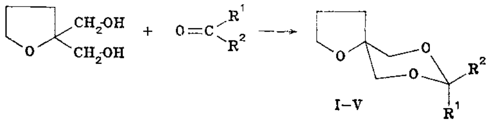
THREE-DIMENSIONAL STRUCTURES OF CYCLIC 2,2-BIS(HYDROXYMETHYL)-TETRAHYDROFURAN ACETALS

R. A. Karakhanov, M. R. Skurko,
T. Yu. Solov'eva, L. Yu. Brezhnev,
L. F. Lapuka, and M. M. Vartanyan

UDC 547.722.3'841'642.07:541.67:543.422.25

2-Substituted spiro[1,3-dioxane-5,2'-tetrahydrofurans] were obtained from 2,2-bis(hydroxymethyl)tetrahydrofuran, and their three-dimensional structures were investigated by ^{1}H and ^{13}C NMR spectroscopy. The tetrahydrofuran ring lies in the plane of symmetry of the 1,3-dioxane ring with an equatorial orientation of the oxygen atom.

Tetrahydrofuran derivatives that are bonded to other heterocycles are well known as biologically active substances [1]. It is also known that the presence of a cyclic acetal fragment in the molecules leads to intensification of the biological activity of preparations [2]. Continuing our research on the chemistry of saturated furans we synthesized and investigated the three-dimensional structures of a number of spiro[1,3-dioxane-5,2'-tetrahydrofurans]. The latter are readily formed in the condensation of 2,2-bis(hydroxymethyl)tetrahydrofuran with aldehydes in the presence of KU-2 cation-exchange resin in the H form or p-toluenesulfonic acid (Table 1):



I–V

I $R^1=R^2=H$; II $R^1=H$, $R^2=C_6H_5$; III $R^1=H$, $R^2=$ 2-furyl IVa $R^1=CH_3$, $R^2=C_5H_{11}$; IVb $R^1=C_5H_{11}$, $R^2=CH_3$; V $R^1=R^2=CH_3$

The condensation of 2,2-bis(hydroxymethyl)tetrahydrofuran with acetone was realized at room temperature in the presence of $CaCl_2$; the yield of acetal V did not exceed 12%.

In the PMR spectrum of I in CCl_4 the protons of the methylene group attached to the acetal carbon atom resonate in the form of an AB quartet. It is known that the relative magnetic nonequivalence and the magnitude of the geminal spin—spin coupling constant (SSCC) of these protons are characteristic and may serve as criteria of the conformation of the 1,3-dioxane system; thus for the canonic chair conformer of 1,3-dioxane $\Delta\delta$ is 0.23-0.34 ppm, and $^2J_{HH}$ = −6.2 Hz [3-5]. In the spectrum of I the difference in the chemical shifts of the equatorial and axial protons attached to $C_{(2)}$ is 0.38 ppm, and $^2J_{HH}$ = −6.0 Hz (Table 2). All of this makes it possible to assert that the 1,3-dioxane ring in the investigated compounds exists primarily in the chair conformation.

The protons of the methylene groups in the equivalent 4 and 6 positions give a typical AB quartet with a geminal constant of −10.6 Hz. The character and magnitude of the splitting, as well as the magnetic nonequivalence of these protons ($\Delta\delta$ = 0.20 ppm), are similar to what was previously observed for the chair conformers of 2,5,5-trialkyl-1,3-dioxanes [6]. The equatorial 2- (δ 4.76 ppm) and 4- and 6-H (3.53 ppm) protons resonate at weaker field than the corresponding axial protons; this is typical for 1,3-heterocycles in the chair conformation [7-9]. The assignment was made on the basis of the observed broadening of the lines of the low-field components of the AB quartets due to long-range spin—spin coupling (LRSSC) of the protons with $^4J_{HH}$ = −1.2 Hz. The LRSSC is stereospecific and characteristic for the protons in the 1,3-diequatorial orientations of the chair conformer, which are separated by planar "zigzag" σ bonds [3, 6, 10, 11]. This fact of LRSSC is also confirmed

---

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow 117913. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 162-166, February, 1984. Original article submitted October 26, 1982; revision submitted March 29, 1983.

0009-3122/84/2002-0128$08.50

TABLE 1. Spiro[1,3-dioxane-5,2'-tetrahydrofurans] I-V

Compound	bp, °C (mm)	n_D^{20}	Found, %		Empirical formula	Calculated, %		Yield, %
			C	H		C	H	
I	84 (18)	1,4611	58,4	8,4	$C_7H_{12}O_3$	58,3	8,3	70
II	124—126 (1)	1,5281	71,8	7,5	$C_{13}H_{16}O_3$	70,9	7,3	65
III	148—150 (11)	1,5018	63,2	7,0	$C_{11}H_{14}O_4$	62,8	6,7	60
IV a, b	99—104 (2)	1,4730	68,9	10,1	$C_{13}H_{24}O_3$	68,4	10,5	55*
V	87—89 (9)	1,4672	63,1	9,4	$C_9H_{16}O_3$	62,8	9,3	12

---

*This is the overall yield of two isomers.

TABLE 2. Chemical Shifts (δ, ppm) and Spin-Spin Coupling Constants (J, Hz) of the Protons of Spiro[1,3-dioxane-5,2'-tetrahydrofurans]

Compound	Solvent	R^1	R^2	4(6)-H_e	4(6)-H_a	3'-H	4'-H	5'-H	$^2J\ H_eH_a$ [a]	$^3J_{HH}$ [b]
I	CCl_4	4,38[c]	4,76[c]	3,53	3,33	1,90—2,05		3,78	−10,6	−6,6
	C_6H_6	4,27[c]	4,73[c]	3,48	3,35	1,68	1,37	3,43	−10,6	6,6
II	CCl_4	5,25	7,10—7,45	3,77	3,57	1,85—2,10		3,66	−10,4	6,6
	C_6H_6	5,15	—	3,63	3,56	1,85	1,39	3,38	−10,0	6,6
III	CCl_4	5,32	6,10—6,40	3,65	3,54	1,85—2,10		3,74	−10,6	6,6
	C_6H_6	5,27	—	3,59	3,49	1,83	1,33	3,39	−10,5	6,6
IVa	CCl_4	1,26	0,82[d]	3,60	3,26	1,75—1,90		3,77	−11,4	—
	C_6H_6	1,18	0,76	3,70	3,34	1,40—1,85		3,44	−10,8	—
IVb	CCl_4	0,83[e]	1,38	3,53	3,27	1,75—1,90		3,77	−11,4	—
	C_6H_6	0,73	1,24	3,65	3,35	1,40—1,85		3,45	−11,2	—
V	CCl_4	1,36	1,25	3,56	3,26	1,75—1,90		3,76	−11,2	—
	C_6H_6	1,25	1,18	3,36	3,34	1,40—1,87		3,43	−11,0	—

---

[a] These are the $J_{44'(66')}$ values. [b] Average vicinal SSCC for the protons of the tetrahydrofuran ring. [c] These are the $^2J_{22'}$ values. [d] Singlet of the terminal protons of the C_5H_{11} group. [e] The shifts of the protons of the CH_2 groups lie at 1.00-1.85 ppm.

by means of homonuclear $^1H-\{^1H\}$ INDOR experiments. The α-methylene protons (5'-H) of the tetrahydrofuran substituent resonate in the form of a triplet (δ 3.69 ppm) with an average vicinal constant of 6.6 Hz, whereas the β-methylene protons (3'- and 4'-H) give an overlapped multiplet with a center of gravity at 1.99 ppm. This constitutes evidence for the rapid (on the time scale) inversion of the $C_{(3')}-C_{(4')}-C_{(5')}$ fragment of the tetrahydrofuran ring. In benzene solution the nonequivalence of the methylene protons (3'- and 4'-H) increases, and they give a triplet with δ 1.68 ppm and a quintet with δ 1.37 ppm, respectively. The primary shielding of one of the β-methylene groups can be explained by the formation of a molecular complex between the solvent molecules and the dissolved substance by direct specific interaction between the π electrons of the benzene ring and the center of partial positive charge in acetal I. The methylene group lying under (over) the plane of the benzene ring will be shielded to a considerably greater extent than the other methylene group.

The position of the signal of the 3'-H protons is characteristic for an axially oriented alkyl substituent in the 5 position of the 1,3-dioxane system. In [12, 13] it was shown that in 5-alkoxy-5-alkyl-2-furyl-1,3-dioxanes the protons of the CH_2 and CH_3 groups of the alkyl substituent attached to the $C_{(5)}$ atom resonate at "anomalously" high field (0.0-1.0 ppm) when the alkyl group is equatorially oriented. However, if the alkyl group is axially oriented, the signal of the protons of the methylene group is shifted to weak field (1.8-1.9 ppm). Thus the three-dimensional structure of I can be depicted as follows:

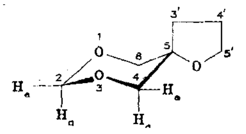
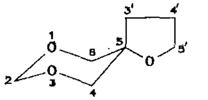
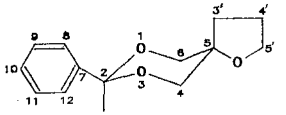
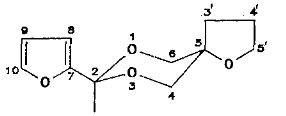
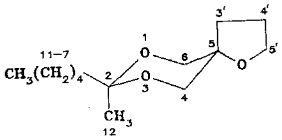
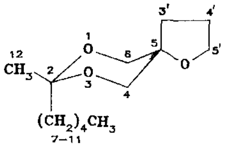
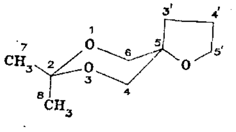


TABLE 3. ^{13}C NMR Spectra of Spiro[1,3-dioxane-5,2'-tetrahydrofurans]

Compound	δ, ppm (J, Hz)											
	$C_{(2)}$	$C_{[4(6)]}$ (t)	$C_{(5)}$ (s)	$C_{(3)}$ (t)	$C_{(4')}$ (t)	$C_{(5')}$ (t)	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	$C_{(10)}$	$C_{(11)}$	$C_{(12)}$
	93,7t (162)	74,2 (132)	76,6	32,7 (134)	26,0 (133)	68,4 (145)	—	—	—	—	—	—
	101,4d (159)	74,8 (143)	75,7	34,6 (130)	26,0 (130)	68,5 (145)	138,8 s	128,1 d (157)	126,7 d (158)	128,7 d (160)	126,7 d (158)	128,1 d (157)
	96,2d (160)	74,6 (144)	75,7	34,6 (132)	26,0 (134)	68,6 (144)	151,4 s	107,8 d (176)	110,6 dd (171,9)	142,7 d (205)	—	—
	99,2s	68,0 (143,5)	77,1	34,5 (132,5)	26,1 (130)	67,6 (143,5)	41,5 t (128)	34,1 t (128)	24,4 t (128)	23,4 t (128)	14,6 q (128)	18,5 q (129)
	99,7s	68,0 (143)	77,4	34,2 (132,5)	26,1 (130)	67,6 (143,5)	41,6 t (128)	34,1 t (128)	24,4 t (128)	23,4 t (128)	14,6 q (128)	18,5 q (129)
	99,4s	68,0 (141)	77,2	34,4 (132)	26,1 (131)	67,5 (143)	18,5 q (128)	18,4 q (128)	—	—	—	—

The deshielding of the axially oriented CH_2 group can evidently be ascribed to the magnetic-anisotropic effect of the unshared pairs of electrons of the oxygen atoms of the 1,3-dioxane ring [8].

Regularities of this sort, which are characteristic for a chair conformer with a tetrahydrofuran ring that lies in the plane of symmetry of the 1,3-dioxane ring, are also observed in the PMR spectrum of V.

A distinctive feature of the spectrum of II is the decrease in the nonequivalence of the axial and equatorial protons in the 4 and 6 positions to 0.11 ppm. Changes in the configuration and the primary conformation as compared with acetal I evidently do not occur, since the carbon chemical shifts of the $C_{(4)}$—$C_{(6)}$ and $C_{(3')}$—$C_{(5')}$ atoms are identical for I and II within the limits of the experimental error (Table 3). The equatorial orientation of the phenyl and furyl substituents in II and III can be judged from the magnitude of the chemical shift of the singlet line of the acetal proton, which resonates at 5.25-5.32 ppm (Table 2), which is characteristic for the axially oriented 2-H proton [7, 12, 13].

The PMR and ^{13}C NMR spectra of III are similar to the spectra of acetal II. Thus II and III are primarily chair trans isomers with an equatorially oriented substituent attached to the $C_{(2)}$ atom and an equatorially oriented oxygen atom of the tetrahydrofuran ring attached to the $C_{(5)}$ atom.

Compound IV is a mixture of two stereoisomers in a ratio of 3:2 that exist primarily in the chair conformation with an equatorially oriented oxygen atom of the tetrahydrofuran ring and different configurations at the $C_{(2)}$ atom (Tables 1 and 2). The methyl substituent in the PMR spectrum of the preponderant isomer gives a signal that is shifted 0.1 ppm to stronger field as compared with the corresponding signal of the second isomer, and this makes it possible to assign an axial orientation to it and, correspondingly, an equatorial orientation to the pentyl group. This assignment does not contradict the results of other researchers [7, 8].

EXPERIMENTAL

The PMR and ^{13}C NMR spectra of solutions of I-V in CCl_4 were recorded at room temperature with BS-497 (100 MHz) and Brucker WH-90 (22.63 MHz) spectrometers, respectively; the chemical shifts were measured on the δ scale relative to hexamethyldisiloxane as the internal standard.

Spiro[1,3-dioxane-5,2'-tetrahydrofurans] (I-IV). A mixture of 0.1 mole of 2,2-bis(hydroxymethyl)tetrahydrofuran [14], 0.1 mole of the corresponding carbonyl compound, and 2 g of KU-2 cation-exchange resin was heated with 80 ml of benzene until the liberation of water ceased, after which the benzene was removed by distillation, and the residue was distilled in vacuo.

Spiro[2,2-dimethyl-1,3-dioxane-5,2'-tetrahydrofuran] (V). A 0.1-mole sample of 2,2-bis(hydroxymethyl)tetrahydrofuran was mixed with 0.2 mole of acetone at room temperature in the presence of one drop of concentrated HCl and 2 g of calcined $CaCl_2$ in 60 ml of chloroform, during which a spontaneous 10° rise in temperature was observed. The reaction mixture was then allowed to stand for 24 h, after which it was filtered, the chloroform was removed from the filtrate by distillation, and the residue was distilled in vacuo.

LITERATURE CITED

1. S. A. Giller, R. A. Zhuk, and M. Yu. Lidak, Dokl. Akad. Nauk SSSR, 176, 332 (1967).
2. U. Herrog and B. Reinshagen, Eur. J. Med. Chem., 11, 415 (1976).
3. K. C. Ramey and J. Messiek, Tetrahedron Lett., No. 49, 4423 (1965).
4. M. Anteunis and J. Swaelens, Org. Magn. Reson., 2, 389 (1970).
5. Yu. Yu. Samitov, Z. I. Zelikman, and V. G. Kul'nevich, Zh. Strukt.Khim., 10, 234 (1969).
6. A. S. Yavorskii, Yu. Yu. Samitov, A. V. Bogat-skii, A. I. Gren', and O. S. Stepanova, Zh. Org. Khim., 13, 1103 (1977).
7. M. Anteunis, D. Tabernier, and F. Borremans, Heterocycles, 4, 293 (1976).
8. Yu. Yu. Samitov, Khim. Geterotsikl. Soedin., No. 12, 1587 (1978).
9. K. Pihlaja and P. Ayras, Acta Chem. Scand., 24, 531 (1970).
10. J. Delman and J. Duplan, Tetrahedron Lett., No. 6, 559 (1966).
11. J. Kotowyzg and R. Lemieux, Chem. Rev., 73, 666 (1973).

12. Yu. Yu. Samitov, Z. I. Zelikman, A. I. Shkrebets, and V. G. Kul'nevich, Khim. Geterotsikl. Soedin., No. 2, 319 (1974).
13. Yu. Yu. Samitov, Atlas of the Nuclear Magnetic Resonance Spectra of Spatial Isomers [in Russian], Vol. 1, Izd. Kazansk Gos. Univ., Kazan (1978), pp. 84, 85.
14. D. S. Eflax and A. P. Dunlop, J. Org. Chem., 26, 2106 (1961).

NEW METHOD FOR THE DETERMINATION OF THE QUANTUM YIELDS IN THE PHOTOISOMERIZATION OF PHOTOCHROMIC EPOXYDIARYLINDANONES

V. M. Zolin, N. D. Dmitrieva,
Yu. E. Gerasimenko, and A. V. Zubkov

UDC 547.665'814.1:535.217:541.621.2:543.422.6

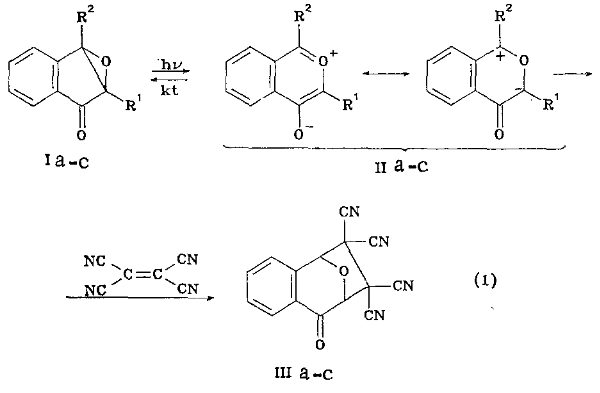
A method for the determination of the quantum yield in the formation of the unstable photoinduced form of 2,3-epoxy-2,3-diphenylindanone based on the reaction with tetracyanoethylene is proposed. The products of 1,3-dipolar addition of tetracyanoethylene to the photoinduced forms of the investigated compounds were isolated and characterized.

Unstable 2-benzopyrylia-4-oxides II are formed as a result of the photochemical valence isomerization of 2,3-epoxyindanones I [1]. We have developed a new simple method for the determination of the quantum yields in the photoisomerization of epoxydiarylindanones.

The measurement of the quantum yields in the photoisomerization of photochromic compounds always presents certain difficulties and requires special procedures for each type of compound [2]. In the case of 2,3-epoxydiarylindanones the complications are due to the fact that decomposition of the photoinduced form, viz., benzopyryliaoxide II, by air oxygen occurs in addition to photochromic transformations (photoelectric coloring and photoelectric and thermal decolorization) during UV irradiation.

The known [1] method for the measurement of the quantum yield in the formation of the photoinduced form of 2,3-epoxy-2,3-diphenylindanone requires prior measurement of the extinction coefficient of the colored form, which is a special problem all by itself [1, 3], as well as thorough removal of the oxygen from the solution of the epoxyindanone to avoid oxidation of the benzopyryliaoxide [1].

The method that we propose is based on the ability of benzopyryliaoxides II to undergo 1,3-dipolar cycloaddition with unsaturated compounds to give adducts III [4].



I a-c

II a-c

III a-c

(1)

A necessary condition for the correct use of this method is the absence of absorption of the adduct in the visible part of the spectrum, as well as a high rate of tying up of the colored form in the adduct that significantly exceeds the rates of the dark reaction and

---

Scientific-Research Institute of Organic Intermediates and Dyes, Moscow 103787. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 167-170, February, 1984. Original article submitted May 24, 1983.