SYNTHESIS OF SOME 5-OXA ANALOGUES OF ACYCLIC JUVENOIDS*

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Numerous esters and amides have been prepared of aliphatic unsaturated 5-oxa acids and their chloro, alkoxy, and epoxy derivatives as analogues of the insect juvenile hormone.

In connection with detailed investigations on the insect juvenile hormone and the relationship between the chemical structure and biological activity of the insect juvenile hormone analogues, the preparation of some corresponding oxa analogues has been studied. In the present paper we wish to report the preparation** of 5-oxa analogues of the insect juvenile hormone. These syntheses have been hitherto described in our Patent applications only[1-4]. The present 5-oxa analogues include the esters of α,β-unsaturated acids, such as of 5-oxaalkenoic acid, -alkatrienoic acid, and -alkatetraenoic acid, esters and amides of α,β-unsaturated 5-oxaalkadienoic acids, and finally, the chloro, alkoxy, and epoxy derivatives of these esters and amides.

As starting compounds in the synthesis of these analogues, we have used terpenic, sesquiterpenic, and aliphatic branched alcohols of a suitable number of carbon atoms. The acid-catalysed reaction of these alcohols with diazoketones has furnished α-alkoxyketones[5] which have been used in the synthesis of esters of α,β-unsaturated 5-oxa acids (by reaction with alkoxycarbonylmethylenetriphenylphosphorane[6,7] or dialkyl esters of alkoxycarbonylmethanephosphonic acid[8]) or of β-hydroxyesters (by the Reformatsky reaction) which have been dehydrated to esters of α,β-unsaturated 5-oxa acids. The amides of α,β-unsaturated 5-oxa acids have been prepared either by the action of dialkyl N-alkyl- or N,N-dialkylaminocarbonylmethanephosphonates on α-alkoxyketones or by reaction of amines with chlorides of 5-oxa acids. The chlorides of 5-oxa acids have been obtained by the action of thionyl chloride on the corresponding acids, prepared in turn by saponification of esters of 5-oxa acids.

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

The thus-obtained esters and amides of α,β-unsaturated 5-oxaalkadienoic acids were converted to the corresponding chloro, alkoxy, and epoxy derivatives by the addition of hydrogen chloride or an alcohol, or by epoxidation.

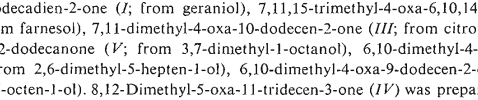
EXPERIMENTAL

The IR spectra were measured in tetrachloromethane. The NMR spectra were taken in deuteriochloroform (tetramethylsilane as internal standard). Chemical shifts are expressed in δ (p.p.m.) and the coupling constants in Hz. The column chromatography was performed on silica gel previously partially deactivated by shaking with 12% of water.

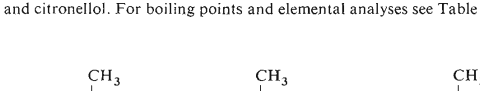
Preparation of α-Alkoxyketones *I*—*VII*

To a solution (precooled to −15°C) of diazomethane (0·12 mol) in ether (350 ml) there was added dropwise under shaking over 15 minutes a solution of the acyl chloride (0·05 mol) in ether (10 ml). The reaction mixture was kept under cooling for 1 h and then concentrated under diminished pressure of a water pump at the temperature up to 0°C to the volume of 20—30 ml. The concentrate was treated with the appropriate alcohol (0·05—0·15 mol), the mixture warmed to 20°C, and treated with ethereal boron trifluoride (0·1—0·2 g in 2—3 portions). The vigorous reaction must be regulated by cooling. When the evolution of nitrogen was finished, the mixture was diluted with water, the ethereal layer washed with aqueous sodium hydrogen carbonate and water, dried, and evaporated. The residue was subjected to fractional distillation. The α-alkoxyketone-containing fractions were chromatographed on silica gel (30—40 parts) with the use of the solvent mixture light petroleum–ether (9 : 1) as eluant. The yields were 20—35%, the recovery was about 50% of the alcohol (with the use of 0·05 mol of the starting alcohol).

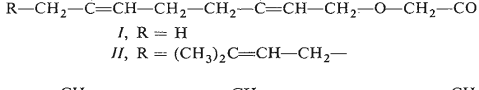
By the reaction with diazoacetone, the following α-alkoxyketones were prepared: 7,11-dimethyl-4-oxa-6,10-dodecadien-2-one (*I*; from geraniol), 7,11,15-trimethyl-4-oxa-6,10,14-hexadecatrien-2-one (*II*; from farnesol), 7,11-dimethyl-4-oxa-10-dodecen-2-one (*III*; from citronellol), 7,11-dimethyl-4-oxa-2-dodecanone (*V*; from 3,7-dimethyl-1-octanol), 6,10-dimethyl-4-oxa-9-undecen-2-one (*VI*; from 2,6-dimethyl-5-hepten-1-ol), 6,10-dimethyl-4-oxa-9-dodecen-2-one (*VII*; from 2,6-dimethyl-5-octen-1-ol). 8,12-Dimethyl-5-oxa-11-tridecen-3-one (*IV*) was prepared from 1-diazo-2-butanone and citronellol. For boiling points and elemental analyses see Table I.



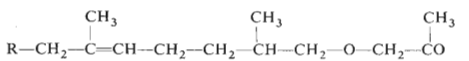
I, R = H
II, R = $(CH_3)_2C{=}CH{-}CH_2{-}$



III, R = H
IV, R = CH_3



V



VI, R = H
VII, R = CH_3

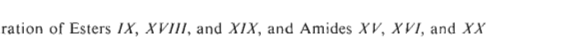
Preparation of Esters *VIII*—*X*, *XII*—*XIV* and *XVIII*

A mixture of alkoxycarbonylmethylenetriphenylphosphorane (0·0135 mol), α-alkoxyketone (0·01 mol), benzoic acid[7] (0·002 mol), and benzene (20 ml) was gently refluxed under nitrogen for 8—12 h, evaporated, and the residual sirup extracted by repeated triturations with light petroleum. The extracts were combined and processed as usual. The crude product was purified by chromatography on silica gel (30—50 parts) with the use of the solvent mixture light petroleum–ether (11 : 1) as eluant. The initial chromatographic fractions contained the individual *cis*-isomer while the *trans*-isomer was present in the final fractions. As indicated by gas chromatography, the ratio of the *cis*- to the *trans*-isomer was 1 : 2—3. The yields were 85—90%.

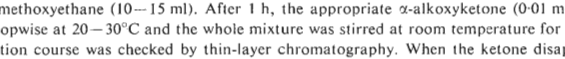
The reaction of methoxycarbonylmethylenetriphenylphosphorane with the ketone *V* afforded methyl 3,8,12-trimethyl-5-oxa-2-tridecenoate (*XIII*). By the reaction of ethoxycarbonylmethylenetriphenylphosphorane with ketones *I*, *II*, *III*, *IV*, *VI*, and *VII*, the following esters were obtained: ethyl 3,8,12-trimethyl-5-oxa-2,7,11-tridecatrienoate (*VIII*), ethyl 3,8,12,16-tetramethyl-5-oxa-2,7,11,15-heptadecatetraenoate (*IX*), ethyl 3,8,12-trimethyl-5-oxa-2,11-tridecadienoate (*X*), ethyl 3-ethyl-8,12-dimethyl-5-oxa-2,11-tridecadienoate (*XII*), ethyl 3,7,11-trimethyl-5-oxa-2,10-dodecadienoate (*XIV*), and ethyl 3,7,11-trimethyl-5-oxa-2,10-tridecadienoate (*XVIII*), see Table I.

Preparation of Esters *IX*, *XVIII*, and *XIX*, and Amides *XV*, *XVI*, and *XX*

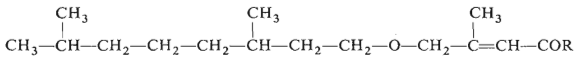
The dialkyl ester of the corresponding substituted alkylphosphonic acid (0·011 mol) was added dropwise under nitrogen with stirring at 20°C to a suspension of sodium hydride (0·0105 mol) in 1,2-dimethoxyethane (10—15 ml). After 1 h, the appropriate α-alkoxyketone (0·01 mol) was added dropwise at 20—30°C and the whole mixture was stirred at room temperature for 2—6 h. The reaction course was checked by thin-layer chromatography. When the ketone disappeared or when the composition of the reaction mixture was constant, the mixture was poured into dilute acetic acid (0·5—1%) and extracted with light petroleum. The extracts were combined and processed as usual. The crude product was purified by column chromatography on silica gel (30—40 parts) with the use of the solvent mixtures 12 : 1 light petroleum–ether (esters of 5-oxa-α,β-unsaturated acids) and 4 : 1 light petroleum–ether (amides of 5-oxa-α,β-unsaturated acids) to obtain the individual *cis*- and *trans*-isomers in the ratio of 1·0 : 2·5—3·0. Yield, 70—85%.



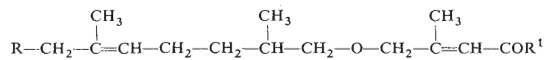
VIII, R = H, $R^1 = OC_2H_5$
IX, R = $(CH_3)_2C{=}CH{-}CH_2{-}$, $R^1 = OC_2H_5$

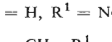


X, R = H, $R^1 = OC_2H_5$
XI, R = H, $R^1 = N(C_2H_5)_2$
XII, R = CH_3, $R^1 = OC_2H_5$



XIII, R = OCH_3



XIV, R = H, $R^1 = OC_2H_5$
XV, R = H, $R^1 = N(C_2H_5)_2$
XVI, R = H, $R^1 = NHC_2H_5$
XVII, R = H, R^1 = 
XVIII, R = CH_3, $R^1 = OC_2H_5$
XIX, R = CH_3, $R^1 = OCH(CH_3)_2$
XX, R = CH_3, $R^1 = N(C_2H_5)_2$

Reaction of diethyl ethoxycarbonylmethanephosphonate with ketones *II* and *VII* afforded compounds *IX* and *XVIII*, resp. Reaction of diisopropyl isopropoxycarbonylmethanephosphonate with ketone *VII* led to isopropyl 3,7,11-trimethyl-5-oxa-2,10-tridecadienaote (*XIX*). Reaction of diethyl N,N-diethylaminocarbonylmethanephosphonate with ketones *VI* and *VII* gave the N,N-diethylamide of 3,7,11-trimethyl-5-oxa-2,10-dodecadienoic acid (*XV*) and the N,N-diethylamide of 3,7,11-trimethyl-5-oxa-2,10-tridecadienoic acid (*XX*), resp. Reaction of diethyl N-ethylaminocarbonylmethanephosphonate with ketone *VI* furnished the N-ethylamide of 3,7,11-trimethyl-5-oxa-2,10-dodecadienoic acid (*XVI*). For analyses and boiling points see Table I.

Preparation of Esters *IX* and *X* by the Reformatsky Reaction

Ethyl bromoacetate (0·011 mol) was added dropwise to a mixture of the α-alkoxyketone (0·01 mol) and activated zinc (0·0105 gramatom) in benzene (20 ml). When the spontaneous reaction was over, the mixture was heated at 80°C for 3 h and processed as usual. A solution of the crude hydroxy acid ester in benzene (10 ml) was added dropwise into a mixture of phosphorus oxychloride (0·012 mol) and pyridine (0·077 mol) in benzene (15 ml) and the whole was then heated at 50–80°C for 1–2 h to accomplish the dehydration. After the usual work-up, the crude product was purified by column chromatography on silica gel. Yields, 30–35%. By this procedure, the ketones *II* and *III* afforded the esters *IX* and *X* (Table I), resp.

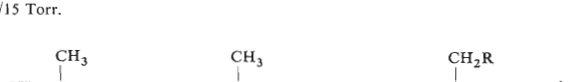
Preparation of Amides *XI*, *XV*, and *XVII* from Acyl Chlorides[9]

A mixture of the ester of 5-oxa acid (3 mmol) and 1–2% ethanolic sodium hydroxide (9 mmol) was refluxed for 90 min and then partially evaporated. The residue was diluted with water, washed with ether, the aqueous phase acidified, and the required acid extracted with ether. A solution of the thus-obtained acid in benzene (5 ml) was treated with pyridine (3 mmol) and thionyl chloride (3 mmol), the whole kept at 20°C for 4 h, cooled down, treated with 7 mmol of the appropriate amine in ether (5 ml), the reaction mixture kept at room temperature for 12 h, and processed as usual. The crude amide was purified by column chromatography on silica gel. Yields, 35–40%.

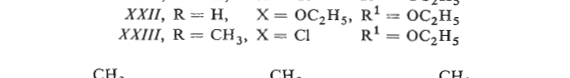
By this procedure, the ester *XIV* was converted to compound *XV* and the morpholide of 3,7,11-trimethyl-5-oxa-2,10-dodecadienoic acid (*XVII*); the ester *X* was transformed into the N,N-diethylamide of 3,8,12-trimethyl-5-oxa-2,11-tridecadienoic acid (*XI*), see Table I.

Preparation of the Chloro Derivatives *XXI* and *XXIII*–*XXVIII*

A solution of the ester or the amide of a 5-oxaalkadienoic acid (50–100 mg) in the solvent mixture (2–4 ml) of ethanol and ether (1 : 1) was saturated with gaseous hydrogen chloride under cooling, the mixture allowed to stand for 10 min, and the solvents evaporated at room temperature under diminished pressure. The residue was diluted with ether, washed with water, dried, and the ether evaporated under diminished pressure. The products were dried to constant weight at 20°C/15 Torr.



XXI, R = H, X = Cl, $R^1 = OC_2H_5$
XXII, R = H, X = OC_2H_5, $R^1 = OC_2H_5$
XXIII, R = CH_3, X = Cl, $R^1 = OC_2H_5$



XXIV, R = H, X = Cl, $R^1 = OC_2H_5$
XXV, R = H, X = Cl, $R^1 = N(C_2H_5)_2$
XXVI, R = H, X = Cl, $R^1 = NHC_2H_5$
XXVII, R = CH_3, X = Cl, $R^1 = OC_2H_5$
XXVIII, R = CH_3, X = Cl, $R^1 = N(C_2H_5)_2$
XXIX, R = CH_3, X = OCH_3, $R^1 = OC_2H_5$
XXX, R = CH_3, X = OCH_3, $R^1 = N(C_2H_5)_2$

By this procedure, the following esters and amides were prepared from compounds *X*, *XII*, *XIV*, *XV*, *XVI*, *XVIII*, and *XX*: ethyl 12-chloro-3,8,12-trimethyl-5-oxa-2-tridecenoate (*XXI*), ethyl 12-chloro-3-ethyl-8,12-dimethyl-5-oxa-2-tridecenoate (*XXIII*), ethyl 11-chloro-3,7,11-trimethyl-5-oxa-2-dodecenoate (*XXIV*), N,N-diethylamide of 11-chloro-3,7,11-trimethyl-5-oxa-2-dodecenoic acid (*XXV*), N-ethylamide of 11-chloro-3,7,11-trimethyl-5-oxa-2-dodecenoic acid (*XXVI*), ethyl 11-chloro-3,7,11-trimethyl-5-oxa-2-tridecenoate (*XXVII*), and N,N-diethylamide of 11-chloro-3,7,11-trimethyl-5-oxa-2-tridecenoic acid (*XXVIII*), see Table I.

Preparation of Epoxy Derivatives *XXXI*–*XXXV*

A solution of 5-oxaalkadienoic acid ester or amide (1·0 mmol) in ether (3 ml) was treated with a solution of *m*-chloroperbenzoic acid (1·05 mmol) in ether (3 ml), the mixture kept in a refrigerator overnight, and processed as usual. The crude residue was chromatographed on a column of neutral alumina (Brockmann activity III; 40–60 parts) with the use of 19 : 1 light petroleum–ether (chromatography of ester) and 4 : 1 light petroleum–ether (chromatography of amides) as eluants. Yields, 60–70%.

By this procedure, compounds *X*, *XIV*, *XV*, *XVIII*, and *XX* were converted into ethyl 11,12-epoxy-3,8,12-trimethyl-5-oxa-2-tridecenoate (*XXXI*), ethyl 10,11-epoxy-3,7,11-trimethyl-5-oxa-2-dodecenoate (*XXXII*), N,N-diethylamide of 10,11-epoxy-3,7,11-trimethyl-5-oxa-2-dodecenoic

TABLE I

Analyses and Boiling Points of the Alkoxy Compounds *I*—*XXXV*

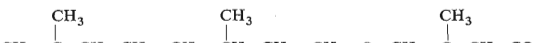
Compound	Formula m.w.	Calculated/Found % C	% H	% Cl	% N	B.p.[a] °C/Torr
I	$C_{13}H_{22}O_2$ 210·3	74·24 74·01	10·55 10·65	—	—	145—150 10
II[b]	$C_{18}H_{30}O_2$ 278·4	77·65 77·37	10·86 10·72	—	—	120—125 0·02
III	$C_{13}H_{24}O_2$ 212·3	73·54 73·44	11·39 11·27	—	—	145—150 12
IV	$C_{14}H_{26}O_2$ 226·4	74·28 74·39	11·58 11·60	—	—	145—150 12
V	$C_{13}H_{26}O_2$ 214·3	72·84 73·04	12·23 12·10	—	—	140—145 10
VI	$C_{12}H_{22}O_2$ 198·3	72·68 72·86	11·19 11·16	—	—	135—140 10
VII	$C_{13}H_{24}O_2$ 212·3	73·54 73·65	11·39 11·48	—	—	140—145 10
VIII	$C_{17}H_{28}O_3$ 280·4	72·82 72·83	10·06 10·10	—	—	125—130 0·01
IX	$C_{22}H_{36}O_3$ 348·5	75·81 76·05	10·41 10·38	—	—	165—170 0·01
X	$C_{17}H_{30}O_3$ 282·4	72·30 72·44	10·71 10·56	—	—	125—130 0·01
XI	$C_{19}H_{35}NO_2$ 309·5	73·73 73·45	11·40 11·20	—	4·53 4·63	150—155 0·05
XII	$C_{18}H_{32}O_3$ 296·4	72·93 73·20	10·88 10·75	—	—	130—135 0·01
XIII	$C_{16}H_{30}O_3$ 270·4	71·07 71·11	11·18 11·20	—	—	115—120 0·01
XIV	$C_{16}H_{28}O_3$ 268·4	71·60 71·75	10·51 10·62	—	—	110—115 0·01
XV	$C_{18}H_{33}NO_2$ 295·5	73·17 73·29	11·26 11·26	—	4·74 4·76	135—140 0·009
XVI	$C_{16}H_{29}NO_2$ 267·4	71·86 71·67	10·93 10·61	— —	5·24 5·13	—
XVII	$C_{18}H_{31}NO_3$ 309·4	—	—	—	4·53 4·54	—
XVIII	$C_{17}H_{30}O_3$ 282·4	72·30 72·35	10·71 10·53	— —	— —	115—120 0·008

TABLE I
(*Continued*)

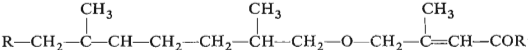
Compound	Formula m.w.	Calculated/Found % C	% H	% Cl	% N	B.p.[a] °C/Torr
XIX	$C_{18}H_{32}O_3$ 296·4	72·93 73·28	10·88 11·05	—	—	120—125 0·008
XX	$C_{19}H_{35}NO_2$ 309·5	73·73 73·46	11·40 11·19	—	4·53 4·51	135—145 0·008
XXI	$C_{17}H_{31}ClO_3$ 318·9	—	—	11·12 11·40	—	—
XXII	$C_{19}H_{36}O_4$ 328·5	69·47 69·16	11·05 10·88	—	—	135—140 0·009
XXIII	$C_{18}H_{33}ClO_3$ 332·9	—	—	10·65 10·26	—	—
XXIV	$C_{16}H_{29}ClO_3$ 304·9	—	—	11·63 11·51	—	—
XXV	$C_{18}H_{34}ClNO_2$ 331·9	—	—	10·68 10·55	—	—
XXVI	$C_{16}H_{30}ClNO_2$ 303·9	—	—	11·67 11·57	—	—
XXVII	$C_{17}H_{31}ClO_3$ 318·9	—	—	11·12 11·18	—	—
XXVIII	$C_{19}H_{36}ClNO_2$ 345·9	—	—	10·25 10·51	—	—
XXIX	$C_{18}H_{34}O_4$ 314·5	68·75 68·85	10·90 10·88	—	—	135—140 0·01
XXX	$C_{20}H_{39}NO_3$ 341·5	—	—	—	4·10 4·20	—
XXXI	$C_{17}H_{30}O_4$ 298·4	68·42 68·81	10·13 10·09	—	—	140—145 0·02
XXXII	$C_{16}H_{28}O_4$ 284·4	67·57 67·87	9·92 9·90	—	—	120—125 0·008
XXXIII	$C_{18}H_{33}NO_3$ 311·5	69·41 69·80	10·68 10·90	—	4·50 4·56	—
XXXIV	$C_{17}H_{30}O_4$ 298·4	68·42 68·69	10·13 10·04	—	—	130—135 0·009
XXXV	$C_{19}H_{35}NO_3$ 325·5	70·11 70·29	10·84 10·75	—	4·30 4·21	— —

[a] Bath temperature. [b] This compound has been prepared earlier by oxidation of the corresponding secondary alcohol[11].

acid (*XXXIII*), ethyl 10,11-epoxy-3,7,11-trimethyl-5-oxa-2-tridecenoate (*XXXIV*), and N,N-diethylamide of 10,11-epoxy-3,7,11-trimethyl-5-oxa-2-tridecenoic acid (*XXXV*), see Table I.



XXXI, R = OC_2H_5



XXXII, R = H, $R^1 = OC_2H_5$
XXXIII, R = H, $R^1 = N(C_2H_5)_2$
XXXIV, R = CH_3, $R^1 = OC_2H_5$
XXXV, R = CH_3, $R^1 = N(C_2H_5)_2$

Preparation of Alkoxy Derivatives *XXII*, *XXIX*, and *XXX*

Treatment of the ester or amide of 5-oxaalkadienoic acid (2 mmol) with mercuric acetate (2·0 mmol) in the appropriate alcohol and then potassium hydroxide (14 mmol) and the subsequent sodium borohydride reduction (1 mmol) afforded a crude alkoxy derivative[10] which was purified by chromatography on a column of silica gel (30—50 parts) with the use of light petroleum–ether as eluant (8 : 1, chromatography of the ester; 7 : 3 with the amide). Yield, 50—80%.

By this procedure, the ester *X* was converted into ethyl 3,8,12,12-tetramethyl-5,13-dioxa--2-pentadecenoate (*XXII*). Addition of methanol to compounds *XVIII* and *XX* afforded ethyl 11-ethyl-3,7,11-trimethyl-5,12-dioxa-2-tridecenoate (*XXIX*) and the N,N-diethylamide of 11-ethyl--3,7,11-trimethyl-5,12-dioxa-2-tridecenoic acid (*XXX*), resp.

Characterisation of Compounds

The structure of the above prepared compounds (Table I) was confirmed by elemental analysis and, in some cases, by IR and NMR spectra.

The purity of compounds and the ratio of the *cis*- to the *trans*-isomer was checked by gas chromatography (Pye Argon Chromatograph with radioactivity ionisation detector). In the chromatography of α-alkoxyketones, esters of 5-oxa acids, their epoxy derivatives, and their alkoxy derivatives, there was used Cellite impregnated with 10% of Apiezon L at 145—155°C (α-alkoxyketones) and at 190—220°C (esters and the alkoxyketone *II*). Compound *IX*, the amides of 5-oxa acids, and their epoxy as well as alkoxy derivatives were chromatographed at 170—190°C on Gas Chrom Q impregnated with 3% of Se-30.

The IR spectra of α-alkoxyketones *II*, *III*, *IV*, *V*, and *VI* showed absorption bands which were attributed to the presence of the CH_3CO— group (1 720—1 723 cm^{-1}, 1 355—1 359 cm^{-1}) and the ethereal oxygen atom (1 115—1 129 cm^{-1}). The structure of ketones *IV* and *VII* was confirmed by NMR spectra as follows. 8,12-Dimethyl-5-oxa-11-tridecen-3-one (*IV*): $C_{(6)}$—CH_3 0·90 (d), J = 6·0 (3 H); $C_{(12)}$ —CH_3 1·06 (t), J = 7·0 (3 H); $C_{(2)}$ 2 × —CH_3 1·59 (bs) (3 H), 1·67 (bs) (3 H); $H_{(4)}$ 1·91 (d), J = 6·5 (1 H); $H_{(4)}$ 2·065 (d), J = 6·5 (1 H); $H_{(12)}$ 2·49 (q), J = 7·0 (2 H); $H_{(8)}$ 3·51 (t), J = 7·0 (2 H); $H_{(10)}$ 4·01 (s) (2 H); $H_{(3)}$ 5·105 (m) (1 H). 6,10-Di-

methyl-4-oxa-9-dodecen-2-one (*VII*): $C_{(7)}$—CH_3 0·93 (d), $J = 6·7$ (3 H); $C_{(2)}$—CH_3 0·94 (t) (3 H); $C_{(3)}$—CH_3 1·60 (bs), $J = <1$; $C_{(3)}$—CH_3 1·65 (bs), $J = 1·2$; $C_{(11)}$—CH_3 2·13 (s) (3 H); $H_{(8)}$ 3·31 (m) (2 H); $H_{(10)}$ 3·94 (s) (2 H); $H_{(4)}$ 5·12 (m) (1 H).

The IR spectra of 5-oxa esters *X*, *XII*, *XIII*, *XIV*, *XVIII*, and *XIX* exhibit absorption bands belonging to an ester group in conjugation with a double bond (at about 1 720, 1 660, 1 220, and 1 155 cm^{-1}) and an absorption band belonging to an ethereal oxygen atom (round 1 115 cm^{-1}). The chloro derivative *XXIV* shows a similar behaviour. The structure of esters *XII* and *XIV* was confirmed by NMR spectra. Ethyl 3-ethyl-8,12-dimethyl-5-oxa-2,11-tridecadienoate (*XII*): $C_{(8)}$—CH_3 0·89 (d), $J = 6·0$ (3 H); $H_{(9)} + H_{(8)} + H_{(7)}$ 1·15—1·80 (m) (5 H); $C_{(12)}$ 2 × —CH_3 1·59 (d) (3 H), 1·67 (d) (3 H); $H_{(10)}$ 1·83—2·05 (m) (2 H); $C_{(3)}$—CH_3 2·08 (d), $J = 1·5$ (3 H); $H_{(6)}$ 3·46 (t), $J = 7·0$ (2 H); $H_{(4)}$ 3·92 (d), $J = 1·5$ (2 H); $H_{(11)}$ 5·10 (t), $J = 7·0$ (1 H); $H_{(2)}$ 5·94 (m) (1 H); —$COOC_2H_5$, —CH_2— 4·17 (q) (2 H), —CH_3 1·27 (t) (3 H). Ethyl *trans*-3,7,11--trimethyl-5-oxa-2,10-dodecadienoate (*XIV*): $C_{(7)}$ —CH_3 0·86 (d), $J = 6·5$ (3 H); $C_{(11)}$ 2 × —CH_3 1·60 (s) (3 H), 1·52 (s) (3 H); $H_{(8)} + H_{(7)}$ 1·60—2·30 (m) (3 H); $H_{(9)}$ 1·75—2·0 (m) (2 H); $C_{(3)}$ —CH_3 2·015 (d), $J = 1·0$ (3 H); $H_{(6)}$ 3·185 (q) (2 H); $H_{(4)}$ 3·75 (d) (2 H); $H_{(10)}$ 5·05 (m) (1 H); —$COOC_2H_5$, —CH_2— 4·105 (q) (2 H), —CH_3 1·20 (t) (3 H).

The IR spectra of amides *XV* and *XX* contained absorption bands which were assigned to a N,N-disubstituted amide group conjugated with a double bond (1 630, 1 658 cm^{-1}) and an absorption band of the ethereal oxygen atom (1 110 cm^{-1}). The spectrum of the chloro derivative *XXV* contained the same absorption bands.

Elemental analyses were performed in the Analytical Department (Dr J. Horáček, Head) of this Institute by Mrs V. Rusová, Mrs E. Šípová, Mrs L. Pejchová, and Mr V. Štěrba. The IR spectra were measured by Mr P. Formánek and interpreted by Dr J. Smolíková. The NMR spectra were measured and interpreted by Dr M. Synáčková and Dr M. Masojídková. The technical assistance of Miss D. Stiborková and Mrs A. Červenclová is gratefully acknowledged.

REFERENCES

1. Jarolím V., Sláma K., Šorm F.: Czechoslov. Pat. Appl. PV 2371—70 (1970), PV 2372—70 (1970), and PV 2373—70 (1970).
2. Jarolím V., Sláma K., Šorm F.: Czechoslov. Pat. Appl. PV 3119—70 (1970), PV 3120—70 (1970), and PV 3121—70 (1970).
3. Jarolím V., Sláma K., Šorm F.: Czechoslov. Pat. Appl. PV 1501—71 (1971).
4. Jarolím V., Šorm F.: Czechoslov. Pat. Appl. PV 2881—72 (1972).
5. Newman M. S., Beal III P. F.: J. Am. Chem. Soc. *72*, 5161 (1950).
6. Maercker A.: *Organic Reactions*, Vol. 14, p. 270. J. Wiley, New York 1965.
7. Rüchardt Ch., Eichler S., Panse P.: Angew. Chem. *75*, 858 (1963).
8. Wadsworth W. S., Emmons W. D.: J. Am. Chem. Soc. *83*, 1733 (1961).
9. Human J. P. E., Mills J. A.: Nature *158*, 877 (1946).
10. Wakabayashi N.: J. Med. Chem. *12*, 191 (1969).
11. Ito Masaaki, Abe Kazuo: Kitami Kogyo Tanki Daigaku, Kenkyu, Hokoku *2*, 97 (1967); Chem. Abstr. *70*, 106674 (1969).

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