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*Heino RANG**, *Tõnis PEHK***, *Sirje VIITMAA**, *Lilja LAHE**,
*Ants ERM**, *Ilme LÕIVEKE**, and *Koit LÄÄTS****SYNTHESIS OF JUVENILE HORMONE ANALOGUES.****15. SYNTHESIS OF NOVEL 1-AROXY-3-METHYL-5-(MONO-, DI-, AND TRIOXA-ALKYL)-2-PENTENES**

The first to synthesize herbicidally and insecticidally active oxa compounds from chloromethyl ether were Mamedov and coworkers [1, 2]. In 1972—1986 a number of oxa compounds, derivatives of benzene and benzodioxolan [3], oxa-alkenyl carboxylic acids [4], oxa-alkenylbenzene [5], and ethers of hydroquinone [6–13] were patented as insecticides, acaricides, and juvenoids. One of the authors with coworkers has earlier worked out a number of oxa compounds [14–18] with juvenoidal activity, of which ephoxene was registered in 1991 [19].

Based on the scheme presented in [18] we have synthesized some novel 1-aroxy-3-methyl-5-(mono-, di-, and trioxa-alkyl)-2-pentenenes with juvenoidal activity which have been tested on leaf louse [20]. These compounds have been synthesized from cyclohexylchloromethyl ether [21] and novel chloromethyl ethers (see Table 1). From the adduct of chloromethyl ether and isoprene a quaternary salt has been obtained with dimethylaniline [15, 22] and alkylated in water solution to the corresponding phenolate [15]. The aroxy compound was separated, vacuum-distilled, and identified by IR and ¹³C NMR spectra.

Experimental**1. Synthesis of chloromethyl ethers**

1-Chloro-3,5-dimethyl-2-oxahexane. 1380 g (13.5 moles) of 4-methyl-2-pentanol and 480 g (16.0 moles) of paraform were stirred and cooled to –5°C. Hydrogen chloride was directed into the mixture. The temperature of the mixture was –5 to 0°C. The reaction was finished when the paraform was dissolved. The organic layer was separated and distilled in vacuum. The yield of 1-chloro-3,5-dimethyl-2-oxahexane was 1899 g (93.2%). The new chloromethyl ethers synthesized are presented in Table 1.

2. Addition of chloromethyl ether to isoprene

Synthesis of the adduct of 1-chloro-3,5-dimethyl-2-oxahexane and isoprene. To 152.6 g (1 mole) of chloromethyl ether (Table 1, No. 1) and 81.6 g (1.2 mole) of isoprene, 1.3 ml of 5.9% solution of tin tetrachloride in dichloroethane was added while stirring in an atmosphere of argon. The reaction temperature was 20–27°C. The density of the mixture increased from 0.835 to 0.913 ($\Delta d = 0.078$). Then 5 g of carbamide was added, the mixture was stirred, settled, and carbamide with the catalyst complex was filtered off. The unreacted substances were evaporated and the mono adduct was distilled from the residue at 93–96°C/1 mm torr, yield 161.9 g (70.4%). Mono adducts are characterized in Table 2.

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Table 1

Characterization of chloromethylethers

No	Starting alcohol	Chloroether	B. t°, °C/torr	n _D ²⁰	d ₄ ²⁰	Yield, %	Purity GLC, %	Mol. mass		Content of Cl, %	
								Calculated	Determined	Calculated	Determined
1	4-Methyl-2-pentanol	1-Chloro-3,5-dimethyl-2-oxahexane	71/5	1.4258	0.9371	93.2	98.7	150.65	149.2	23.53	23.5
2	2-Ethyl-1-hexanol	1-Chloro-4-ethyl-2-oxaoktane	100—101/10	1.4372	0.9454	98.0	98.1	178.70	177.8	19.84	19.8
3	3-Oxa-1-pentanol	1-Chloro-2,5-dioxahexane	62/10	1.4285	1.0623	97.1	98.2	138.60	138.1	25.58	25.6
4	3,6-Dioxa-1-oktanol	1-Chloro-2,5,8-trioxadecane	107—108/5	1.4432	1.0954	96.7	97.3	182.59	183.3	19.42	19.4

Table 2

Characterization of mono adducts

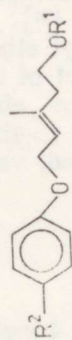
No.	Starting chloromethyl-ether	Mono adduct	B. p., °C/torr	n_D^{20}	Mol. mass			Content of Cl, %		Yield, %
					Calculated	Determined	*Calculated	Primary	Saponified	
1	1-Chloro-3,5-dimethyl-2-oxahexane	$C_{12}H_{23}ClO$	93—96/1	1.4565—1.4585	288.77	277.2	16.21	14.8	16.2	66.0
2	1-Chloro-4-ethyl-2-oxaoktane	$C_{14}H_{27}ClO$	110—115/0.1	1.4700	246.82	239.2	14.36	12.4	13.9	62.1
3	1-Chloro-2,5-dioxaheptane	$C_{10}H_{19}ClO_2$	95—99/1	1.4578—1.4583	206.71	203.9	17.15	14.03	16.7	52.8
4	1-Chloro-2,5,8-trioxadecane	$C_{12}H_{23}ClO_3$	113—114/0.1	1.4660 eq	250.77	248.1	14.14	9.0	13.0	60.6
5	Cyclohexyl chloromethyl ether	$C_{12}H_{21}ClO$	110—115/1	1.4840	216.75	212.4	16.36	14.0	15.9	64.5



Characterization of bisoxa compounds

Table 3

Characterization of phenoxy compounds



No.	R ¹	R ²	B. p., °C/torr	n _D ²⁰	Mol. mass		Purity, GLC			IR spectrum, cm ⁻¹	Relative retention time, 1.0
					Calculated	Determined	E+Z isomers, %	from this isomer, %	Yield, %		
1	2	3	4	5	6	7	8	9	10	11	12
1	(CH ₃) ₂ CHCH ₂ CH(CH ₃)	Cl	122—126/0.1	1.5058	310.87	308.6	95.4	71.5	53.9	650; 660; 690; 840; 1020; 1100; 1250; 1370; 1400; 1410; 1490; 1510; 1600; 1620; 2880; 2940; 2980; 3060; 3100	1.23
2	(CH ₃) ₂ CHCH ₂ CH(CH ₃)	CH ₃	123—126/0.1	1.4990	290.45	289.1	93.2	76.7	67.2	820; 1020; 1090; 1240; 1380; 1470; 1510; 1590; 1620; 2880; 2930; 2960; 3040; 3070; 3100	1.22
3	(CH ₃) ₂ CHCH ₂ CH(CH ₃)	C ₂ H ₅	124—130/0.15	1.4980	304.48	303.2	90.1	70.3	65.4	830; 1020; 1100; 1240; 1380; 1390; 1470; 1510; 1580; 1610; 2870; 2940; 2970; 3040; 3060; 3100	1.20
4	(CH ₃) ₂ CHCH ₂ CH(CH ₃)	i-C ₃ H ₇	127—130/0.1	1.4945	318.51	317.6	91.2	81.6	70.5	830; 1010; 1100; 1240; 1380; 1390; 1480; 1520; 1590; 1620; 2870; 2940; 2970; 3040; 3070	1.23

Table 3 continued

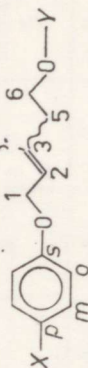
1	2	3	4	5	6	7	8	9	10	11	12
5	$\text{CH}_3(\text{CH}_2)_3\text{CH}(\text{C}_2\text{H}_5)\text{CH}_2$	C_3H_5	138—140/0.04	1.4958	332.54	330.1	93.2	76.5	63.2	830; 1020; 1120; 1240; 1380; 1470; 1520; 1590; 1620; 2870; 2940; 2970; 3040	1.21
6	$\text{CH}_3(\text{CH}_2)_3\text{CH}(\text{C}_2\text{H}_5)\text{CH}_2$	Cl	137/0.03	1.5054	338.92	336.7	96.7	67.4	58.2	640; 650; 680; 830; 1020; 1110; 1240; 1390; 1470; 1500; 1590; 1600; 2880; 2950; 2970; 3060; 3100	1.23
7	Cyclohexyl	CH_3	135—136/0.2	1.5182	288.43	280.5	92.1	66.4	65.2	830; 1020; 1120; 1250; 1360; 1380; 1400; 1460; 1520; 1600; 1620; 2870; 2950; 3040; 3070; 3100	1.21
8	Cyclohexyl	C_2H_5	146—147/0.1	1.5200	302.46	300.9	93.3	72.5	64.8	830; 1020; 1110; 1240; 1360; 1370; 1390; 1460; 1520; 1590; 1620; 2870; 3040; 3070; 3100	1.24
9	Cyclohexyl	Cl	148—149/0.1	1.5320	308.85	307.6	97.1	71.9	53.9	640; 650; 680; 840; 1020; 1110; 1250; 1360; 1380; 1400; 1460; 1500; 1590; 1610; 2870; 2950; 3040; 3080; 3100	1.24
10	$\text{C}_2\text{H}_5\text{OCH}_2\text{CH}_2$	CH_3	126—130/0.3	1.5040	278.39	272.1	96.0	54.0	40.8	820; 1020; 1120; 1250; 1360; 1390; 1460; 1520; 1590; 1620; 2880; 2940; 3040; 3070	1.20

Table 3 continued

1	2	3	4	5	6	7	8	9	10	11	12
11	$C_2H_5OCH_2CH_2$	ClH^{β}	138—139/0.2	1.5032	298.81	295.3	93.8	58.4	39.2	630; 640; 670; 830; 1010; 1120; 1240; 1360; 1390; 1470; 1500; 1590; 1600; 2870; 2930; 2980; 3040; 3080; 3100	1.21
12	$C_2H_5OCH_2CH_2$	C_2H_5	120—126/0.07	1.5021	292.42	291.5	95.2	61.0	47.1	830; 1020; 1120; 1240; 1360; 1380; 1460; 1520; 1590; 1610; 2880; 2940; 2970; 3030; 3060	1.20
13	$C_2H_5O(CH_2)_2OCH_2CH_2$	H	132—135/0.06	1.5022	308.42	305.9	93.0	76.0	32.5	700; 760; 1000; 1010; 1040; 1120; 1240; 1370; 1390; 1460; 1500; 1590; 1600; 2880; 2950; 2980; 3030; 3070; 3470	1.23
14	$C_2H_5O(CH_2)_2OCH_2CH_2$	Cl	135—139/0.03	1.5114	342.87	336.9	91.2	80.0	29.8	640; 650; 680; 840; 1010; 1050; 1100; 1140; 1240; 1360; 1400; 1480; 1500; 1530; 1590; 1600; 2880; 2950; 2980; 3050; 3080; 3100; 3470	1.24
15	$C_2H_5O(CH_2)_2OCH_2CH_2$	CH_3	130—133/0.03	1.5016	322.44	320.1	93.4	81.8	38.2	820; 1020; 1120; 1240; 1350; 1380; 1460; 1510; 1580; 1610; 2880; 2920; 2980; 3030; 3060; 3480;	1.23

1	2	3	4	5	6	7	8	9	10	11	12			
11	$C_6H_5OCH_2CH_3$	CH_3	$120-1260.2$	1.5079	253.01	255.3	99.8	19.4	39.3	630	640	670	830	1.21
12	$C_6H_5OCH_2CH_3$	CH_2	$120-1260.07$	1.5071	222.57	241.5	93.3	51.0	47.1	400	400	1100	1210	1.30
13	$C_6H_5O(CH_2)_2OCH_2CH_3$	H	$132-1350.06$	1.5025	308.45	315.9	33.0	76.3	33.5	1300	1300	1600	1800	1.23

Table 4

 ^{13}C chemical shifts of *E* and *Z* isomers of

X	Y	Isomer	s	o	m	p	1	2	3	4	5	6	Y	X		
$(CH_3)_2CH-$	$CH(CH_3)CH_2CH(CH_3)_2$	<i>E</i> 3.5	156.63	114.02	126.56	140.06	64.14	121.20	137.06	16.39	39.54	66.32	73.05	22.13	22.73	
		<i>Z</i>				140.02	64.05	122.18	137.22	23.40	32.94	66.09	73.19	22.14	22.67	
CH_3-	$CH_2-CH_2-O-CH_2-CH_3$	<i>E</i> 1.5	156.10	113.80	129.06	128.71	63.93	121.00	136.73	16.08	38.69	69.04	69.46	69.13	65.77	
		<i>Z</i>				128.68	63.82	121.99	136.81	23.11	32.12	68.81	69.60	69.17	65.79	
$Cl-$	$CH_2-CH_2OCH_2CH_2OCH_2CH_3$	<i>E</i> 5.8	156.59	115.08	128.24	124.25	64.01	120.13	137.15	15.84	38.44	68.63	69.22	69.59	68.91	
		<i>Z</i>	156.61			124.20	63.96	121.22	137.07	22.78	31.92	68.41	69.36	69.65	68.89	
CH_3CH_2-	C_6H_{11}	3.2	156.51	114.01	128.03	135.46	64.11	122.02	137.41	23.44	32.93	65.58	76.77	31.70	23.46	
		<i>Z</i>				135.66	64.34	121.31	137.42	16.50	39.24	69.31	73.33	39.46	23.57	25.46
CH_3-CH_2-	$CH_2CH(C_2H_5)CH_2CH_2CH_2CH_3$	<i>E</i> 3.6	156.72	114.21	128.21	135.64	64.23	122.18	137.58	23.52	32.64	69.06	73.46	39.51	23.70	24.80
		<i>Z</i>				135.64	64.23	122.18	137.58	23.52	32.64	69.06	73.46	39.51	23.70	24.80

3. Synthesis of aroxy compounds

1-(4-Chlorophenyl)-1,7-dioxa-4,8,10-trimethyl-3-undecene. 100 g of the adduct of 1-chloro-3,5-dimethyl-2-oxahexene and isoprene (0.43 mole of primary chlorides), 65.4 g (0.54 mole) of dimethylaniline, and 55 ml of methanol were stirred at 50°C for 5 h; quaternary salt was obtained. The mixture was cooled, 200 ml of water and 100 ml of toluene were added, and stirred. The water solution of the quaternary salt was separated and alkalified to pH=9, then extracted with toluene. 55.3 g (0.43 mole) of 4-chlorophenol and 86 g of 20% sodium hydroxide solution (0.43 mole) were stirred. At 70°C the extracted water solution of the quaternary salt was added to the phenolate solution obtained and stirred at the same temperature for 4 h. The mixture was cooled and extracted with toluene. The toluene solution was washed with 10% sodium hydroxide solution and then with water. Toluene and dimethylaniline were distilled from the toluene solution in vacuum. From the residue 1-(4-chlorophenyl)-1,7-dioxa-4,8,10-trimethyl-3-undecene was distilled at 122—126°C/0.1 torr. The yield was 75.5 g (53.9%). The phenoxy compounds obtained are presented in Table 3 and the ¹³C NMR spectra in Table 4.

Chloride compounds were analysed by means of a gas chromatograph Chrom 5 (Laboratorne Pristroje, Czechoslovakia) on glass capillary column 1—24 m, i.d. — 0.27 mm coated with TCEP — 1,2,3-tris-(2-cyanoethoxy)propane. Temperature of column oven 70—100°C, temperature of injection port 150—180°C, carrier gas N₂, flow rate 1.2 cm³/min.

Phenoxy compounds were analysed by means of a gas chromatograph Chrom 5 (Laboratorne Pristroje, Czechoslovakia) on glass capillary column 1—47 m, i.d. — 0.3 mm coated with PDEAS (phenyldiethanol-aminesuccinate), temperature of column oven 200°C, temperature of injection port 270°C, carrier gas N₂, flow rate 2.0 cm³/min.

Infrared spectra were taken on a Specord 75 IR spectrometer (Zeiss, Jena) in the region 400—4000 cm⁻¹ using the KBr window.

Mol. mass is determined ebullioscopically, ¹³C NMR spectra were measured from CDCl₃ solutions with Bruker AM-500 spectrometer. Standard pulse programmes for 2D correlations were used.

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JUVENILHORMOONI ANALOOGIDE SÜNTEES.

15. UUTE 1-AROKSÜ-3-METÜÜL-5-(MONO-, DI- ja TRIOKSAALKÜÜL)-2-PENTEENIDE SÜNTEES

Saadi rida 1-aroksü-3-metüül-5-(mono-, di- ja trioksaalküül)-2-penteene, mida isoleerimustati infrapunaste ja ^{13}C TMR-spektritega. Süntees teostati isopreeni haloalküüleerimisel vastavate klorometüüleetriega ja järgneval asendatud fenoolide o-alküüleerimisel saadud aduktidega.

Хейно РАНГ, Тынис ПЕХК, Сирье ВИИТМАА, Лилья ЛАХЕ, Антс ЭРМ, Ильме ЛЫИВЕКЕ, Коит ЛЭЭТС

СИНТЕЗ АНАЛОГОВ ЮВЕНИЛЬНОГО ГОРМОНА.

15. СИНТЕЗ НОВЫХ 1-АРОКСИ-3-МЕТИЛ-5-(МОНО-, ДИ- И ТРИОКСА-АЛКИЛ)-2-ПЕНТЕНОВ

Получен ряд 1-арокси-3-метил-5-(моно-, ди- и триоксаалкил)-2-пентенов, которые охарактеризованы ИК- и ^{13}C ЯМР-спектрами. Синтез осуществлен галоалкилированием изопрена соответствующими хлорметиловыми эфирами и последующим o-алкилированием замещенных фенола получаемыми галоаддуктами.