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THIONYLATION OF 5-ALKYL-3H-FURAN-2-ONES AND THEIR NON-CYCLIC 4-OXOALKANOATE ESTER ANALOGS

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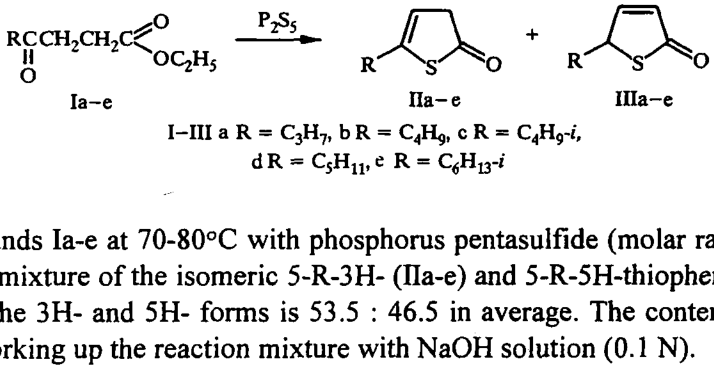
We have studied thionylation of 5-R-3H-furan-2-ones and 4-oxoalkanoates using phosphorus pentasulfide and the Lawesson reagent. It was found that the structure of the reaction products depended on the thionylating agent. Preparative methods have been developed for the synthesis of 5-R-5H- and 5-R-3H-thiophen-2-ones and 5-R-3H-furan-2-thiones.

5-Alkyl-3H-thiophen-2-ones belong to a little studied group of heterocyclic compounds and this is related to preparative difficulties in their synthesis. Promising synthons of the indicated heterocycles are 4-oxoalkanoates containing two electrophilic centers, the position of which determines their susceptibility to heterocyclization.

A method has previously been suggested [1] for preparation of 5-R-3H-thiophen-2-ones based on the treatment of 4-oxoalkanoates with hydrogen sulfide in acidic medium. In this way a mixture of products was obtained and the yield of the desired thiophen-2-one was only 9-15%.

In this work, we present the results of an investigation of reactions of ethyl 4-oxoalkanoates with phosphorus pentasulfide in the absence of solvent and also the thionylation of 5-alkyl-3H-furan-2-ones using phosphorus pentasulfide and the Lawesson reagent.



Ia–e IIa–e IIIa–e

I–III a R = C_3H_7, b R = C_4H_9, c R = C_4H_9-*i*,
d R = C_5H_{11}, e R = C_6H_{13}-*i*

By heating compounds Ia-e at 70-80°C with phosphorus pentasulfide (molar ratio of I:P_2S_5 = 5:1) in CO_2 atmosphere we obtained a mixture of the isomeric 5-R-3H- (IIa-e) and 5-R-5H-thiophen-2-ones (IIIa-e). According to GLC data, the ratio of the 3H- and 5H- forms is 53.5 : 46.5 in average. The content of the 3H- isomer can be increased to 65-69% by working up the reaction mixture with NaOH solution (0.1 N).

Differences in the physicochemical properties permit the separation of the isomeric thiophen-2-ones by fractionation *in vacuo* and isolation of the pure compounds IIa-e and IIIa-e (Table 1).

The structure of IIa-e and IIIa-e was confirmed from IR and PMR spectral data. Hence, the absorption band for the C=O group of the nonconjugated thiolactones IIa-e is found at 1750-1745 cm^{-1}. In the spectra of IIIa-e this band is shifted to longer wavelength and is seen at 1710-1695 cm^{-1}.

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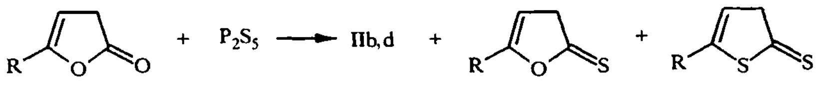
TABLE 1. Chacteristics of Compounds Synthesized

Compound	Empirical formula	Found, % Calculated, %			Bp / 10 mm Hg, °C	n_D^{20}	Yield, %
		C	H	S			
IIa	$C_7H_{10}OS$	59,37 59,15	7,27 7,04	22,78 22,53	130...132	1,4575	52
IIb	$C_8H_{12}OS$	61,76 61,53	7,73 7,69	20,78 20,51	135...137	1,4634	52
IIc	$C_8H_{12}OS$	61,84 61,53	7,81 7,69	20,93 20,51	130...132	1,4671	55
IId	$C_9H_{14}OS$	63,81 63,52	8,56 8,23	19,10 18,81	144...145	1,4671	52
IIe	$C_{10}H_{16}OS$	65,35 65,27	8,83 8,77	17,55 17,43	150...152	1,4685	56
IIIa	$C_7H_{10}OS$	59,33 59,15	7,10 7,04	22,70 22,53	137...139	1,5002	18
IIIb	$C_8H_{12}OS$	61,66 61,53	7,75 7,69	20,43 20,51	142...145	1,5045	15
IIIc	$C_8H_{12}OS$	61,70 61,53	7,75 7,69	20,76 20,51	135...138	1,5055	15
IIId	$C_9H_{14}OS$	63,76 63,52	8,43 8,23	19,10 18,81	150...153	1,5075	17
IIIe	$C_{10}H_{16}OS$	65,40 65,27	8,85 8,77	17,60 17,43	155...158	1,5083	12
Va	$C_8H_{12}OS$	61,66 61,53	7,80 7,69	19,90 20,51	138...140	1,4638	35
Vb	$C_9H_{14}OS$	63,70 63,52	8,30 8,23	18,95 18,81	140...143	1,4650	45

The PMR spectra of products IIa-e have a triplet signal for the vinyl proton at 5.42-5.45 ppm and a doublet for the two protons of the ring $C_{(3)}$ atom at 3.34-3.36 ppm. In the regions 6.02-6.25 (d) and 7.30-7.50 (m) the signals for the vinyl protons at the $C_{(3)}$ and $C_{(4)}$ atoms are found and the multiplet for the proton at $C_{(5)}$ is seen at 4.40-4.43 ppm (Tables 2, 3).

Study of thionylation of 3H-furan-2-ones (IVa,b) (being the internal esters of the enolic form of 4-oxoalkanoic acids) using phosphorus pentasulfide and the Lawesson reagent leading, in the majority of cases, to a quantitative yield of products [2], showed that the structure of the compounds obtained in this way depends on the thionylating reagent used.



IVa,b Va,b VIa,b

IV–VI a R = C_4H_9, b R = C_5H_{11}

Hence refluxing furanones IVa,b in xylene with phosphorus pentasulfide gives a mixture of three products. Of these, the predominant product from GLC data (and the only one separated from the reaction mixture preparatively) is 5-R-3H-thiophen-2-one IIb,d. Other products (the corresponding 5-alkyl-3H-furan-2-thiones Va,b

TABLE 2. PMR Spectral Chacteristics of 5-R-3H-Thiophen-2-ones (II)

Compound	Chemical shift of protons, δ, ppm		
	R (m)	3-H (d, 2H)	4-H (t, 1H)
IIa	0,87...2,30 (7H)	3,34	5,42
IIb	0,87...2,30 (9H)	3,36	5,40
IIc	0,89...2,32 (9H)	3,35	5,44
IId	0,89...2,35 (11H)	3,36	5,42
IIe	0,87...2,40 (13H)	3,36	5,45

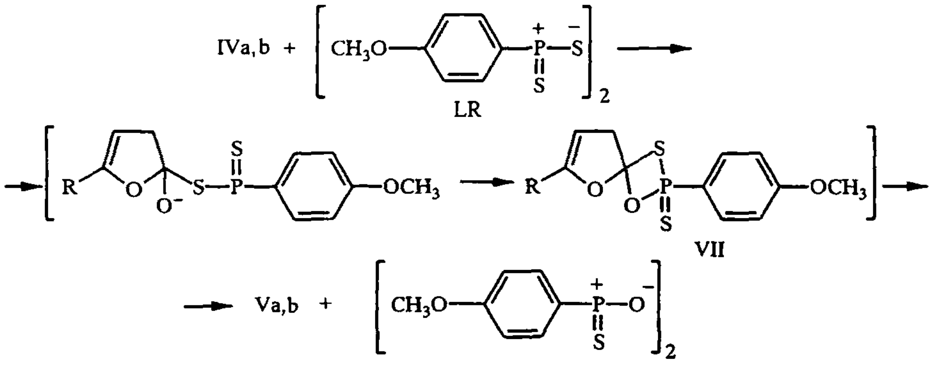
TABLE 3. PMR Spectral Chacteristics of 5-R-5H-Thiophen-2-ones (III)

Compound	Chemical shift of protons, δ, ppm			
	R (m)	3-H (d, 1H)	4-H (t, 1H)	5-H (m, 1H)
IIIa	0,87...2,30 (7H)	6,10	7,40	4,43
IIIb	0,87...2,30 (9H)	6,21	7,50	4,42
IIIc	0,89...2,32 (9H)	6,02	7,30	4,40
IIId	0,89...2,35 (11H)	6,25	7,55	4,42
IIIe	0,87...2,40 (13H)	6,20	7,42	4,40

and 5-alkyl-3H-thiophen-2-thiones VIa,b) were identified by GLC using previously prepared reference substances. The ratio of compounds IIb: Va: VIa was 45: 20: 35 and of compounds IId: Vb: VIb was 48: 24: 28.

5H-Forms of the corresponding thiophen-2-ones, furan-2-thiones, and thiophen-2-thiones were not recorded by us.

Use of the Lawesson reagent (LR) for thionylation causes the reaction to proceed more selectively. Only exchange of the carbonyl group in the starting compounds IVa,b for thiocarbonyl occurs to give 3H-furanthiones (Va,b) in yields up to 45%.



The probable mechanism of thionylation involves reaction of the Lawesson reagent with the furanones IVa,b at the carbonyl group with subsequent formation of the four-membered intermediate VII.

The structure of compounds Va,b was confirmed by the presence of an absorption band in their IR spectra in the region 1025-1020 (characteristic of C=S groups), 1050, 1125 (intense ether group bands), and 1695-1685 cm^{-1} (typical of an unconjugated C=C bond).

Hence the use of phosphorus pentasulfide for thionylation of ethyl 4-oxoalkanoates gives "thiolactonization" of the starting substrates and is the most convenient preparative method for preparing 5-R-3H-thiophen-2-ones II. At the same time, the Lawesson reagent appears to be a more convenient for preparation of 5-R-3H-furan-2-thiones V.

EXPERIMENTAL

PMR spectra were recorded on a Varian FT-80A spectrometer with $CDCl_3$ as solvent and internal standard TMS. IR spectra were taken on a Specord M-80 spectrometer in a capillary layer. The reaction course and purity of the products obtained was monitored by GLC. The chromatograph was LCM-8MD with flame ionization detector and TND-TS-M grade brick sorbent (0.25-0.35 mm fraction) modified with 2% KOH and impregnated with 15% of Apiezon L.

The starting ethyl 4-oxoalkanoates (Ia-e) were prepared by method [3] and the 5-R-3H-furan-2-ones (IVa,b) by the method reported in [4]. The Lawesson reagent was prepared by a known method [2].

Parameters for the compounds synthesized IIa-e, IIIa-e, and Va,b are reported in Table 1.

5-R-3H-Thiophen-2-ones (IIa-e) and 5-R-5H-thiophen-2-ones (IIIa-e). A mixture of ethyl 4-oxoalkanoate (I, 0.1 mole) and phosphorus pentasulfide (0.05 mole) was held in a stream of inert gas (CO_2) at 95-100°C for 1 h. NaOH solution (20%, 10 ml) was added to the reaction mixture cooled to 0°C, and the product extracted with ether. The extract was dried with $MgSO_4$, solvent removed, and the residue distilled in vacuo to give products IIa-e and IIIa-e.

5-R-3H-Furan-2-thiones (Va,b). A mixture of furanone IV (0.01 mole) and the Lawesson reagent (0.005 mole) was refluxed in absolute xylene (10 ml) for 2 h. After cooling, the solvent was distilled off, and the residue purified on an Al_2O_3 column, eluting product V with hexane.

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