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TRANSFORMATION OF ALKYL ESTERS OF 4-OXO-3-PHENYLTHIOALKANOIC ACIDS INTO SUBSTITUTED 4-PHENYLTHIO-2(5H)-FURANONES AND 3-PHENYLTHIOFURANS

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When the solutions of methyl and ethyl esters of 4-oxo-3-phenylthioalkanoic acids are boiled in toluene in the presence of p-toluene sulfonic acid, substituted 4-phenylthio-2(5H)-furanones are formed in good yields. In the reaction with diisobutylaluminum hydride or organomagnesium compounds, the latter convert into the corresponding 3-phenylthiofurans.

4-Oxoalkaloic acids are successfully used in the synthesis of compounds in the furan series [1, 2]. Information on the use of this class of compounds in the synthesis of alkylthio- and aryl-thiofurans and their derivatives, representatives of which have interesting chemical [3-5] and biological properties [6, 7], is limited to examples of the preparation of substituted 4-phenylthiotetrahydro-2-furanones [5, 8]. In the present work, conditions were found for converting esters of 4-oxo-3-phenylthioalkanoic acids (Ia-i) [9] into substituted 4-phenylthio-2(5H)-furanones (IIa-i) and 3-phenylthiofurans (IIIa-h).

TABLE 1. Physicochemical Characteristics of Compounds Synthesized

Compound	mp, °C [bp, °C]	n_D^T	T, °C	Found, %		Empirical formula	Calculated, %		Yield, %
				C	H		C	H	
IIa	69—70*			64,1	5,0	$C_{11}H_{10}O_2S$	64,1	4,9	56
IIb	35—36*			65,6	6,0	$C_{12}H_{12}O_2S$	65,4	5,5	95
IIc		1,5782	16	66,4	6,2	$C_{13}H_{14}O_2S$	66,6	6,0	85
IId	[171—172 (2 hPa)	1,5592	17	68,8	7,0	$C_{15}H_{18}O_2S$	68,7	6,9	94
IIe	42—43*			71,8	5,3	$C_{17}H_{14}O_2S$	72,3	5,0	85
IIf		1,5763	16	65,5	5,6	$C_{12}H_{12}O_2S$	65,4	5,5	85
IIg	[169—170 (2 hPa)	1,5526	17	66,7	6,1	$C_{13}H_{14}O_2S$	66,6	6,0	81
IIh		1,5528	20	67,4	6,6	$C_{14}H_{16}O_2S$	67,7	6,5	80
IIi		1,5506	20	68,2	7,1	$C_{15}H_{18}O_2S$	68,7	6,9	71
IIIa		1,5411	17	71,1	6,4	$C_{13}H_{14}OS$	71,5	6,5	35
IIIb		1,5917	15	70,2	5,9	$C_{12}H_{12}OS$	70,5	5,9	40
IIIc		1,5547	18	72,8	7,4	$C_{15}H_{18}OS$	73,1	7,4	45
IIId		1,5738	17	71,0	6,4	$C_{13}H_{14}OS$	71,5	6,5	86
IIIe		1,5682	17	72,0	7,1	$C_{14}H_{16}OS$	72,4	6,9	88
IIIf	63—64*			76,9	5,8	$C_{18}H_{16}OS$	77,1	5,7	75
IIIg		1,5478	17	74,7	8,0	$C_{17}H_{22}OS$	74,4	8,1	82
IIIh		1,6108	15	78,0	6,9	$C_{21}H_{22}OS$	78,2	6,9	90

*From 2-propanol.

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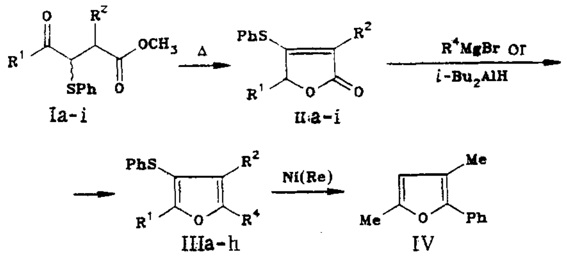
TABLE 2. PMR Spectra of 4-Phenylthio-2(5H)-furanones IIa-i*

Compound	Chemical shift, δ, ppm (J, Hz)		
	5-H	R^1	R^2
IIa	4,15 (1H, q, $J=2$)	4,15 (1H, q, $J=2$)	1,71 (3H, t, $J=2$)
IIb	4,65 (1H, m, $J_1=2$, $J_2=7$)	1,20 (3H, d, $J=7$)	1,71 (3H, d, $J=2$)
IIc	4,4—4,7 (1H, m)	0,77 (3H, t, $J=7$); 1,0—1,6 (2H, m)	1,71 (3H, d, $J=2$)
IId	4,4—4,7 (1H, m)	0,75 (3H, t, $J=7$); 0,9—1,5 (6H, m)	1,67 (3H, d, $J=2$)
IIe	5,3—5,4 (1H, m)	6,5—7,2 (5H, m)	1,77 (3H, d, $J=2$)
IIf	4,7—5,0 (1H, m)	0,94 (3H, t, $J=7$); 1,5—2,1 (2H, m)	5,12 (1H, d, $J=1$)
IIg	4,7—5,0 (1H, m)	0,97 (3H, t, $J=7$); 1,1—1,9 (4H, m)	5,12 (1H, d, $J=1$)
IIh	4,7—5,0 (1H, m)	0,91 (3H, t, $J=7$); 1,1—2,1 (6H, m)	5,12 (1H, d, $J=1$)
IIi	4,7—5,0 (1H, m)	0,85 (3H, t, $J=6$); 1,1—2,1 (8H, m)	5,12 (1H, d, $J=1$)

*In the IR spectra, the $\nu_{C=C}$ and $\nu_{C=O}$ bands are observed in the region of 1630, 1760 cm^{-1}, respectively, for compounds IIa-e and 1575, 1760 cm^{-1} for compounds IIf-i. The proton signals of the phenylthio group appear in the form of multiplets in the 7.0-7.6 ppm region.

2(5H)-Furanones IIa-i are formed in yields of 56-95% when solutions of compounds Ia-i are boiled in toluene in the presence of equimolar amounts of p-toluenesulfonic acid. Cyclization of compounds Ia-e containing a methyl substituent at the α-position to the ester group proceeds much more rapidly than in the case of compounds If-i. To complete the reaction, about 1 h is required in the first case, while in the second case the reaction mixture must be boiled for 24 h.



I, IIa $R^1=H$, $R^2=Me$; b $R^1=R^2=Me$; c $R^1=Et$, $R^2=Me$; d $R^1=Bu$, $R^2=Me$; e $R^1=Ph$, $R^2=Me$; f $R^1=Et$, $R^2=H$; g $R^1=Pr$, $R^2=H$; h $R^1=Bu$, $R^2=H$; i $R^1=C_5H_{11}$, $R^2=H$; III a $R^1=Pr$, $R^2=R^4=H$; b $R^1=R^2=Me$, $R^4=H$; c $R^1=Bu$, $R^2=Me$, $R^4=H$; d $R^1=R^2=R^4=Me$; e $R^1=R^2=Me$, $R^4=Et$; f $R^1=R^2=Me$, $R^4=Ph$; g $R^1=Bu$, $R^2=Me$, $R^4=Et$; h $R^1=Bu$, $R^2=Me$, $R^4=Ph$

Compounds IIb,d,g were converted into 3-phenylthiofurans IIIa-c by the known reaction with diisobutylaluminum hydride [10, 11]. It is worth noting that compounds IIb,d convert fairly smoothly into 2,4,5-trisubstituted 3-phenylthiofurans IIId-h also in the reaction with Grignard reagents.

Thus, although up to the present, there are many publications dealing with methods of synthesis of substituted 4-phenylthio-2(5H)-furanones [4, 12-14] and 3-phenyl-thiofurans [6, 7, 12, 14], the approach used in the present work makes available many compounds, which are difficult to synthesize. An example illustrating the possible use of substituted 3-phenylthiofurans in the synthesis of 2,3,5-trisubstituted furans that are difficult to obtain, is the preparation of furan IV by desulfurization of compound IIIf by Raney nickel.

EXPERIMENTAL

The PMR spectra of 5-10% solutions of the compounds studied in CCl_4 were run on a Tesla BS-467A spectrometer (60 MHz) using HMDS as internal standard. The IR spectra of the compounds were recorded on a Specord 75-IR spectrophotometer. The purity of the compounds obtained was controlled by TLC on aluminum oxide (neutral grade II activity) as well as on silica gel (development by iodine vapors). The characteristics of the compounds synthesized are listed in Tables 1-3.

TABLE 3. PMR Spectra of 3-Phenylthiofurans IIIa-h*

Compound	Chemical shift, δ, ppm (J, Hz)		
	R^1	R^2	R^4
III a	0,77 (3H, t, J=7); 1,0—1,7 (2H, m); 2,55 (2H, t, J=7)	6,13 (1H, d, J=2)	7,12 (1H, d, J=2)
III b	2,22 (3H, s)	1,75 (3H, d, J=1)	7,03 (1H, q, J=1)
III c	0,76 (3H, t, J=6); 0,9—1,6 (4H, m); 2,55 (2H, t, J=7)	1,74 (3H, d, J=1)	6,98 (1H, q, J=1)
III d	2,17 (3H, s)	1,65 (3H, s)	2,08 (3H, s)
III e	2,23 (3H, s)	1,71 (3H, s)	1,12 (3H, t, J=7); 2,43 (2H, q J=7)
III f	2,33 (3H, s)	2,07 (3H, s)	6,6—7,5 (5H, m)
III g	0,76 (3H, t, J=6); 1,0—1,7 (4H, m); 2,2—2,7 (2H, m)	1,67 (3H, s)	1,09 (3H, t, J=7); 2,2—2,7 (2H, m)
III h	0,80 (3H, t, J=6); 1,0—1,7 (4H, m); 2,66 (2H, t, J=7)	2,06 (3H, s)	6,6—7,5 (5H, m)

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*The signals of the phenylthio group protons appear in the form of multiplets in the 6.6-7.1 ppm region. In the IR spectra of compounds IIIa-h, the absorption of the furan ring is observed in the 1585 cm^{-1} region.

4-Phenylthio-2(5H)-furanones (IIa-i). A mixture of 100 mmoles of compound Ia-i [9] and 19 g of p-toluenesulfonic acid monohydrate in 300 ml of toluene was boiled with a Dean—Stark adapter for 1 h (esters Ia-e) or for 24 h (esters If-i). A 100 ml portion of water was added to the reaction mixture, the organic layer was separated, and the aqueous layer was extracted by ether. The organic layers were combined, washed with a saturated solution of sodium chloride, and were fractionally distilled in vacuo to yield compounds IIa,b,d,e,g. Compounds IIc,f,h,i were isolated by chromatography on a column with silica gel, using a 2:1 hexane—ether mixture as eluent.

2-Propyl-, 2,4-Dimethyl-, 2-Butyl-4-methyl-3-phenylthiofuran (IIIa-c). A solution of 15 mmoles of diisobutylaluminum hydride in 30 ml of petroleum ether was added dropwise, with stirring, to a solution of 6 mmoles of 2(5H)-furanone IIb,d,g in 3 ml of absolute ether, while the temperature was maintained by cooling at 20-22°C. The mixture was stirred for 20 more min, and then decomposed by 5% hydrochloric acid (15 ml). The organic layer was separated, and the aqueous layer was extracted by ether (3 × 5 ml). The combined extracts were washed with a saturated aqueous solution of sodium chloride, and dried over anhydrous sodium sulfate. The solvent was distilled, the residue was chromatographed on a column with silica gel, using a 2:1 hexane—ether mixture as eluent.

2,4,5-Trisubstituted 3-Phenylthiofurans (IIId-h). A solution of 4 mmoles of 4-phenylthio-2(5H)-furanone IIb,d in an equal volume of ether was added in the course of 2 min, with stirring, to alkyl(aryl)magnesium bromide, obtained from 12 mmoles of Mg and 12 mmoles of alkyl(aryl) bromide, in 4 ml of absolute ether. The mixture was stirred for 20 more min, and then hydrolyzed by 5% hydrochloric acid (10 ml). The organic layer was separated, and the aqueous layer was extracted by ether (3 × 5 ml). The combined ether extracts were washed with a saturated aqueous solution of sodium chloride and sodium bicarbonate, and dried over anhydrous sodium sulfate. The solvent was distilled, and the residue was chromatographed on a column with silica gel, using hexane as eluent.

3,5-Dimethyl-2-phenylfuran (IV) was obtained by reduction of 1 g (3.6 mmoles) of 3-phenylthiofuran (IIIf) over Raney nickel (4 g) with boiling the reaction mixture in 20 ml of isopropanol. Compound IV was isolated by column chromatography on silica gel in the form of an oily liquid. Yield 0.37 g (60%), n_D^{15} 1.5868. PMR spectrum, δ: 2.10 (3H, d, J = 1 Hz, CH_3); 2.20 (3H, d, J = 1 Hz, CH_3); 5.70 (1H, br. s, CH); 6.6-7.5 ppm (5H, m, C_6H_5). Found, %: C 83.2, H 7.1%. $C_{12}H_{12}O$. Calculated, %: C 83.7, H 7.0%.

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SYNTHESIS OF DERIVATIVES OF 4,5-DIHYDROFURAN, FURAN, AND HEXAHYDROBENZOFURAN FROM CONJUGATED ALKENYNES*

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The regiochemistry of the reaction of 1,2- and 1-substituted derivatives of 1-buten-3-yne and its 4- and 2,4-substituted derivatives of the isoprenoid type with acetoacetic ester and acetylacetone in the presence of the manganese(III) acetate—copper(II) acetate oxidative system was studied. Derivatives of 4,5-dihydrofuran, furan, and hexahydrobenzofuran were obtained.

The radical reactions of conjugated systems with β-dicarbonyl compounds initiated by manganese acetate have recently been the subject of detailed investigation [2-6]. It was shown that in the case of 1-alken-3-ynes the regiochemistry of the process basically depends on the structure of the substrate. 1-Buten-3-yne reacts nonregioselectively with α,α-dioxoalkyl radicals with the commensurable participation of both the double bond and the triple bond [2, 3], while in the case of 2-, 4-, and 2,4-substituted 1-buten-3-ynes the reaction proceeds selectively at the double bond [3, 5, 6].

In the present research we studied the regiochemistry of the reaction of conjugated alkenynes with acetoacetic ester and acetylacetone in the presence of manganese(III) acetate using 1,2- and 1-substituted derivatives of 1-buten-3-yne, as well as its 4- and 2,4-substituted derivatives of the isoprenoid type, as the substrates.

Cyclohexenylacetylene was selected as a 1,2-disubstituted derivative of 1-buten-3-yne. Its reaction with acetoacetic ester under the conditions used in the analogous reactions of 1-alken-3-ynes [60-70°C, substrate:Mn(III):addend:Cu(II) molar ratio 1:1:2:0.07] led only to resinification products, evidently as a consequence of rapid polymerization of the vinyl radical-adducts formed in the addition of an α-carbethoxyacetonyl radical to the triple bond of the substrate [3]. The role of copper(II) acetate in this reaction consists in the oxidation

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*Communication 137 from the series "Reactions of unsaturated compounds." See [1] for communication 136.

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