der Veen, and H. Fujiwara, Heterocycles, 7, 1227 (1977).
3. I. Attia and Z. Siemion, Roczn. Chem., 50, 2063 (1976).
4. K. C. R. Pachler, Spectrochim. Acta, 29, 581 (1961).
5. Ziauddin, K. D. Kopple, and C. A. Bush, Tetrahedron Lett., No. 6, 483 (1972).
6. A. Mouneyrat, Chem. Ber., 33, 2393 (1900).