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O-ACYLATON OF KETOXIMES OF THE FURAN AND THIOPHENE SERIES IN THE LIQUID–SOLID BODY SYSTEM UNDER INTERPHASE CATALYSIS CONDITIONS

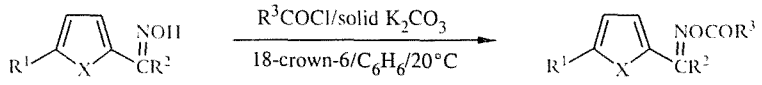
É. Abele, Yu. Popelis, M. Gavars, A. Gaukman, M. Shimanska, and É. Lukevich

The acylation of 2-furanyl- and 2-thienylalkylketoximes by acyl chlorides in a two-phase catalytic system (solid K_2CO_3–C_6H_6–18-crown-6) at room temperature leads to a selective formation of the corresponding O-acetylketoximes in the form of a mixture of E- and Z-isomers.

O-Acylated derivatives of furan- and thiophenealdoximes and ketoximes exhibit antibacterial [1, 2], antifungal [2], and also insecticidal [1, 3], acaricidal [1, 3], fungicidal [4], herbicidal [5], pesticidal [6], and plant-regulating [7] activities. 2-Acetylfuran O-acetyloxime causes coagulation of thrombocytes in rabbits and guinea pigs [8]. Acylaldoximes are used in petrochemistry as additives to lead-containing benzines to increase the octane number [9]. Compounds of this series were less studied than the corresponding O-ethers [10].

The O-acyl derivatives of oximes of the furan and thiophene series are usually obtained by the acylation of the corresponding oximes by acyl chlorides in the presence of pyridine [5, 11-15] of triethylamine [4]. The furan-containing aldoximes are acylated by acetic anhydride in the presence of pyridine, but the reaction is accompanied by a Beckmann rearrangement [16, 17].

We have carried out the acylation of 2-furyl- and 2-thienylalkylketoximes I-VII by carboxylic acid chlorides (R^3COCl) in a two-phase catalytic system (solid K_2CO_3–C_6H_6–18-crown-6) at room temperature. Under these conditions the acylation of oximes leads readily and selectively to the formation of O-acyl derivatives isolated by crystallization or by distillation *in vacuo* in yields of 42-95% in the form of a mixture of E- and Z-isomers.



I–VII

Ia-c; IIa,c; IIIa,c; IVa,c,d; Va,b; VIa,c; VIIa-c

I X = O, R^1 = H, R^2 = CH_3; II X = O, R^1 = H, R^2 = *i*-C_3H_7; III X = O, R^1 = CH_3, R^2 = *i*-C_3H_7; IV X = S, R^1 = H, R^2 = CH_3; V X = S, R^1 = H, R^2 = *i*-C_3H_7; VI X = S, R^1 = Br, R^2 = CH_3; VII X = S, R^1 = Br, R^2 = C_2H_5; a R^3 = CH_3; b R^3 = C_2H_5; c R^3 = C_6H_5; d R^3 = 2-thienyl; e R^3 = *t*-C_4H_9

The formation of nitrones and Beckmann rearrangement products does not occur under these conditions. The O-acylation method that has been developed does not require boiling the reaction mixture to complete the reaction.

The starting ketoximes I-VII were obtained by the reaction of the corresponding ketones with hydroxylamine hydrochloride in ethanol [18]. Ketoximes II-IV, VI, VII are mixtures of E- and Z-isomers [1]. We succeeded in isolating compound I in the form of an E-isomer, and oxime V as in Z-isomer.

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TABLE 1. Acylation Conditions of Furyl- and Thineylalkylketoximes I-VII and Physicochemical Characteristics of O-Acyl Derivatives Obtained

Oxime (ratio of E- and Z-isomers)*	Acyl chloride	Duration of reaction, h	Reaction product	mp or bp	Yield, %
I (100 : 0)	CH_3COCl	2	Ia	67...87*2	70
	C_2H_5COCl	1,5	Ib	104...105	72
	PhCOCl	3,5	Ic	98...99*3	84
	(2-thienyl)COCl	2	Id	69...75	82
	$(CH_3)_3CCOCl$	1,5	Ie	72...76	72
II (20 : 80)	CH_3COCl	1,5	IIa	53...59	42
	PhCOCl	2	IIc	Oil	79
III (45 : 55)	CH_3COCl	1,5	IIIa	142...143/10	69
	PhCOCl	2	IIIc	142...143/0,5	72
IV (40 : 60)	CH_3COCl	2	IVa	115...123	77
	PhCOCl	1,5	IVc	66...70	80
	(2-thienyl)COCl	2,5	IVd	53...56	65
V (0 : 100)	CH_3COCl	2,5	Va	115...117/1,5	51
	C_2H_5COCl	2,5	Vb	123...125/1	57
VI (25 : 75)	CH_3COCl	1,5	VIa	69...77	94
	PhCOCl	3	VIc	103...111	59
VII (35 : 65)	CH_3COCl	1,5	VIIa	51...55	95
	C_2H_5COCl	1,5	VIIb	46...48	77
	PhCOCl	3	VIIc	55...59	77

*The ratio of E and Z-isomers in oximes I-V and VII was established by PMR spectroscopy; the procedure has been described previously in [1].

*2According to the literature data, mp 75°C (Z-isomer); 95°C (E-isomer) [13].

*3According to the literature data, mp 84°C (Z-isomer); 97-98°C (E-isomer) [13].

The structure of the O-acyl derivatives of oximes obtained was confirmed by PMR spectroscopy. In the PMR spectra of the O-acyloximes there are two sharply differing groups of resonance signals. In the 6.1-8.3 ppm range multiplets are observed with chemical shifts and SSCC characteristic for three or two protons of the heterocyclic ring and also of the benzene and thiophene rings in the R^3 substituent. The protons of the alkyl substituents of groups R^1, R^2 and R^3 were recorded in the 1.2-3.6 ppm range. The oxime group has a descreening effect [19], and therefore the weak-field signals of the α-protons of the R^2 substituent appearing at 1.2-3.6 ppm are assigned to the E-isomer, while the similar multiplets in stronger fields are assigned to the Z-isomer. Since the ratio of the E- and Z-isomers in the initial ketoximes and in the acylation reaction products does not coincide in most cases, a partial E/Z-isomerization probably takes place.

Thus, the acylation method of 2-furyl- and 2-thienylalkylketoximes that has been developed is convenient, mild and selective for the synthesis of the corresponding O-acyl derivatives.

EXPERIMENTAL

The mass spectra were studied using solutions in $CDCl_3$ on a Bruker WH-90/DS spectrometer, using TMS as a standard. The mass spectra were recorded on a Kratos MS-25 chromato-mass spectrometer (70 eV) and on a MS-50 mass spectrometer (AEI) at an ionizing voltage of 70 eV, and the temperature of the ionizing chamber of 200°C. The GLC analysis was carried out on a Chrom-5 chromatograph with a flame-ionization detector and using a glass column filled with a 5% OV-17 on a chromosorb W-HP (80-100 mesh), at a thermostat temperature of 160-230°C. The melting points were determined on a Boetius type stage and are given uncorrected. 2-Bromothiophene, 18-crown-6 and pivaloyl chloride were products from the firm Fluka. The acetyl, propionyl and benzoyl chlorides were produced by Reakhim. 2-Thiophenecarbonyl chloride was

TABLE 2. Chemical Shifts (δ, ppm) of Protons of E- and Z-Isomeric O-Acylketoximes*

Reaction product	Stereoisomers, %	The furan and thiophene ring protons			Protons of substituents R^2 and R^3
		3-H	4-H	5-H (CH_3)	
1	2	3	4	5	6
Ia	65 (*E*)	6,91	6,49	7,54	2,25 (CH_3); 2,31 ($COCH_3$)
	35 (*Z*)	7,36	6,59	7,55	2,28 (CH_3); 2,40 ($COCH_3$)
Ib	100 (*E*)	6,92	6,49	7,54	1,26 ($CH_2\underline{CH_3}$); 2,31 (CH_3); 2,54 (CH_2)
Ic	100 (*E*)	7,00	6,52	7,58	2,45 (CH_3); 7,4...7,7 & 8,0...8,2 (C_6H_5)
Id	70 (*E*)	6,98	6,51	7,57	2,43 (CH_3); 7,16 (4'-H); 7,63 (5'-H); 7,94 (3'-H)
	30 (*Z*)	7,50	6,62	7,58	2,48 (CH_3); 7,19 (4'-H); 7,65 (5'-H); 7,98 (3'-H)
Ie	100 (*E*)	6,93	6,49	7,54	1,33 (CMe_3); 2,31 (CH_3)
IIa	90 (*E*)	6,90	6,47	7,53	1,34 ($CH\underline{Me_2}$); 2,24 (CH_3); 3,51 (CH)
	10 (*Z*)	7,35	6,57	*2	1,32 ($CH\underline{Me_2}$); 2,28 (CH_3); 3,51 (CH)
IIc	15 (*E*)	6,98	6,50	*2	1,42 ($CH\underline{Me_2}$); 3,56 (CH); 7,3...7,8 & 8,0...8,3 (C_6H_5)
	85 (*Z*)	7,32	6,59	7,59	1,39 ($CH\underline{Me_2}$); 3,40 (CH); 7,3...7,8 & 8,0...8,3 (C_6H_5)
IIIa	40 (*E*)	6,79	6,08	(2,35)	1,34 ($CH\underline{Me_2}$); 2,24 (CH_3); 3,41 (CH)
	60 (*Z*)	7,26	6,19	(2,37)	1,31 ($CH\underline{Me_2}$); 2,27 (CH_3); 3,31 (CH)
IIIc	100 (*Z*)	7,21	6,19	(2,39)	1,38 ($CH\underline{Me_2}$); 3,37 (CH); 7,3...7,6 & 8,0...8,2 (C_6H_5)
IVa	65 (*E*)	7,44	7,07	7,42	2,26 (CH_3); 2,40 ($COCH_3$)
	35 (*Z*)	7,58	7,15	7,67	2,32 (CH_3); 2,50 ($COCH_3$)
IVc	80 (*E*)	7,50	7,09	7,44	2,53 (CH_3); 7,4...7,6 & 8,1...8,3 (C_6H_5)
	20 (*Z*)	7,61	7,17	7,68	2,59 (CH_3); 7,4...7,6 & 8,1...8,3 (C_6H_5)
IVd	70 (*E*)	7,49	7,09	7,44	2,51 (CH_3); 7,16 (4'-H); 7,62 (5'-H); 7,94 (3'-H)
	30 (*Z*)	7,63	7,17	7,67	2,57 (CH_3); 7,19 (4'-H); 7,69 (5'-H); 8,08 (3'-H)
Va	100 (*Z*)	7,59	7,14	7,62	1,36 ($CH\underline{Me_2}$); 2,29 (CH_3); 3,28 (CH)
Vb	100 (*Z*)	7,58	7,14	7,62	1,27 ($CH_2\underline{CH_3}$); 1,37 ($CH\underline{Me_2}$); 2,59 ($\underline{CH_2}CH_3$); 3,28 (CH)
VIa	40 (*E*)	7,15	7,02	—	2,25 (CH_3); 2,33 ($COCH_3$)
	60 (*Z*)	7,29	7,13	—	2,33 (CH_3); 2,45 ($COCH_3$)
VIc	30 (*E*)	7,21	7,05	—	2,46 (CH_3); 7,4...7,6 & 8,0...8,3 (C_6H_5)
	70 (*Z*)	7,34	7,14	—	2,54 (CH_3); 7,4...7,6 & 8,0...8,3 (C_6H_5)
VIIa	60 (*E*)	7,16	7,13	—	1,32 ($CH_2\underline{CH_3}$); 2,33 (CH_3); 2,85 ($\underline{CH_2}CH_3$)
	40 (*Z*)	7,31	7,04	—	1,21 ($CH_2\underline{CH_3}$); 2,25 (CH_3); 2,78 ($\underline{CH_2}CH_3$)

*The SSCC of the ring protons differ little for the E- and Z-isomers and are practically independent from the substituents R^2 and R^3: $J_{3,4}$ = 3.4, $J_{3,5}$ = 0.8 and $J_{4,5}$ = 1.8 Hz (for furan rings); $J_{3,4}$ = 3.9, $J_{3,5}$ = 1.2 and $J_{4,5}$ = 5.0 Hz (for thiophene rings).

*2The signal is masked by the signals of the second isomer.

TABLE 2 (continued)

Reaction product	Stereo-isomers, %	The furan and thiophene ring protons			Protons of substituents R^2 and R^3
		3-H	4-H	5-H (CH_3)	
1	2	3	4	5	6
VIIb	100 (*Z*)	7,30	7,13	—	1,30 ($CH_2\underline{CH_3}$); 1,32 ($COCH_2\underline{CH_3}$); 2,61 ($\underline{CH_2}CH_3$); 2,85 ($CO\underline{CH_2}CH_3$)
VIIc	40 (*E*)	7,22	7,06	—	1,33 (CH_3); 2,90 (CH_2); 7,4...7,7 & 8,0...8,3 (C_6H_5)
	60 (*Z*)	7,36	7,15	—	1,37 (CH_3); 2,94 (CH_2); 7,4...7,7 & 8,0...8,3 (C_6H_5)

TABLE 3. Mass Spectral Data of O-Acylketoximes*

Compound	m/z (I_{rel}, %)
Ia	167 (9, M^+), 125(68), 108(16), 93(15), 68(26), 53(9), 43 (100), 39(58)
Ib	181 (4, M^+), 125 (51), 109 (42), 94 (100), 68 (12), 64 (24), 57 (82), 37 (69)
Ic*2	229 (18, M^+), 122 (18), 105 (100), 77 (60), 51 (60), 39 (60)
Id*2	235 (13, M^+), 210 (2), 111 (100), 93 (4), 83 (5), 66 (5), 57 (5), 39 (27)
Ie	209 (5, M^+), 125 (16), 108 (7), 94 (14), 85 (15), 68 (6), 57 (100), 41 (25)
IIa	195 (7, M^+), 153 (38), 138 (17), 125 (30), 93 (52), 78 (14), 64 (26), 43 (100)
IIc*2	257 (16, M^+), 226 (3), 198 (12), 122 (42), 105 (100), 94 (59), 77 (61), 65 (18), 51 (59), 43 (60), 39 (60), 27 (60)
IIIa	209 (10, M^+), 167 (38), 152 (14), 139 (27), 107 (62), 78 (40), 60 (16), 52 (43), 43 (100)
IIIc*2	271 (4, M^+), 198 (3), 122 (11), 105 (100), 77 (45), 51 (22), 43 (7)
IVa	183 (3, M^+), 139 (45), 123 (46), 108 (100), 95 (7), 82 (27), 67 (9), 56 (11), 41 (50)
IVc*2	245 (2, M^+), 122 (5), 110 (6), 105 (100), 77 (38), 51 (13), 39 (13)
IVd*2	251 (8, M^+), 210 (2), 128 (5), 124 (5), 110 (100), 83 (7), 57 (6), 45 (6), 39 (25)
Va*2	211 (9, M^+), 168 (67), 151 (33), 140 (25), 109 (38), 96 (11), 77 (9), 42 (100), 38 (24)
Vb	225 (2, M^+), 169 (20), 152 (8), 109 (60), 57 (100), 45 (46), 39 (34)
VIa	261 (3, M^+), 221 (19), 203 (30), 188 (43), 164 (9), 109 (15), 82 (20), 60 (15), 43 (100)
VIc*2	323 (11, M^+), 202 (4), 187 (10), 122 (13), 105 (100), 82 (46), 77 (60), 65 (24), 51 (61), 39 (18)
VIIa	275 (7, M^+), 233 (44), 216 (29), 190 (100), 138 (48), 109 (29), 82 (48), 64 (45)
VIIb*2	289 (4, M^+), 232 (22), 215 (5), 187 (7), 122 (5), 82 (7), 57 (100), 45 (6), 29 (42)
VIIc*2	337 (11, M^+), 187 (25), 122 (41), 105 (100), 82 (55), 77 (60), 51 (58), 45 (34), 39 (26)

*The mass spectra of the E- and Z-isomers are identical.

*2The mass spectra were run on a MS-30 apparatus (AEI).

obtained by the reaction of the corresponding acid with thionyl chloride according to a method described in [20]. The oximes of 2-acetylfuran (I), 2-methyl-1-(2-furyl)-1-propanone (II), 2-methyl-1-(5-methyl-2-furyl)-1-propanone (III), 2-acetylthiophene (IV), 2-methyl-1-(2-thienyl)-1-propanone (V), and 1-(5-bromo-2-thienyl)-1-propanone (VII), were obtained by the reaction of the corresponding ketones with hydroxylamine hydrochloride in the presence of KOH in ethanol [10]. 5-Bromo-2-acetylthiophene was obtained by the acylation of 2-bromothiophene with acetyl chloride according to Friedel–Crafts [21]. The oxime of 5-bromo-2-acetylthiophene (VI) was obtained by the reaction of the ketone with $NH_2OH \cdot HCl/KOH$ in ethanol [18]. Oxime VI was isolated in a yield of 60% in the form of a mixture of E- and Z-isomers (the E/Z ratio 25:75 according to the PMR spectroscopy data).

The results of the elemental analysis of the synthesized compounds correspond to the calculated data.

General Method of Acylation of Oximes I-VII by Acyl Chlorides under an Interphase Catalysis Condition (on the example of the acylation of 2-acetylfuran oxime (I) with acetyl chloride). A 4.15 g (30 mmoles) portion of a powdered

K_2CO_3 was added to a solution of 1.25 g (10 mmoles) of oxime 1 and 0.26 g (1 mmole) of 18-crown-6 in 30 ml of anhydrous benzene, and then a solution of 1.42 ml (20 mmoles) of acetyl chloride in 5 ml of benzene was added dropwise in the course 30 min. The mixture obtained was stirred at room temperature for another 1.5 h (GLC control, 180°C). At the end of the reaction, the mixture was washed with water, the organic layer was separated, dried over $CaCl_2$, and filtered, benzene was evaporated at a reduced pressure, and the residue was crystallized from hexane. Yield, 1.1 g (70%) of compound Ia, mp 67-68°C in the form of a mixture of E- and Z-isomers (the E/Z ratio 65:35). The O-acylketoximes Ib-e, IIa, IVa, c, d, VIa, c and VIIa-c were obtained in a similar way. Compounds IIIa, c and Va, b were isolated by distillation *in vacuo*. The characteristics of the compounds obtained are listed in Tables 1-3.

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