REACTION OF 2,2-DIALKOXY-2,3-DIHYDROFURANS WITH BENZENESULFENYL CHLORIDE. CONVENIENT METHOD FOR OBTAINING 4-OXO-3-PHENYLTHIOALKANOIC ACID ESTERS

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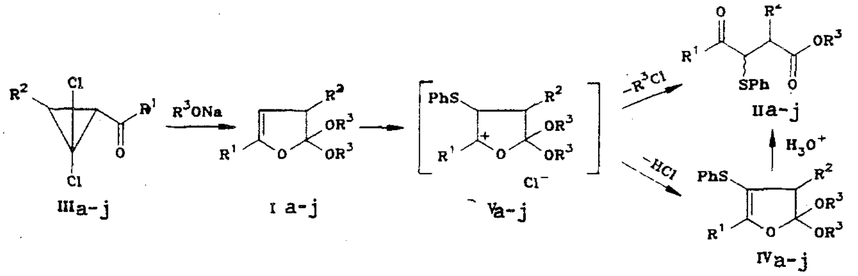
UDC 547.722.3.07:541.632

The reaction of 2,2-dimethoxy(ethoxy)-2,3-dihydrofurans with benzenesulfenyl chloride with subsequent treatment with dilute hydrochloric acid leads to the corresponding 4-oxo-3-phenylthioalkanoic acid esters in high yields.

Substituted 2,2-dialkoxy-2,3-dihydrofurans are quite accessible on the basis of reactions of diazo carbonyl compounds with ketene dialkylacetals [1] or gem-dichlorocyclopropyl ketones with sodium alkoxides [2, 3]. The presence in these compounds of latent carbonyl and ester functions together with a nucleophilic carbon—carbon double bond makes their use effective in the synthesis of 1,4-bifunctional compounds and derivatives of the furan series [1-6]. We have found that the electrophilic addition of benzene sulfenyl chloride to the double bond of 2,2-dialkoxy-2,3-dihydrofurans Ia-j with subsequent opening of the heteroring is a convenient method for obtaining 4-oxo-3-phenylthioalkanoic acid alkyl esters IIa-j. Some possibilities of the use of representatives of this class of substances in the synthesis of 2(5H)-furanone derivatives and other compounds were demonstrated in [7, 8]; however, the known method for obtaining them [7] has substantial limitations with respect to the synthesis of alkyl esters of 2-substituted 4-oxo-3-phenylthioalkanoic acids.

Compounds Ia-c were obtained from 1-acyl-2,2-dichlorocyclopropanes IIIa-e by a method similar to that previously described for obtaining Id-j [9]. The reaction of dihydrofurans Ia-j with benzenesulfenyl chloride was carried out in methylene chloride in the presence of pyridine at −60°C to −70°C with subsequent treatment of the reaction mixture with dilute hydrochloric acid. Compounds IIa-j were obtained in 76-84% yields; 2-methyl-substituted IIb-f were obtained in the form of mixtures of diastereomers with substantial preponderance of one of them.



I—V a $R^1=R^2=H$, $R^3=Et$; b $R^1=H$, $R^2=Me$, $R^3=Et$; c $R^1=Bu$, $R^2=R^3=Me$; d $R^1=R^2=R^3=Me$; e $R^1=Et$, $R^2=R^3=Me$; f $R^1=Ph$, $R^2=R^3=Me$; g $R^1=Et$, $R^2=H$, $R^3=Me$; h $R^1=Pr$, $R^2=H$, $R^3=Me$; i $R^1=Bu$, $R^2=H$, $R^3=Me$; j $R^1=C_5H_{11}$, $R^2=H$, $R^3=Me$

Monitoring of the course of the reaction of Ia-j with benzenesulfenyl chloride by TLC shows that, prior to treatment of the reaction mass with aqueous acid, products with higher chromatographic mobilities are formed in significant amounts along with IIa-j. In the case of the reactions of Id, g the preacidification products were isolated in an approximately equimolar ratio with IId, g and were identified as dihydrofurans IVd, g. Treatment of them with dilute hydrochloric acid leads to IId, g in quantitative yields. At the same time, we were unable to substantially change the ratios of the products of the reaction of dihydrofurans IIa-j with benzenesulfenyl chloride in favor of the primary production of 4-phenylthiohydrofurans IVa-j by using thoroughly dried reagents and solvents and by carrying out the reaction in an atmosphere of dry argon. Thus IIa-j under these conditions cannot be products of hydrolytic transformations, and splitting out of an alkyl chloride from carbonium ion intermediates Va-j is the probable scheme of their formation.

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0009-3122/88/2402-0132$12.50

TABLE 1. Physicochemical Characteristics of the Synthesized Compounds

Compound	bp, °C (hPa)	n_D (T, °C)	Found, %		Empirical formula	Calc., %		Yield, %
			C	H		C	H	
Ia	67—68 (16)	1,4296 (19)	60,3	9,0	$C_8H_{14}O_3$	60,7	8,9	45
Ib	70—71 (16)	1,4291 (22)	62,4	9,5	$C_9H_{16}O_3$	62,8	9,4	50
Ic	102—104 (16)	1,4423 (20)	65,4	10,3	$C_{11}H_{20}O_3$	66,0	10,1	82
IIa	137—141 (2)	1,5428 (22)	60,3	5,8	$C_{12}H_{14}O_3S$	60,5	5,9	78
IIb	147—150 (2)	1,5378 (21)	61,8	6,5	$C_{13}H_{16}O_3S$	61,9	6,4	78
IIc	162—164 (2)	1,5223 (17)	65,6	7,7	$C_{16}H_{22}O_3S$	65,3	7,5	82
IId	132—135 (2)	1,5408 (24)	61,6	6,2	$C_{13}H_{16}O_3S$	61,9	6,4	84
IIe	137—138 (2)	1,5302 (14)	63,3	6,7	$C_{14}H_{18}O_3S$	63,1	6,8	77
IIf	190—195 (2)	1,5452 (14)	68,3	5,8	$C_{18}H_{18}O_3S$	68,8	5,8	76
IIg	124—126 (2)	1,5386 (16)	62,2	6,3	$C_{13}H_{16}O_3S$	61,9	6,4	84
IIh	130—132 (2)	1,5306 (16)	63,0	7,1	$C_{14}H_{18}O_3S$	63,1	6,8	83
IIi	145—146 (2)	1,5292 (23)	64,3	7,1	$C_{15}H_{20}O_3S$	64,3	7,2	80
IIj	150—154 (2)	1,5278 (22)	65,7	7,6	$C_{16}H_{22}O_3S$	65,3	7,5	81
IVd*	Oily liquid		62,7	7,0	$C_{14}H_{18}O_3S$	63,1	6,8	42
IVg*	Oily liquid		62,7	6,9	$C_{14}H_{18}O_3S$	63,1	6,8	42

*Isolated chromatographically with a column packed with silica gel and hexane as the eluent.

TABLE 2. PMR Spectra of 2,2-Dialkoxy-2,3-dihydrofurans Ia-c and 2,2-Dimethoxy-4-phenylthio-2,3-dihydrofurans IVd, g

Compound	Chemical shift, δ, ppm (J, Hz)				
	3-H	4-H	R^1	R^2	R^3
Ia	2,47 (1H, t, J=2)	4,7—5,0 (1H, m)	6,1—6,4 (1H, m)	2,47 (1H, t, J=2)	1,11 (6H, t, J=7), 3,47 (4H, q, J=7)
Ib	2,6—3,0 (1H, m)	4,7—4,8 (1H, m)	6,0—6,2 (1H, m)	0,99 (3H, d, J=7)	1,11 (6H, t, J=7), 3,45 (2H, q, J=7), 3,60 (2H, q, J=7)
Ic	2,6—3,0 (1H, m)	4,3—4,4 (1H, m)	0,7—1,5 (7H, m), 1,8—2,1 (2H, m)	0,87 (3H, d, J=7)	3,10 (3H, s), 3,18 (3H, s)
IVd*	2,80 (1H, m, J_1=2, J_2=7)		1,94 (3H, d, J=2)	0,95 (3H, d, J=7)	3,19 (3H, s), 3,28 (3H, s)
IVg*	2,54 (1H, t, J=2)		1,04 (3H, t, J=7), 2.33 (2H, m, J_1=2, J_2=7)	2,54 (1H, t, J=2)	3,18 (6H, s)

*The signals of the protons of the phenylthio grouping show up in the form of a multiplet at 6.8-7.3 ppm.

EXPERIMENTAL

The PMR spectra of 5-10% solutions of the compounds in CCl_4 were recorded with a Tesla BS-467A spectrometer (60 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The IR spectra of the substances were recorded with a Specord 75-IR spectrometer. The purity of the investigated compounds was monitored by TLC on aluminum oxide (neutral, activity II), as well as on silica gel. The characteristics of the synthesized substances are presented in Tables 1-3.

trans-3-Methyl-1-(1-oxopentyl)-2,2-dichlorocyclopropane (IIIc). This compound was synthesized by the method in [10] from 30 g of trans-3-methyl-1-formyl-2,2-dichlorocyclopropane and butylmagnesium bromide with subsequent oxidation of the resulting carbinol with sodium dichromate in the presence of sulfuric acid. The yield of IIIc, with bp 85-86°C (2 hPa) and n_D^{27} 1.4664, was 27 g (66%). IR spectrum: 1715 cm^{-1} (C=O). PMR spectrum, δ: 0.94 (3H, t, J = 6 Hz), 1.23 (3H, d, J = 5.5 Hz), 1.1-1.6 (4H, m), 1.9-2.6 ppm (4H, m). Found C 51.2; H 6.9%. $C_9H_{14}Cl_2O$. Calculated: C 51.7; H 6.7%.

2,2-Dialkoxy-2,3-dihydrofurans Ia-c. These compounds were obtained by a method similar to that described in [9] from 1-acyl-2,2-dichlorocyclopropanes IIIa-c and sodium alkoxide at 0-5°C.

TABLE 3. PMR Spectra of 2-Alkyl-4-oxo-3-phenylthioalkanoic Acid Esters IIa-j*

Compound	Chemical shift, δ, ppm (J, Hz)				
	2-H	3-H	R^1	R^2	R^3
IIa	2,43 (1H, dd, $J_1=7, J_2=16$)	3,89 (1H, m, $J_1=1, J_2=7$)	9,46 (1H, d, $J=1$)	2,82 (1H, dd., $J_1=7, J_2=16$)	1,22 (3H, t, $J=7$), 4,07 (2H, q, $J=7$)
IIb	2,3—3,1 (1H, m)	3,5—3,8 (1H, m)	9,31 (0,4H, d, $J=2$), 9,41 (0,6H, d, $J=2$)	1,33 (3H, d, $J=7$)	1,15 (3H, t, $J=7$), 4,11 (2H, q, $J=7$)
IIc †	2,3—3,1 (1H, m)	3,54 (1H, d, $J=10$)	0,7—1,5 (7H, m), 2,3—2,8 (2H, m)	1,31 (3H, d, $J=7$)	3,48 (3H, s)
IId ‡	2,3—3,1 (1H, m)	3,56 (1H, d, $J=10$)	2,17 (3H, s)	1,31 (3H, d, $J=7$)	3,48 (3H, s)
IIe ‡	2,3—3,0 (1H, m)	3,54 (1H, d, $J=10$)	0,97 (3H, t, $J=7$), 2,3—2,9 (2H, m)	1,31 (3H, d, $J=7$)	3,48 (3H, s)
IIf †	2,5—3,5 (1H, m)	2,5—3,5 (1H, m)	6,8—7,8 (5H, m)	1,09 (3H, d, $J=7$)	3,47 (3H, s)
IIg	**	3,79 (1H, dd $J_1=6, J_2=9$)	0,95 (3H, t, $J=7$), 2,2—3,0 (4H, m)	**	3,47 (3H, s)
IIh	**	3,79 (1H, dd., $J_1=6, J_2=9$)	0,83 (3H, t, $J=7$), 1,3—1,8 (2H, m), 2,2—2,9 (4H, m)	**	3,48 (3H, s)
IIi	**	3,85 (1H, dd., $J_1=6, J_2=9$)	0,87 (3H, t, $J=7$), 1,0—1,7 (4H, m), 2,2—2,9 (4H, m)	**	3,48 (3H, s)
IIj	**	3,79 (1H, dd $J_1=6, J_2=9$)	0,75 (3H, t, $J=6$), 1,0—1,6 (6H, m), 2,2—2,9 (4H, m)	**	3,48 (3H, s)

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*The signals of the protons of the phenylthio group show up in the form of multiplets at 6.9-7.4 ppm. In the IR spectra the absorption of carbonyl groups is observed at 1690-1735 cm^{-1}.

†The data from the PMR spectrum of the preponderant diasteromer are presented. According to measurements of the integral intensities of the signals of the methoxy protons, the percentage of the minor component in the mixtures of stereoisomers is 10-15%.

‡Parameters of the PMR spectrum obtained with a Bruker-360 spectrometer (360 MHz) with $CDCl_3$ as the solvent and hexamethyldisiloxane (HMDS) as the internal standard, δ (J, Hz): 1.15 (0.3H, d, J = 7), 1.39 (2.7H, d, J = 7), 2.20 (0.3H, s), 2.27 (2.7H, s), 2.7-2.8 (0.9H, m), 2.9-3.0 (0.1H, m), 3.53 (2.7H, s), 3.69 (0.9H, d, J = 10), 3.68 (0.3H, s), 3.75 (0.1H, d, J = 8), 7.1-7.4 ppm (5H, m).

**The signal of the proton is included in the multiplet at 2.2-3.0 ppm (4H).

4-Oxo-3-phenylthioalkanoic Acid Esters IIa-j. A solution of 15.9 g of benzenesulfenyl chloride in 200 ml of methylene chloride was added dropwise in the course of 1 h in an atmosphere of dry argon at −60°C to −70°C to a solution of 0.1 mole of dihydrofuran Ia-j and 0.2 mole of pyridine in 200 ml of dry methylene chloride, and the mixture was stirred at this temperature for another hour. The mixture was then heated to 0°C, 100 ml of 5% hydrochloric acid was added, and the mixture was stirred at room temperature for 30 min. The organic layer was separated, and the aqueous layer was extracted with methylene chloride (three 50-ml portions). The combined organic extracts were washed successfully with 5% hydrochloric acid (10 ml) and a saturated solution of sodium bicarbonate (20 ml), dried with anhydrous sodium sulfate, and distilled in vacuo.

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PYRYLOCYANINES. 25*

THREE-DIMENSIONAL STRUCTURES OF PYRYLO-2-MONOMETHINECYANINES AND THEIR HETEROANALOGS

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UDC 547.812.5'818.1'821.3:541.63:543.422.25

Symmetrical tetra-tert-butyl-substituted pyrylo-2- and thiopyrylo-2-monomethinecyanines were synthesized by the condensation of 2-methyl-4,6-di-tert-butylpyrylium and -thiopyrylium salts, respectively, with 2-(alkylthio)-4,6-di-tert-butylpyrylium and -thiopyrylium salts. The pyrylo-2-cyanine obtained was converted to a tetra-tert-butyl-substituted pyrido-2-monomethinecyanine by treatment with methylamine. It was shown by PMR spectroscopy that, in contrast to pyrido-2-monomethinecyanine, which exists in the E,E form, its oxygen-containing analog exists in the E,Z form, and its sulfur-containing analog exists in the Z, Z configuration.

The regularities in the absorption spectra of pyrylo-2-cyanines and their sulfur- and nitrogen-containing analogs have been studied in detail [1]. However, in the investigation of these regularities the possibility of the existence of these dyes in different stereoisomeric forms has not yet been taken into account, since, in contrast to polylmethine dyes constructed from nitrogen-containing heterocycles [2], data on the three-dimensional structures of pyrylo- and thiopyrylocyanines have not been available. Information regarding the fine chemical structures of the indicated dyes would also facilitate their purposeful synthesis for the spectral sensitization of electrophotographic materials [3] and quantum electronics [4], in which they find practical application.

In the present research we set out to use PMR spectroscopy to investigate the three-dimensional structures of symmetrical pyrylo-2-, thiopyrylo-2-, and pyrido-2-monomethinecyanines. Tetra-tert-butyl-substituted dyes were selected as the subjects of the study in view of the considerably greater ease of interpretation of their PMR spectra as compared with the spectra of their tetraphenyl-substituted analogs.

The pyrylo- and thiopyrylomonomethinecyanines were obtained by the usual method for the synthesis of monomethinecyanines — by condensation of the corresponding 2-methyl-substituted heterocyclic salts with their 2-alkylthio analogs. We have previously described 2,4-di-tert-butyl-6-methylpyrylium tetrafluoroborate (Ia) and 2,4-di-tert-butyl-6-methylthiopyrylium perchlorate (Ib) [1].

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*See [1] for Communication 24.

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev 252660. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 167-171, February, 1988. Original article submitted September 16, 1986.