SYNTHESIS OF SOME 9-OXA AND 10-OXA ANALOGUES OF ACYCLIC JUVENOIDS*

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A series of esters and amides of 9-oxa-2-alkenoic acids, 10-oxa-2-alkenoic acids, and 10-oxa--2,6-alkadienoic acids has been prepared. The substances are analogues of the insect juvenile hormone.

In connection with effort to obtain further analogues of the insect juvenile hormone we have now prepared some 9-oxa and 10-oxa compounds; their synthesis is the object of the present communication.** The 9-oxa analogues comprise esters and amides of 9-oxa-2-alkenoic acids and the 10-oxa analogues relate to (*cf.* the corresponding Czechoslovak Patent Applications[1]) esters and amides of 10-oxa-2-alkenoic acid and 10-oxa-2,6-alkadienoic acids.

In the preparation of 10-oxa analogues (Scheme 1), there were used as the starting materials 3-alkoxy-2-butanones, namely, 4-(1,1-dimethylethoxy)-2-butanone (*Ia*), 4-(1-methyl-propoxy)-2-butanone (*IIa*), and 4-(1-ethylpropoxy)-2-butanone (*IVa*), obtained by reaction of the corresponding alcohols with methyl vinyl ketone[2]. The preparation of 9-oxa analogues was performed from 1-alkoxy-2-propanones, namely, 1-(2-methyl-propoxy)-2-propanone (*Va*), 1-(2,2-dimethylpropoxy)-2-propanone (*VIa*), and 1-(1,1-dimethylethoxy)-2-propanone (*VIIa*), obtained by the acid-catalysed reaction of the corresponding alcohols with diazoacetone[3]. Reaction of thus-prepared alkoxybutanones and alkoxypropanones with diethyl ethoxycarbonylmethanephosphonate[4,5] or ethoxycarbonylmethylenetriphenylphosphorane[6,7] yielded esters of α,β-unsaturated oxa acids which were reduced with lithium aluminium hydride (either directly or after the previous hydrogenation) to afford the corresponding oxa alcohols. By the action phosphorus tribromide in the presence of pyridine or on treatment with bromine and triphenylphosphine[8] in dimethylformamide, the oxa alcohols

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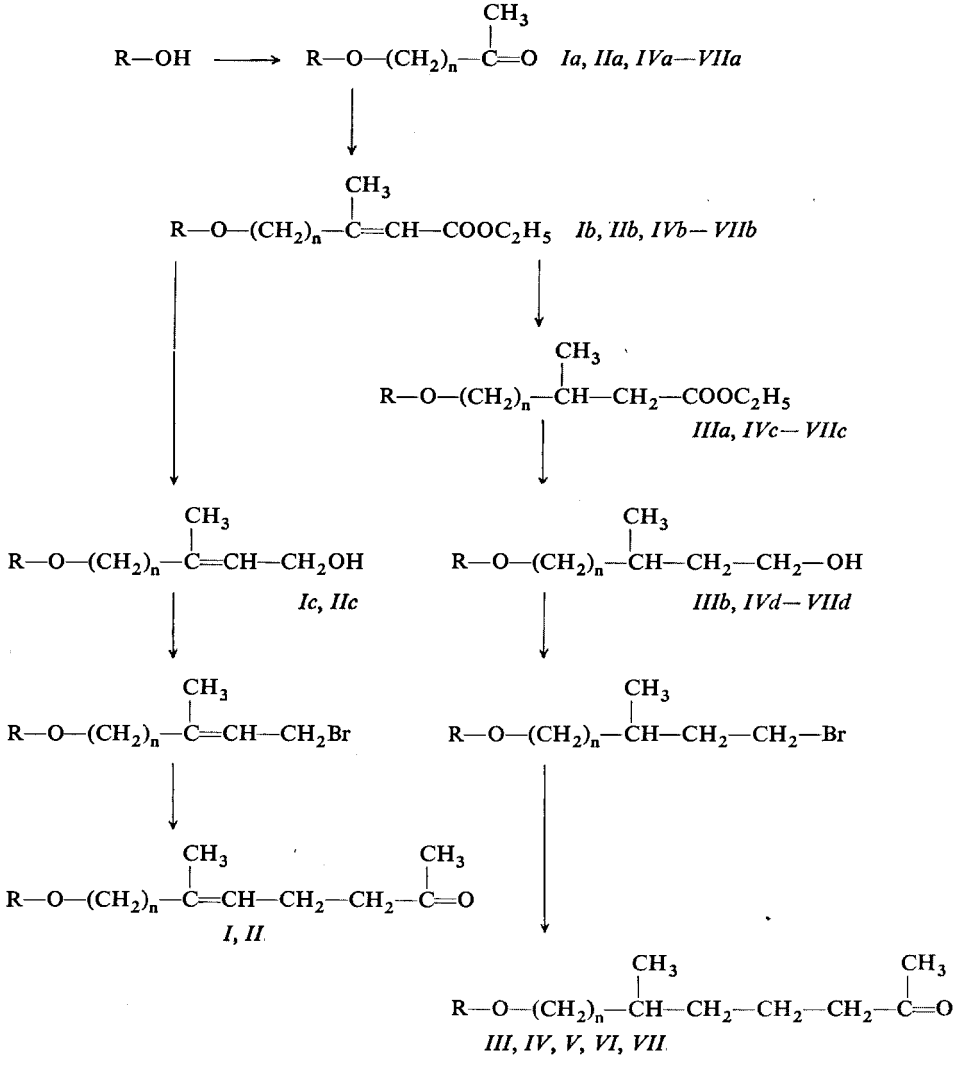
** The biological activity of the present substances will be reported elsewhere in collaboration with workers of the Institute of Entomology, Czechoslovak Academy of Sciences, Prague.

were converted to the corresponding bromides which afforded the oxa ketones *I–VII* by reaction with ethyl acetoacetate and the subsequent ketonic hydrolysis.

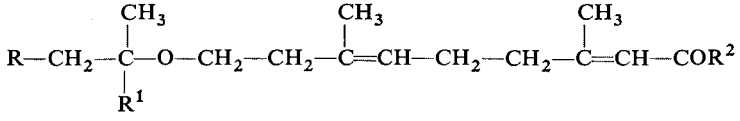
The thus-prepared oxa ketones *I–IV* were converted to esters and amides



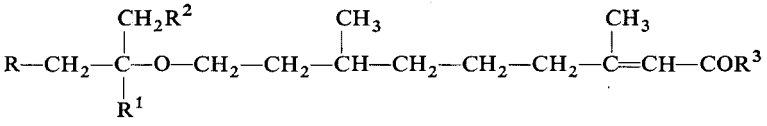
I, n = 2, R = $(CH_3)_3C$—
II, n = 2, R = $(C_2H_5)(CH_3)CH$—
III, n = 2, R = $(CH_3)_3C$—
IV, n = 2, R = $(C_2H_5)_2CH$—
V, n = 1, R = $(CH_3)_2CH$—CH_2
VI, n = 1, R = $(CH_3)_3CCH_2$—
VII, n = 1, R = $(CH_3)_3C$—

SCHEME 1

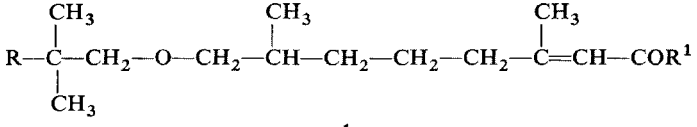
of 10-oxa-2-alkenoic acids or 10-oxa-2,6-alkadienoic acids *VIII–XVII* by reaction with ethoxycarbonylmethylenetriphenylphosphorane, dialkyl alkoxycarbonylmethanephosphonate or diethyl esters of N-substituted or N,N-disubstituted aminocarbonylmethanephosphonic acids. Analogous reactions were used to convert the oxa ketones *V–VII* into esters and amides of 9-oxa-2-alkenoic acids *XVIII–XXV*.



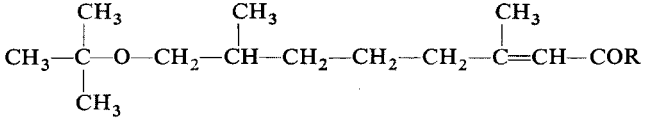
VIII, R = H, $R^1 = CH_3$, $R^2 = OC_2H_5$
IX, R = CH_3, R^1 = H, $R^2 = OC_2H_5$
X, R = CH_3, R^1 = H, $R^2 = N(C_2H_5)_2$



XI, R = H, $R^1 = CH_3$, R^2 = H, $R^3 = OC_2H_5$
XII, R = H, $R^1 = CH_3$, R^2 = H, $R^3 = OCH(CH_3)_2$
XIII, R = H, $R^1 = CH_3$, R^2 = H, $R^3 = N(C_2H_5)_2$
XIV, R = H, $R^1 = CH_3$, R^2 = H, $R^3 = NHC_2H_5$
XV, R = CH_3, R^1 = H, $R^2 = CH_3$, $R^3 = OC_2H_5$
XVI, R = CH_3, R^1 = H, $R^2 = CH_3$, $R^3 = OCH(CH_3)_2$
XVII, R = CH_3, R^1 = H, $R^2 = CH_3$, $R^3 = N(C_2H_5)_2$



XVIII, R = H, $R^1 = OC_2H_5$
XIX, R = H, $R^1 = N(C_2H_5)_2$
XX, R = CH_3, $R^1 = OC_2H_5$
XXI, R = CH_3, $R^1 = OCH(CH_3)_2$
XXII, R = CH_3, $R^1 = N(C_2H_5)_2$
XXIII, R = CH_3, $R^1 = NHC_2H_5$



XXIV, R = OC_2H_5
XXV, R = $N(C_2H_5)_2$

EXPERIMENTAL

The IR spectra were taken in tetrachloromethane. The NMR spectra were measured in deuteriochloroform; tetramethylsilane was used as internal standard; chemical shifts are given in δ (p.p.m.) and coupling constants in Hz. Column chromatography was performed on silica gel partially deactivated by 12% water. Gas chromatography was carried out on a Pye Argon Chromatograph apparatus with a radioactive ionisation detector.

Preparation of 4-Alkoxy-2-butanones *Ia*, *IIa*, and *IVa*

A mixture of the corresponding alcohol (0·5 g), red mercuric oxide (0·1 g), and boron trifluoride etherate (0·1 g) was heated to 80—100°C, cooled down to 20°C, treated with the corresponding alcohol (0·2—0·4 mol) and methyl vinyl ketone (0·18 mol), and the whole mixture kept at room temperature for 36—80 h. The course of the reaction was checked by thin-layer chromatography. The mixture was then diluted with water, extracted with ether, and the ethereal extract processed as usual, finally by fractional distillation of the residue to afford 4-(1,1-dimethylethoxy)-2-butanone[9] (*Ia*), 4-(1-methylpropoxy)-2-butanone (*IIa*), and 4-(1-ethylpropoxy)-2-butanone (*IVa*) in 20—30%, 65%, and 70% yields, resp.

Preparation of 1-Alkoxy-2-propanones *Va*—*VIIa*

To a solution of diazomethane (0·19 mol) in ether (350ml) there was added dropwise at —15°C a solution of acetyl chloride (0·07 mol) in ether (10 ml), the cooled mixture kept for 1 h, and then concentrated under diminished pressure at —5 to 0°C to the volume of 20—30 ml. The corresponding alcohol (0·15—0·25 mol) and boron trifluoride etherate (0·2—0·3 g) were added to the concentrate and the mixture heated to 20—30°C (evolution of nitrogen). When the reaction was complete water was added, the product extracted with ether, the extract processed as usual, and the residue subjected to fractional distillation to afford 1-(2-methylpropoxy)-2-propanone (*Va*), 1-(2,2-dimethylpropoxy)-2-propanone (*VIa*), and 1-(1,1-dimethylethoxy)-2-propanone (*VIIa*) in 60, 60, and 25% yields, resp.

Preparation of Ethyl Esters of α,β-Unsaturated Oxa Acids *Ib*, *IIb*, *IVb*—*VIIb*

A. To a solution of diethyl ethoxycarbonylmethanephosphonate (0·055 mol) in dimethylformamide (50 ml) there was added dropwise under nitrogen at 20—30°C ethanolic sodium ethoxide (from 0·052 gramatom of sodium and 15 ml of ethanol). After 1 h, the alkoxy ketone (0·05 mol) was added, and the mixture kept 1 h at room temperature and 1—3 h at 50—70°C. The reaction course was checked by thin-layer chromatography. The mixture was then diluted with 0·5% aqueous acetic acid, extracted with light petroleum, and processed as usual to afford the crude ester which was purified by distillation. The yields were 10—40% in reactions of 4-alkoxy-2-butanones and 75—84% in reactions of 1-alkoxy-2-propanones. The following esters were prepared: ethyl 3,7,7-trimethyl-6-oxa-2-octenoate (*Ib*), ethyl 3,7-dimethyl-6-oxa-2-nonenoate (*IIb*), ethyl 3,7-dimethyl-5-oxa-2-octenoate (*Vb*), and ethyl 3,6,6-trimethyl-5-oxa-2-heptenoate (*VIIb*).

B. To a suspension of sodium hydride (0·052 mol) in 1,2-dimethoxyethane or dimethylformamide (40—50 ml) there was added dropwise under nitrogen at 20—30°C diethyl ethoxycarbonylmethanephosphonate (0·055 mol), the whole stirred for 1 h, treated with the alkoxy ketone (0·05 mol), and processed analogously to procedure *A* to afford esters *Ib*, *IIb*, ethyl 7-ethyl-3-methyl-6-oxa-2-nonenoate (*IVb*), and ethyl 3,7,7-trimethyl-5-oxa-2-octenoate (*VIb*) in 75—93% yields.

C. A mixture of ethoxycarbonylmethylenetriphenylphosphorane (0·025 mol), the alkoxy ketone (0·020 mol), benzoic acid (0·002 mol), and benzene (40 ml) was refluxed in nitrogen atmo-

sphere and the reaction course checked by thin-layer chromatography. Reaction of 1-alkoxy--2-propanones was complete after 8—12 h. In the case of 4-alkoxy-2-butanones, the mixture was heated for 16—20 h, treated with an additional portion (0·013 mol) of ethoxycarbonylmethylenetriphenylphosphorane and benzoic acid (0·001 mol), and the reflux continued for further 16—20 h. The benzene was then evaporated and the residue triturated repeatedly with light petroleum. The light petroleum extracts were combined and processed as usual to afford the crude ester which was purified by distillation. The yields were 80—90% in reactions of 1-alkoxy-2-propanones and 70—80% in reactions of 4-alkoxy-2-butanones. By this route, compounds *Ib*, *IIb*, *Vb*, and *VIb* were prepared.

Preparation of Ethyl Oxaalkanoates *IIIa*, *IVc*—*VIIc*

The appropriate ethyl oxaalkenoate (0·025 mol) in ethanol (20 ml) was hydrogenated over 5% Pd-C catalyst (200 mg), the mixture filtered, the filtrate diluted with water, and extracted with ether to afford (yields, about 90%) ethyl 3,7,7-trimethyl-6-oxa-octanoate (*IIIa*), ethyl 7-ethyl--3-methyl-6-oxanonanoate (*IVc*), ethyl 3,7-dimethyl-5-oxaoctanoate (*Vc*), ethyl 3,7,7-trimethyl--5-oxaoctanoate (*VIc*), and ethyl 3,6,6-trimethyl-5-oxaheptanoate (*VIIc*).

Preparation of Oxa Alkanols and Oxa Alkenols *Ic*, *IIc*, *IIIb*, and *IVd*—*VIId*

A suspension of lithium aluminium hydride (0·012 mol) in ether (40 ml) was treated dropwise with 0·02 mol of the appropriate ethyl oxaalkenoate (at −10°) or ethyl oxaalkanoate (at 10—20°C), the mixture stirred at room temperature for 1 h and refluxed for 1 h. The excess reagent was decomposed, the mixture acidified, and processed as usual to afford the crude product which was purified by distillation. By this route, the following compounds were prepared in 85—95% yields: 3,7,7-trimethyl-6-oxa-2-octen-1-ol (*Ic*), 3,7-dimethyl-6-oxa-2-nonen-1-ol (*IIc*), 3,7,7-trimethyl-6-oxa-1-octanol (*IIIb*), 7-ethyl-3-methyl-6-oxa-1-nonanol (*IVd*), 3,7-dimethyl--5-oxa-1-octanol (*Vd*), 3,7,7-trimethyl-5-oxa-1-octanol (*VId*), and 3,6,6-trimethyl-5-oxa-1-heptanol (*VIId*).

Preparation of Bromo Oxa Alkanes and Bromo Oxa Alkenes

A. To a solution of the appropriate oxaalkanol or oxaalkenol (0·023 mol) in pyridine (0·007 mol) and light petroleum (b.p. 50°C; 40 ml) there was added dropwise at −10°C over 15 min a solution of phosphorus tribromide (0·0104 mol) in light petroleum (5 ml), the whole mixture stirred for additional 30 min, and processed as usual to afford a crude product which was purified by distillation. By this route, the following bromides were obtained in 55—70% yields: 8-bromo-2,2,6-trimethyl-3-oxa-6-octene (b.p.* 135—140°C/15 Torr), 9-bromo-3,7-dimethyl-4-oxa--7-nonene (b.p.* 125—130°C/14 Torr), 8-bromo-2,2,6-trimethyl-3-oxaoctane (b.p.* 125—130°C/ /15 Torr), 8-bromo-2,6-dimethyl-4-oxaoctane (b.p.* 130—135°C/14 Torr), and 7-bromo-2,2,5-trimethyl-3-oxaheptane (b.p.* 130—138°C/18 Torr).

B. To a solution of the appropriate oxaalkanol (0·02 mol) and triphenylphosphine (0·0203 mol) in dimethylformamide (20 ml) there was added dropwise with stirring at 10—20°C over 20—30 min a solution of bromide (0·0202 gramatom) in dichloromethane (5 ml), the whole mixture stirred for 1 h, diluted with water (2—3 ml), and extracted with five portions of light petroleum (b.p 50°C). The extracts were combined and washed successively with water (three 2 ml portions)

* Bath temperature.

TABLE I

Analyses and Boiling Points of Intermediates

Compound	Formula m.w.	Calculated/Found % C	% H	B.p., °C Torr
		Alkoxy ketones		
IIa	$C_8H_{16}O_2$	66·62	11·18	115–120[a]
	144·2	66·91	10·95	65
IVa	$C_9H_{18}O_2$	68·31	11·46	104–105
	158·2	68·68	11·31	35
Va[b]	$C_7H_{14}O_2$	64·57	10·84	80–85
	130·2	64·55	11·10	50
VIa	$C_8H_{16}O_2$	66·62	11·18	90–95[a]
	144·2	66·59	11·01	40
VIIa[c]	$C_7H_{14}O_2$	64·57	10·84	92–95[a]
	130·2	64·41	10·88	65
	Esters of α,β-unsaturated oxa acids			
Ib	$C_{12}H_{22}O_3$	67·25	10·35	116–119
	214·3	67·41	10·38	13
IIb	$C_{12}H_{22}O_3$	67·25	10·35	144–148[a]
	214·3	67·33	10·31	22
IVb	$C_{13}H_{24}O_3$	68·39	10·60	136–139
	228·3	68·58	10·45	14
Vb	$C_{11}H_{20}O_3$	65·95	10·06	116–123[a]
	200·3	65·84	10·06	11
VIb	$C_{12}H_{22}O_3$	67·25	10·35	120–130[a]
	214·3	67·03	10·25	15
VIIb	$C_{11}H_{20}O_3$	65·95	10·06	125–132[a]
	200·3	65·88	9·89	17
	Esters of oxa acids			
IIIa	$C_{12}H_{24}O_3$	66·63	11·18	110–112
	216·3	66·51	11·25	14
IVc	$C_{13}H_{26}O_3$	67·79	11·38	135–140[a]
	230·3	67·81	11·49	15
Vc	$C_{11}H_{22}O_3$	65·30	10·96	117–125[a]
	202·3	65·73	10·71	23
VIc	$C_{12}H_{24}O_3$	66·63	11·18	113–116[a]
	216·3	66·93	11·02	19
VIIc	$C_{11}H_{22}O_3$	65·29	10·96	130–137[a]
	202·3	65·47	10·84	38

TABLE I
(*Continued*)

Compound	Formula m.w.	Calculated/Found % C	% H	B.p., °C Torr
		Oxa alcohols		
Ic	$C_{10}H_{20}O_2$	69·70	11·70	135–145[a]
	172·3	69·58	11·82	17
IIc	$C_{10}H_{20}O_2$	69·70	11·70	135–142[a]
	172·3	70·01	11·65	17
IIIb	$C_{10}H_{22}O_2$	68·90	12·72	120–128[a]
	174·3	68·88	12·63	14
IVd	$C_{11}H_{24}O_2$	70·16	12·85	127–128
	188·3	70·32	12·63	13
Vd	$C_9H_{20}O_2$	67·43	12·58	130–138[a]
	160·3	67·71	12·48	37
VId	$C_{10}H_{22}O_2$	68·90	12·72	120–128[a]
	174·3	68·75	12·60	20
VIId	$C_9H_{20}O_2$	67·43	12·58	125–130[a]
	160·3	67·72	12·56	30
		Oxa ketones		
I	$C_{13}H_{24}O_2$	73·54	11·39	130–135[a]
	212·3	73·41	11·20	10
II	$C_{13}H_{24}O_2$	73·54	11·39	130–135[a]
	212·3	73·35	11·17	12
III	$C_{13}H_{26}O_2$	72·84	12·23	135–140[a]
	214·3	72·87	12·09	15
IV	$C_{14}H_{28}O_2$	73·63	12·36	148–153[a]
	228·4	73·62	12·27	13
V	$C_{12}H_{24}O_2$	71·95	12·08	130–135[a]
	200·3	72·19	12·10	13
VI	$C_{13}H_{26}O_2$	72·84	12·23	132–137[a]
	214·3	72·60	12·12	12
VII	$C_{12}H_{24}O_2$	71·95	12·08	135–140[a]
	200·3	71·60	12·09	16

[a] Bath temperature; [b,c] these compounds have been prepared earlier by another procedure[10,11].

aqueous sodium hydrogen carbonate, and water. The solvent was evaporated and the residual crude bromo derivative distilled. This route afforded 8-bromo-2,2,6-trimethyl-3-oxaoctane,

9-bromo-3-ethyl-7-methyl-4-oxanonane (b.p.* 135—140°C/15 Torr), and 8-bromo-2,2,6-trimethyl-4-oxaoctane (b.p.* 130—137°C/14 Torr) in 70—85% yields.

Preparation of Oxa Ketones *I*—*VII*

Ethyl acetoacetate (0·017 mol) and the appropriate bromo oxa alkane or alkene (0·015 mol) were added dropwise to ethanolic sodium ethoxide (from 0·016 gramatom of sodium and 20 ml of ethanol) and the mixture heated at 70—80°C for 8 h. Aqueous sodium hydroxide (10%; 25 ml) was then added and the heating continued for additional 3 h. Usual work-up afforded a crude product which was distilled and the distillate chromatographed on silica gel (30 parts by weight) in 9 : 1 light petroleum–ether as eluant. The folowing oxa ketones were prepared in 40—50% yield by this route: 6,10,10-trimethyl-9-oxa-5-undecen-2-one (*I*), 6,10-dimethyl-9--oxa-5-dodecen-2-one (*II*), 6,10,10-trimethyl-9-oxa-2-undecanone (*III*), 10-ethyl-6-methyl-9-oxa--2-dodecanone (*IV*), 6,10-dimethyl-8-oxa-2-undecanone (*V*), 6,10,10-trimethyl-8-oxa-2-undecanone (*VI*), and 6,9,9-trimethyl-8-oxa-2-decanone (*VII*).

Preparation of Esters *VIII*, *IX*, *XI*, *XVIII*, and *XXIV*

From ethoxycarbonylmethylenetriphenylphosphorane (2 mmol), the appropriate oxa ketone (1 mmol), benzoic acid (0·2 mmol), and benzene (6 ml) there was prepared (analogously to procedure *C* in the above synthesis of esters of α,β-unsaturated oxa acids) a crude ester which was purified by chromatography on silica gel (40—60 parts by weight) with 93 : 7 light petroleum–ether as eluant. From the first fractions of the effluent, there was obtained the *cis*-isomer while the last fractions afforded the *trans*-isomer. The ratio of the *cis*- to the *trans*-isomer was 1 : 1·5—2·0 and the yields were 70—85%. By this route, the ketones *I*, *II*, *III*, *V*, and *VII* were converted to ethyl 3,7,11,11-tetramethyl-10-oxa-2,6-dodecadienoate (*VIII*), ethyl 3,7,11- trimethyl-10-oxa-2,6-tridecadienoate (*IX*), ethyl 3,7,11,11-tetramethyl-10-oxa-2-dodecenoate (*XI*), ethyl 3,7,11-trimethyl-9-oxa-2-dodecenoate (*XVIII*), and ethyl 3,7,10,10-tetramethyl-9-oxa-2-undecenoate (*XXIV*), resp.

Preparation of Amides *X*, *XIII*, *XIV*, *XIX*, and *XXV*

From diethyl N-substituted aminocarbonylmethanephosphonate (2·3 mmol), ethanolic sodium ethoxide (from 2·2 milligramatom of sodium and 2 ml of ethanol), the appropriate oxa ketone (2 mmol), and dimethylformamide (6—10 ml) there was prepared (analogously to procedure *A* in the above synthesis of esters of α,β-unsaturated acids) the crude amide which was purified by chromatography on silica gel (40—60 parts by weight) with the use of 85 : 15 light petroleum–ether as eluant. The first fractions of the effluent afforded the *cis*-isomer and the last fractions contained the *trans*-isomer. Yields, 70—80%.

By this route, the ketones *II*, *V*, and *VII* were converted into the N,N-diethylamide of 3,7,11--trimethyl-10-oxa-2,6-tridecadienoic acid (*X*), the N,N-diethylamide of 3,7,11-trimethyl-9-oxa--2-dodecenoic acid (*XIX*), and the N,N-diethylamide of 3,7,10,10-tetramethyl-9-oxa-2-undecenoic acid (*XXV*), resp. The ketone *III* afforded the N,N-diethylamide of 3,7,11,11-tetramethyl--10-oxa-2-dodecenoic acid (*XIII*) and the N-ethylamide of 3,7,11,11-tetramethyl-10-oxa-2-dodecenoic acid (*XIV*).

* Bath temperature.

TABLE II

Analyses and Boiling Points of Oxa Compounds *VIII*—*XXV*

Compound	Formula m.w.	Calculated/Found % C	% H	% N	B.p.[a], °C Torr
VIII	$C_{17}H_{30}O_3$	72·30	10·71	—	102—115
	282·4	72·45	10·87		0·009
IX	$C_{17}H_{30}O_3$	72·30	10·71	—	120—125
	282·4	72·57	10·66		0·009
X	$C_{19}H_{35}NO_2$	73·73	11·40	4·53	160—165
	309·5	73·95	11·54	4·71	0·02
XI[b]	$C_{17}H_{32}O_3$	71·78	11·34	—	115—120
	284·4	72·12	11·11		0·02
XII	$C_{18}H_{34}O_3$	72·40	11·48	—	110—120
	298·5	72·65	11·09		0·01
XIII[b]	$C_{19}H_{37}NO_2$	73·26	11,97	4·50	150—155
	311·5	73·15	12·09	4·65	0·013
XIV[b]	$C_{17}H_{33}NO_2$	72·03	11·73	4·94	155—160
	283·4	71·76	11·69	5·19	0·01
XV	$C_{18}H_{34}O_3$	72·40	11·48	—	118—125
	298·5	72·62	11·37		0·008
XVI	$C_{19}H_{36}O_3$	73·03	11·61	—	120—127
	312·5	73·29	11·55		0·008
XVII	$C_{20}H_{39}NO_2$	73·79	12·08	4·30	140—150
	325·5	73·78	12·10	4·61	0·008
XVIII	$C_{16}H_{30}O_3$	71·07	11·18	—	115—120
	270·4	71·36	11·22		0·009
XIX	$C_{18}H_{35}NO_2$	72·67	11·86	4·71	145—150
	297·5	72·87	12·10	5·02	0·015
XX	$C_{17}H_{32}O_3$	71·78	11·34	—	105—115
	284·4	72·06	11·21		0·009
XXI	$C_{18}H_{34}O_3$	72·40	11·48	—	112—117
	298·5	72·64	11·48		0·009
XXII	$C_{19}H_{37}NO_2$	73·26	11·97	4·50	135—145
	311·5	73·44	12·00	4·44	0·008
XXIII	$C_{17}H_{33}NO_2$	72·03	11·73	4·94	
	283·4	72·06	11·98	4·96	
XXIV	$C_{16}H_{30}O_3$	71·07	11·18	—	93—100
	270·4	71·21	11·10		0·01
XXV	$C_{18}H_{35}NO_2$	72·67	11·86	4·71	140—145
	297·5	72·82	12·01	4·76	0·015

[a] Bath temperature; [b] the biological activity on some insect species and preparation of this compound has been reported earlier[12].

Preparation of Esters *XII*, *XV*, *XVI*, *XX*, and *XXI* as well as Amides *XVII*, *XXII*, and *XXIII*

From diethyl ethoxycarbonylmethanephosphonate, diisopropyl isopropoxycarbonylmethanephosphonate or diethyl N-substituted aminocarbonylmethanephosphonate (1·73 mmol each), sodium hydride (1·65 mmol), the appropriate oxa ketone (1·5 mmol), and 1,2-dimethoxyethane (6—10 ml) there was prepared (analogously to procedure *B* in the above synthesis) the crude product which was purified by chromatography on silica gel with the use of 93 : 7 light petroleum–ether (in the case of esters) and 85 : 15 light petroleum–ether (in the case of amides) as eluants. The ratio of the *cis*-isomer to the *trans*-isomer was 1 : 2·0—2·5. Yields, 80—90% of esters and 75—85% of amides.

By this route, the ketone *III* was converted into isopropyl 3,7,11,11-tetramethyl-10-oxa-2-dodecenoate (*XII*) and the ketone *IV* afforded ethyl 11-ethyl-3,7-dimethyl-10-oxa-2-tridecenoate (*XV*), isopropyl 11-ethyl-3,7-dimethyl-10-oxa-2-tridecenoate (*XVI*), and the N,N-diethylamide of 11-ethyl-3,7-dimethyl-10-oxa-2-tridecenoic acid (*XVII*). From the ketone *VI* there were prepared ethyl 3,7,11,11-tetramethyl-9-oxa-2-dodecenoate (*XX*), isopropyl 3,7,11,11-tetramethyl-9-oxa-2-dodecenoate (*XXI*), the N,N-diethylamide of 3,7,11,11-tetramethyl-9-oxa-2-dodecenoic acid (*XXII*), and the N-ethylamide of 3,7,11,11-tetramethyl-9-oxa-2-dodecenoic acid (*XXIII*).

Characteristics of the Above Oxa Analogues and Intermediates

The structure of the title substances was confirmed by elemental analysis (Tables I and II) supplemented in some cases by analysis of IR and NMR spectra.

The purity of substances and the ratio of the *cis*-isomer to the *trans*-isomer was determined by gas chromatography. The alkoxy ketones and esters of oxa acids and oxa alcohols were chromatographed on Cellite impregnated with 10% Apiezon L at temperatures of 50—70°C (alkoxyketones *Ia*—*VIIa*), 110—140°C (esters of 5-oxa and 6-oxa acids as well as 5-oxa and 6-oxa alcohols), 140—155°C (oxa ketones *I*—*VII*), and 200—210°C (esters of 10-oxa and 9-oxa acids.) Gas chromatography of amides of 9-oxa alkenoic acids, of 10-oxaalkenoic acids, and of 10-oxaalkadienoic acids was performed on Gas Chrom Q impregnated with 3% SE 30 at the temperature of 175—185°C.

The IR spectra of alkoxy ketones *Ia*—*VIIa* exhibited absorption bands corresponding to the $-COCH_3$ group (at about 1720 and 1360 cm^{-1}) and the ethereal oxygen atom (1105 of 1125 to 1130 cm^{-1}). The structure of 1-(2,2-dimethylpropoxy)-2-propanone (*VIa*) was confirmed by NMR spectrum: $C_{(6)}$ 3× $-CH_3$ 0·94 (s), (9 H); $C_{(2)}$ $-CH_3$ 2·17 (s) (3 H); $H_{(3)}$ 3·12 (s) (2 H); $H_{(5)}$ 3·95 (s) (2 H).

The IR spectra of 8-oxa and 9-oxa ketones *I*—*VII* contained absorption bands attributable to the $-COCH_3$ group (at about 1720 and 1360 cm^{-1}) and the ethereal oxygen atom (1115 to 1120 cm^{-1}). The structure of ketones *I*, *VI*, and *VII* was confirmed by NMR spectra as follows. 6,10,10-Trimethyl-9-oxa-5-undecen-2-one (*I*): $C_{(10)}$ 3× $-CH_3$ 1·18 (s) (9 H); $C_{(6)}$ $-CH_3$ 1·63 (s); $C_{(6)}$ $-CH_3$ 1·69 (s); $C_{(2)}$ $-CH_3$ 2·12 (s) (3 H); $H_{(3)} + H_{(4)} + H_{(7)}$ 2·0—2·55 (m) (6 H); $H_{(8)}$ 3·36 (m) (2 H); $H_{(5)}$ 5·14 (m) (1 H). 6,10,10-Trimethyl-8-oxa-2-undecanone (*VI*): $C_{(6)}$—CH_3 0·91 (d), $J = 7·0$ (3 H); $C_{(10)}$ 3× $-CH_3$ 0·90 (s) (9 H); $H_{(4)} + H_{(5)}$ 1·05—1·75 (compl. multipl.) (4 H); $H_{(6)}$ 1·78 (m), $J = 6·9$ (1 H); $C_{(2)}$—CH_3 2·13 (s) (3 H); $H_{(3)}$ 2·41 (m) (2 H); $H_{(9)}$ 3·02 (s) (2 H); $H_{(7)}$ 3·21 (m) (2 H). 6,9,9-Trimethyl-8-oxa-2-decanone (*VII*): $C_{(6)}$—CH_3 0·88 (d), $J = 6·6$ (3 H); $C_{(9)}$ 3× $-CH_3$ 1·16 (s) (9 H); $H_{(4)} + H_{(5)} + H_{(6)}$ 1·20—1·80 (m) (5 H); $C_{(2)}$ $-CH_3$ 2·12 (s) (3 H); $H_{(3)}$ 2·40 (m) (2 H); $H_{(7)}$ 3·14 (m) (2 H).

The IR spectra of esters *VIII*, *IX*, *XV*, *XVIII*, *XX*, *XXI*, and *XXIV* contained absorption bands corresponding to the ester group in conjugation with a double bond (at 1720, 1650, 1220, and 1150 cm^{-1}) and absorption bands of the ethereal oxygen atom (1080—1110 cm^{-1}). The structure of ethyl *trans*-11-ethyl-3,7-dimethyl-10-oxa-2-tridecenoate (*XV*) was confirmed by analysis

of the NMR spectrum: $C_{(12)}$ + $C_{(11)}$ (ethyl) 2× —CH_3 0·88 (m) (6 H); $C_{(7)}$ —CH_3 0·90 (d) (3 H); 4× —CH_2— + $H_{(7)}$ 1·10—1·90 (compl. multipl.); $C_{(3)}$—CH_3 2·12 (d), J = 1·15 (3 H); $H_{(11)}$ 3·06 (m) (1 H); $H_{(9)}$ 3·44 (m) (2 H); $H_{(2)}$ 5·62 (m), J = 1·15 (1 H); isopropyl (ester) 2× CH_3 1·22 (d) (6 H); CH 5·03 (m). The *cis*-isomer differed in the value of $C_{(3)}$—CH_3 1·86 (d), J = 1·3.

The IR spectra of amides *XIII*, *XVII*, *XXII*, and *XXV* contained absorption bands due to the presence of a N,N-disubstituted amide group in conjugation with a double bond (1 640—1 650 and 1 630 cm^{-1}) and an absorption band of the ethereal grouping (1 080—1 110 cm^{-1}). The structure of amides *XIII* and *XXV* was confirmed by analysis of NMR spectra. N,N-Diethylamide of *cis*-3,7,11,11-tetramethyl-10-oxa-2-dodecenoic acid (*XIII*): $C_{(7)}$ —CH_3 0·86 (d), J = 6·0 (3 H); 2× —CH_3 (ethyl) 1·12 (t) (6 H); $C_{(11)}$ 3× —CH_3 1·16 (s) (9 H); $C_{(3)}$ —CH_3 1·80 (d), J = 1·1 (3 H); $H_{(9)}$ + 2× —CH_2— (ethyl) 3·2—3·55 (m) (6 H); $H_{(2)}$ 5·77 (bs) (1 H). N,N-Diethylamide of *trans*-3,7,11,11-tetramethyl-10-oxa-2-dodecenoic acid (*XIII*): $C_{(7)}$ —CH_3 0·88 (d), J = 6·0 (3 H); 2× —CH_3 (ethyl) 1·13 (t) (6 H); $C_{(11)}$ 3× —CH_3 1·17 (s) (9 H); $C_{(3)}$—CH_3 1·89 (d), J = 1·1 (3 H); $H_{(9)}$ + 2× —CH_2— (ethyl) 3·15—3·6 (m) (6 H); $H_{(2)}$ 5·78 (bs) (1 H). N,N-Diethylamide of *cis*-3,7,10,10-tetramethyl-9-oxa-2-undecenoic acid (*XXV*): $C_{(7)}$—CH_3 0·87 (d), J = 6·1 (3 H); $C_{(10)}$ 3× —CH_3 1·14 (s) (9 H); $C_{(3)}$—CH_3 1·81 (d), J = 1·1 (3 H); $H_{(4)}$ 2·2—2·45 (m) (2 H); $H_{(8)}$ 3·0—3·16 (m) (2 H); $H_{(2)}$ 5·78 (m) (1 H); ethyl, 2× —CH_3 1·12 (t), J = 6·5 (6 H); 2× —CH_2— 3·37 (q) (4 H). N,N-Diethylamide of *trans*-3,7,10,10-tetramethyl-9-oxa--2-undecenoic acid (*XXV*): $C_{(7)}$ —CH_3 0·88 (d), J = 6·1 (3 H); $C_{(10)}$ 3× —CH_3 1·15 (s) (9 H); $C_{(3)}$ —CH_3 1·89 (d), J = 1·1 (3 H); $H_{(4)}$ 1·95—2·2 (m) (2 H); $H_{(8)}$ 3·0—3·36 (m) (2 H); $H_{(2)}$ 5·78 (bs) (1 H); ethyl, 2× —CH_3 1·13 (t) (6 H); 2× —CH_2— 3·37 (q) (4 H).

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