PREPARATION OF SOME 8-OXA DERIVATIVES OF 2,4-DIENOIC ACID ESTERS

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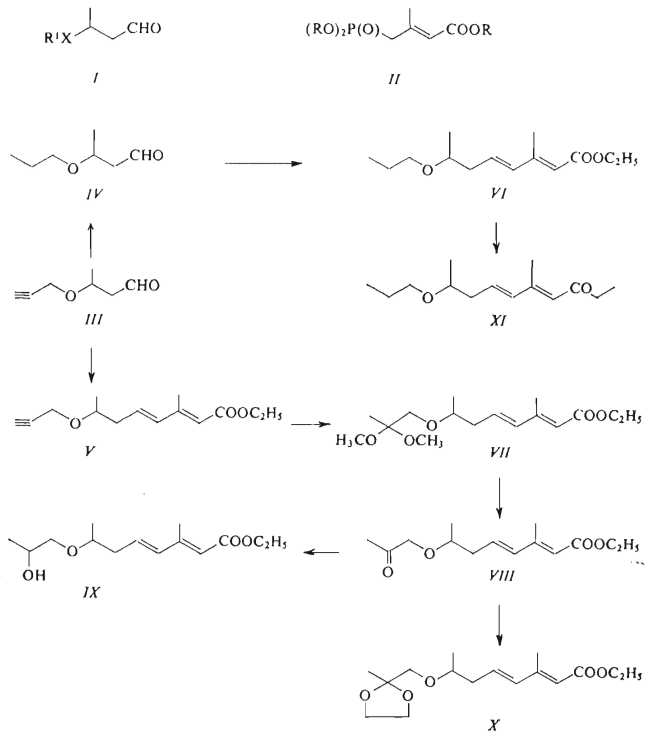
The method of preparation of the esters of 8-oxa-2,4-dienoic acids is described, utilizing 3-methyl--4-oxa-6-heptynal (*III*) as the key intermediate which was prepared on addition of 2-propyn-1-ol to 2-butenal.

Substances imitating the effect to the insect juvenile hormone (juvenoids) are considered as potential non-traditional insecticides[1,2]. In the past decade much effort was devoted to the study of the relationship between their chemical structure and biological activity[3,4]. One of the prospective types of juvenoids are α,β-γ,δ-unsaturated esters[5,6]. The key intermediate[8] for their synthesis are aldehydes *I* giving on further reaction dienoates, for example with trialkyl phosphonosenecioates of general formula *II* (ref.[6,7]). One of the factors determining the accessibility of the juvenoids of this type is therefore the availability of the mentioned aldehydes.

It is known that under suitable conditions the addition of alcohols to the double bond of α,β-unsaturated carbonyl compounds takes place under formation of corresponding oxa derivatives[8]. In our study we made use of this fact for the addition of 2-propyn-1-ol to 2-butenal, endeavouring to obtain the relatively easily accessible 4-oxa-aldehydes *I* (X = O), utilizable for the synthesis of oxa esters possessing juvenile hormone activity. 3-Methyl-4-oxa-6-heptynal (*III*), formed in relatively good yield (45–48%) on reaction of both mentioned substances under catalysis with aqueous sodium hydroxide solution, afforded 3-methyl-4-oxa-heptanal (*IV*) by low-pressure hydrogenation on palladium. On reaction of aldehydes *III* or *IV* with phosphonosenecioate *II* (R = C_2H_5) we obtained the esters *V* or *VI*, respectively. The triple bond in ester *V* enabled us to prepare further derivatives. By methoxylation under catalysis with the boron trifluoride etherate – mercuric oxide complex[9–11] we obtained dimethyl acetal *VII* from which keto ester *VIII* was prepared by trans- ketalization in acetone. The reduction of ester *VIII* with tetramethylammonium borohydride gave hydroxy ester *IX*. On reaction with ethylene glycol keto ester *VIII* gave ethylene acetal X. Alkaline saponification of dienoate *VI* and the reaction of the acid formed with ethyllithium[12] in ether at 0°C gave α,β-γ,δ-unsaturated ketone *XI*.



The analysis of the ^{1}H NMR spectra showed that in the preparation of compounds *V*–*X* as well as *XI* no isomerization of the double bonds in the α,β-γ,δ-unsaturated system took place.

The biological activities of the prepared substances ranged from 1 to 100 μg per individual (ID_{50} Morph., in the bug Dysdercus cingulatus).

EXPERIMENTAL

The majority of the substances were isolated by means of column chromatography on silica gel (Gebr. Herrmann, Köln-Ehrenfeld). Their purity was checked by means of thin-layer chromatography on silica gel G (Merck) or GLC (Perkin–Elmer F-11 with FID). The IR spectra were

measured in CCl_4 on a UR 20 spectrometer (Carl Zeiss, Jena). The ^1H NMR spectra were measured on a HA-100 spectrometer in $CDCl_3$ (tetramethylsilane as internal reference) and the mass spectra on a AEI MS-902 instrument. Ethylene glycol was distilled through a Vigreux column of 1·2 × 8 cm dimensions and the fraction distilling within the 180–185°C (1·6 kPa) interval was collected. It was stored over anhydrous potassium carbonate.

3-Methyl-4-oxa-6-heptyn-1-al (*III*)

2-Butenal (45 g, 0·64 mol) was added dropwise over 30 min to a stirred mixture of 2-propyn-1-ol (112 g, 2·3 mol) and a 40% potassium hydroxide solution (1 ml) kept at −10°C. The reaction was stopped by addition of a mixture of glacial acetic acid (5 ml) and 85% orthophosphoric acid (1·5 g) and then rectified on a Vigreux column (1·2 × 5 cm). The main fraction distilled from 70–73°C/1·6 kPa. Yield, 38·7 g (48%). For $C_7H_{10}O_2$ (126·2) calculated: 66·64% C, 7·99% H; found: 66·18% C, 7·89% H. IR (cm^{-1}): 3 315, 2 730, 2 125, 1 725, 1 140, 1 104. Mass spectrum: $m/z = 98$ ($M^+ - 28$). ^1H NMR (ppm): 1·26 (d, 3 H, 6·5), 2·43 (d, 1 H, 2·4), 2·47 (dq, 1 H, 2·1, 2·1, 6·0, −16·7), 2·69 (dq, 1 H, 2·3, 7·0, −16·5), 4·00–4·35 (m, 1 H), 4·17 (dt, 2 H, 2·4, 1·0).

3-Methyl-4-oxaheptanal (*IV*)

Aldehyde *III* (6·5 g, 51·4 mmol) was hydrogenated in methanol (25 ml) at atmospheric pressure and room temperature and under catalysis with 5% palladium on calcium carbonate (0·6 g). After distillation 4·2 g (63%) of a product of b.p. 121–124°C/17·3 kPa were obtained. For $C_7H_{14}O_2$ (130·2) calculated: 64·58% C, 10·84% H; found: 64·13% C, 10·63% H. Infrared spectrum (cm^{-1}): 2 730, 1 729, 1 145, 1 110, 1 080.

α,β-γ,δ-Unsaturated Ketones *V* and *VI*

Using the procedure according to Pattenden-Weedon[7] aldehyde *III* (0·5 g, 3·9 mmol) in 10 ml of 1,2-dimethoxyethane was reacted with a 50% suspension of sodium hydride in oil (0·19 g, 4 mmol) and triethyl phosphonosenecioate (1·1 g, 4·4 mmol) to give ethyl 3,7-dimethyl-8-oxa-2,4-undecadien-10-ynoate (*V*, 0·15 g, 16%). Similarly, from aldehyde *IV* (1·0 g, 7·7 mmol) ethyl 3,7-dimethyl-8-oxa-2,4-undecadienoate (*VI*, 0·55 g, 30%) was prepared. Their physical data are given in Table I.

Ethyl 10,10-Dimethoxy-3,7-dimethyl-2,4-undecadienoate (*VII*)

A mixture of red mercuric oxide (0·065 g), freshly distilled boron trifluoride etherate (0·05 ml) and 0·1 ml of methanol were heated at 70°C for 10 min. After cooling with ice a mixture of ester *V* (1·3 g, 5·5 mmol) in 0·6 ml of methanol was added and the mixture stirred under cooling for 30 min and at room temperature for another 15 min. Anhydrous potassium carbonate (1·0 g) was added and the mixture stirred at room temperature for 15 min. The solution was filtered, potassium carbonate washed with two 3 ml portions of methanol and the combined methanolic fractions were evaporated under reduced pressure. After chromatography and distillation 1·1 g (67%) of the product were obtained. ^1H NMR spectrum (ppm): 1·18 (d, 3 H, 6), 1·21 (t, 3 H, 7·0), 1·34 (s, 3 H), 1·98 (d, 1·2), 2·27 (d, 1·2), 2·41 (m, 2 H), 3·22 (s, 6 H), 3·42 (s, 2 H), 5·62; 5·69 (s, 1 H), 6·27–6·90 (m, 2 H).

Ethyl 10-Oxo-3,7-dimethyl-8-oxa-2,4-undecadienoate (*VIII*)

A mixture of ester *VII* (0·19 g, 0·63 mmol) *p*-toluenesulfonic acid (16 mg) and 1·5 ml of acetone was heated at 80–90°C for 30 min. After evaporation of the solvent the residue was diluted

with 2 ml of water, extracted with three 10 ml portions of ether, the extract washed twice with 10 ml of a 5% aqueous sodium hydrogen carbonate solution and finally dried over anhydrous sodium sulfate. Chromatography of the mixture and distillation gave a pure product (0·14 g, 84·5%). ^{1}H NMR (ppm): 1·19 (d, 3 H, 6·0), 1·28 (t, 3 H, 7·0), 1·99 (d, 1·2), 2·16 (d, 1·2), 2·28 (d, 1·2), 2·45 (m, 2 H), 3·58 (m, 1 H), 4·04 (s, 2 H), 5·71 (s, 1 H), 5·95—6·35 (m, 2 H).

Ethyl 10-Hydroxy-3,7-dimethyl-8-oxa-2,4-undecadienoate (*IX*)

Ester *VIII* (0·3 g, 1·18 mmol) was reduced with tetramethylammonium borohydride (0·6 g, 7 mmol) in methanol (20 ml) at 0°C. After working up 0·29 g (96%) of the product were obtained. ^{1}H NMR spectrum (ppm): 0·65 (d, 3 H, 6·0), 0·69 (d, 3 H, 6·0), 0·78 (t, 3 H, 7·0), 1·98 (d, 1·2), 2·28 (d, 1·2), 2·42 (m, 2 H), 3·00—3·70 (m, 2 H), 3·70—4·20 (m, 1 H), 5·71 (s, 1 H), 5·63 (s, 1 H).

TABLE I

Properties of compounds *V*—*XI*

Compound[a] B.p., °C	Mass M^+	IR cm^{-1}	Formula (m.w.)	Calculated/Found % C	% H
V 131—136	236	3 820, 3 125, 1 714, 1 642, 1 610, 1 245, 1 158, 1 089	$C_{14}H_{20}O_3$ (236·3)	71·16 71·19	8·53 8·43
VII 133—141	300	2 840, 1 713, 1 641, 1 607, 1 245, 1 157, 1 123, 1 052	$C_{16}H_{28}O_5$ (300·4)	63·97 63·50	9·40 9·48
VIII 129—135	254	1 721, 1 714, 1 642, 1 608, 1 357, 1 245, 1 158, 1 139, 1 115	$C_{14}H_{22}O_4$ (254·3)	66·11 66·57	8·72 8·48
IX 134—138	256	3 595, 1 714, 1 640, 1 607, 1 247, 1 150, 997, 951	$C_{14}H_{24}O_4$ (256·3)	65·59 65·52	9·44 9·68
X 136—144	298	1 714, 1 652, 1 607, 1 247, 1 148, 1 118, 1 100, 955	$C_{16}H_{26}O_5$ (298·4)	64·40 64·86	8·78 8·71
VI 130—138	240	1 711, 1 639, 1 611, 1 242, 1 158, 1 196, 1 110	$C_{14}H_{24}O_3$ (240·3)	69·96 69·80	10·07 10·12
XI 131—139	224	1 686, 1 634, 1 588, 1 127, 1 150, 981	$C_{14}H_{24}O_2$ (224·3)	74·95 74·81	10·78 10·63

[a] Bath temperature; vacuum 13 Pa.

Ethyl 10-Ethylenedioxy-3,7-dimethyl-8-oxa-2,4-undecadienoate (*X*)

A mixture of keto ester *VIII* (0·3 g, 1·18 mmol), ethylene glycol (0·15 g, 2·38 mmol) and *p*-toluenesulfonic acid (9 mg) in 20 ml of benzene was heated under simultaneous distillation off of benzene for 1 h. The residue was diluted with 15 ml of ether and the solution was washed with 10 ml of an aqueous solution of sodium hydrogen carbonate and then dried over anhydrous sodium sulfate. After working up the yield was 0·14 g (40%) of the product. ^{1}H NMR spectrum (ppm): 1·17 (d, 3 H, 6·5), 1·27 (t, 3 H, 7·0), 1·99 (d, 1·2), 2·27 (d, 1·2), 2·41 (m, 2 H), 3·41 (s, 2 H), 3·97 (s, 4 H), 5·62 (s), 5·70 (s).

5,9-Dimethyl-10-oxa-trideca-4,6-dien-3-one (*XI*)

Ester *VI* (1·4 g, 5·8 mmol) was hydrolyzed with an aqueous-ethanolic alkali. The acid obtained was dissolved in 20 ml of anhydrous ether and a solution of ethyllithium was added to it dropwise. Ethyllithium was prepared from ethyl bromide (1·2 g) and lithium (0·16 g) in 30 ml of ether under cooling with a mixture of ice and water, with stirring. The mixture was allowed to stand for 15 min in a refrigerator and then decomposed with ice. After working up and chromatography 0·4 g (31%) of the product were obtained. Its physical constants are given in Table I.

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