SYNTHESIS OF SOME DIOXA ANALOGUES OF ACYCLIC JUVENOIDS*

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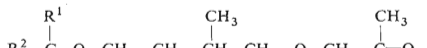
Received September 20th, 1976

A series of aliphatic branched esters and amides of 5,8-, 5,9-, and 5,10-dioxa-2-alkenoic acids was prepared as bioanalogues of the insect juvenile hormone. Some of them are particularly active on some representants of *Diptera*.

The occurrence of some biologically active substances[1] among the oxa analogues of the insect juvenile hormone prompted us to examine the dioxa series. The object of the present paper is preparation of dioxa analogues, one of the oxygen atoms being always placed at position 5. The thus-prepared compounds *V–XVI* include esters and amides of 3,7,11,11-tetramethyl-5,10-dioxa-2-dodecenoic acid, 11-ethyl--3,7-dimethyl-5,10-dioxa-2-tridecenoic acid, 3,7,11-trimethyl-5,9-dioxa-2-dodecenoic acid, and 3,7,10-trimethyl-5,8-dioxa-2-undecenoic acid (Table I).

In the synthesis of compounds *V–XVI*, the ketones *I–IV* were used as key intermediates. Ketones *I* and *II* were prepared from 6,6-dimethyl-5-oxa-2-heptanone and 6-ethyl-5-oxa-2-octanone, resp. Thus, the Darzens reaction with ethyl chloro-

Ia, $R^1 = R^2 = R^3 = CH_3$
IIa, $R^1 = R^2 = C_2H_5$, $R^3 = H$



I, $R^1 = R^2 = R^3 = CH_3$
II, $R^1 = R^2 = C_2H_5$, $R^3 = H$

* Part XXXIII in the series Natural and Synthetic Materials with the Insect Hormone Activity; Part XXXII: This Journal *41*, 1253 (1975).

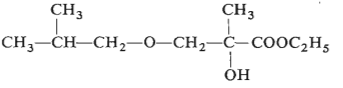
TABLE I

Elemental Analyses and Boiling Points of Compounds *I*–*XVI*

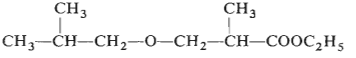
Compound	Formula (mol.wt.)	Calculated/Found			Distils at[a] °C/Torr
		% C	% H	% N	
I	$C_{12}H_{24}O_3$	66·63	11·18	—	125–135
	(216·3)	66·99	11·34	—	13
II	$C_{13}H_{26}O_3$	67·78	11·38	—	147–155
	(230·3)	67·86	11·47	—	13
III	$C_{11}H_{22}O_3$	65·30	10·96	—	115–125
	(202·3)	65·90	11·00	—	15
IV	$C_{10}H_{20}O_3$	63·78	10·71	—	120–125
	(188·3)	63·96	10·89	—	16
V	$C_{16}H_{30}O_4$	67·09	10·56	—	100–110
	(286·4)	67·02	10·78	—	0·009
VI	$C_{17}H_{32}O_4$	67·96	10·74	—	105–120
	(300·4)	68·30	10·60	—	0·009
VII	$C_{18}H_{35}NO_3$	68·96	11·25	4·47	
	(313·5)	69·22	11·32	4·51	
VIII	$C_{16}H_{31}NO_3$	—	—	4·91	
	(285·4)	—	—	5·00	
IX	$C_{17}H_{32}O_4$	67·96	10·74	—	118–128
	(300·4)	68·21	10·63	—	0·008
X	$C_{19}H_{37}NO_3$	69·68	11·39	4·28	137–147
	(327·5)	69·81	11·47	4·28	0·008
XI	$C_{15}H_{28}O_4$	66·14	10·36	—	107
	(272·4)	66·50	10·18	—	0·01
XII	$C_{17}H_{33}NO_3$	68·19	11·11	4·68	140–150
	(299·4)	68·39	11·13	4·72	0·009
XIII	$C_{14}H_{26}O_4$	65·10	10·15	—	95–105
	(258·3)	65·08	10·07	—	0·008
XIV	$C_{15}H_{28}O_4$	66·14	10·36	—	95–100
	(272·4)	66·50	10·30	—	0·008
XV	$C_{16}H_{31}NO_3$	67·33	10·95	4·91	107–115
	(285·4)	67·37	10·78	5·05	0·008
XVI	$C_{14}H_{27}NO_3$	65·32	10·57	5·44	140
	(257·4)	65·05	10·62	5·45	0·009

[a] Bath temperature is given.

acetate in the presence of sodium hydride afforded the corresponding glycide esters which were saponified and the acids decarboxylated to yield the corresponding aldehydes. The lithium aluminium hydride reduction of the aldehydes afforded the primary alcohols *Ia* and *IIa* from which the dioxa ketones *I* and *II* were prepared by reaction with diazoacetone[2] under catalysis of boron trifluoride etherate. The ketone *III* was obtained in several steps from 6-methyl-4-oxa-2-heptanone. Addition of hydrogen cyanide yielded a cyanohydrin which was saponified in acidic media in the presence of ethanol to afford the hydroxy ester *IIIa*. Dehydration of the ester *IIIa* with phosphorus oxychloride in pyridine and hydrogenation of the resulting unsaturated ester on Pd/C catalyst afforded the saturated ester *IIIb*. The lithium aluminium hydride reduction of the ester *IIIb* gave the alcohol *IIIc* from which the



IIIa



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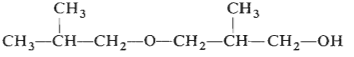
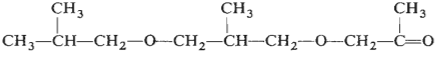
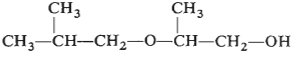


IIIc

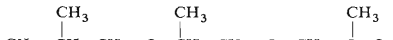


III

ketone *III* was prepared by an acid-catalysed reaction with diazoacetone. In the synthesis of the ketone *IV*, the sulfuric acid-catalysed reaction of isobutyl alcohol with 2-methyloxirane[3] yielded a mixture of 6-methyl-4-oxa-2-heptanol and 2,5-dimethyl-3-oxa-1-hexanol (*IVa*). The primary alcohol *IVa* was isolated from the mixture by heating with phthalic anhydride in benzene and saponification of the resulting hydrogen phthalate. The recovered alcohol *IVa* was treated with diazoacetone in the presence of boron trifluoride etherate to afford the dioxa ketone *IV*.



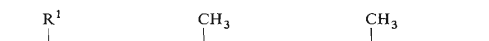
IVa



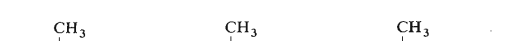
IV

By reaction with ethoxycarbonylmethylenetriphenylphosphorane[4,5] and dimethylaminocarbonylmethylenetriphenylphosphorane[4], the ketone *I* yielded the ester *V* and the N,N-diethylamide *VII*, resp. On treatment with diethyl ethoxycarbonylmethanephosphonate[6] or diisopropyl isopropoxycarbonylmethanephosphonate in the presence of sodium hydride as the base, the ketones *I*–*IV* were converted into the ethyl and isopropyl esters *V*, *VI*, *IX*, *XI*, *XIII*, and *XIV*. The N,N-diethylamides and N-ethylamides *VII*, *VIII*, *X*, *XII*, *XV*, and *XVI* were prepared from the ketones *I*–*IV* by reaction with diethyl diethylaminocarbonylmethanephosphonate or diethyl ethylaminocarbonylmethanephosphonate.

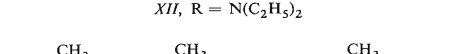
The juvenile activity assays are mentioned in the experimental part (for details see ref.[1]).



V, $R^1 = R^2 = R^3 = CH_3$, $R = OC_2H_5$
VI, $R^1 = R^2 = R^3 = CH_3$, $R = OCH(CH_3)_2$
VII, $R^1 = R^2 = R^3 = CH_3$, $R = N(C_2H_5)_2$
VIII, $R^1 = R^2 = R^3 = CH_3$, $R = NHC_2H_5$
IX, $R^1 = R^2 = C_2H_5$, $R^3 = H$, $R = OC_2H_5$
X, $R^1 = R^2 = C_2H_5$, $R^3 = H$, $R = N(C_2H_5)_2$



XI, $R = OC_2H_5$
XII, $R = N(C_2H_5)_2$



XIII, $R = OC_2H_5$
XIV, $R = OCH(CH_3)_2$
XV, $R = N(C_2H_5)_2$
XVI, $R = NHC_2H_5$

EXPERIMENTAL

The IR spectra were taken in tetrachloromethane. The ^{1}H-NMR spectra were measured in deuteriochloroform with the use of tetramethylsilane as internal standard. Chemical shifts are ex-

pressed in δ (ppm) and coupling constants in Hz. Chromatography was performed on the Pitra macroporous silica gel (12% of water), produced by Service Laboratories of this Institute. Gas chromatography was carried out on a Pye Argon Chromatograph with a radioactive ionisation detection. Mass spectra were taken on an A.E.I. MS 902 apparatus.

Alcohols *Ia* and *IIa*

At −15°C, sodium hydride (2·8 g) was added over 2 h with stirring to a solution of 6,6-dimethyl--5-oxa-2-heptanone or 6-ethyl-5-oxa-2-octanone (0·11 mol each) and ethyl chloroacetate (16·5 g) in hexane (50 ml). The mixture was stirred for 3 h, poured into water preacidified with acetic acid, extracted with ether, and the extract processed as usual. The residue (24−26 g) was treated at −10°C with 10% aqueous sodium hydroxide (50 ml), the mixture stirred with cooling for 3 h, the acidic portion extracted with ether, and the extract worked up, and the residue distilled to afford the aldehydic fractions boiling at 90−95°C/20 Torr and 104−108°C/20 Torr, resp., in 25−30% yields. These fractions were directly subjected to reduction.

The appropriate aldehyde (0·03 mol) was added dropwise with cooling to a suspension of lithium aluminium hydride (0·5 g) in ether (50 ml); the mixture was stirred at 20°C for 2 h and then refluxed for 1 h. The excess reagent was decomposed with water, the mixture acidified with hydrochloric acid, and the ethereal layer worked up to afford 95% yields of distilled alcohols.

2,6,6-Trimethyl-5-oxa-1-heptanol (*Ia*), b.p. 105−110°C/16 Torr. For $C_9H_{20}O_2$ (160·3) calculated: 67·45% C, 12·58% H; found: 67·20% C, 12·40% H. 6-Ethyl-2-methyl-5-oxa-1-octanol (*IIa*), b.p. 120−125°C/15 Torr. For $C_{10}H_{22}O_2$ (174·3) calculated: 68·90% C, 12·72% H; found: 69·20% C, 12·92% H.

Ethyl 2-Hydroxy-2,6-dimethyl-4-oxaheptanoate (*IIIa*)

At 0°C to −5°C, 40% aqueous sulfuric acid (66 g) was added dropwise over 5 h to a mixture of 6-methyl-4-oxa-2-heptanone (33 g), potassium cyanide (21·5 g), ethanol (200 ml), and water (30 ml). The mixture was stirred for 2 h, diluted with water, extracted with ether, and the extract worked up. The crude cyanohydrin (50 g) was dissolved in ethanol (100 ml) and hydrochloric acid (30 ml) was added. The mixture was saturated with gaseous hydrogen chloride and refluxed for 4 h. The saturation and refluxing was repeated twice more. The mixture was then diluted with water, extracted with ether, and the neutral portion isolated. Yield, 56% of the ester *IIIa*, b.p. 103−105°C/14 Torr. For $C_{10}H_{20}O_4$ (204·3) calculated: 58·79% C, 9·87% H; found: 59·12% C, 9·87% H.

Ethyl 2,6-Dimethyl-4-oxaheptanoate (*IIIb*)

Ethyl 2-hydroxy-2,6-dimethyl-4-oxaheptanoate (28 g) was added dropwise with stirring at 20 to 30°C into a mixture of phosphorus oxychloride (17 ml), pyridine (135 ml), and benzene (150 ml). The mixture was stirred for 1 h, heated at 80−90°C for 2 h, cooled down, poured into water, extracted with ether, and the neutral portion isolated in 66% yield (b.p. 110−115°C/18 Torr). The thus-prepared unsaturated ester (16 g) was hydrogenated in ethanol over 5% Pd/C catalyst (400 mg). Yield, 85% of the ester *IIIb*, b.p. 95−98°C/18 Torr. For $C_{10}H_{20}O_3$ (188·3) calculated: 63·78% C, 10·71% H; found: 63·64% C, 10·71% H.

2,6-Dimethyl-4-oxa-1-heptanol (*IIIc*)

At −10°C to 0°C, ethyl 2,6-dimethyl-4-oxaheptanoate (9·4 g) was added dropwise with stirring into a suspension of lithium aluminium hydride (1·5 g) in ether (250 ml). The mixture was stirred

with cooling for 2 h and refluxed for 20 min. The excess reagent was decomposed with water, the mixture acidified with hydrochloric acid, and worked up to afford a 82% yield of the alcohol *IIIc*, b.p. 100—104°C/30 Torr. For $C_8H_{18}O_2$ (146·2) calculated: 65·72% C, 12·41% H; found: 66·08% C, 12·36% H.

2,5-Dimethyl-3-oxa-1-hexanol (*IVa*)

2-Methyloxirane (52 g) in isobutyl alcohol (50 ml) was added dropwise with stirring at 100°C over 4 h into a mixture of isobutyl alcohol (200 ml) and sulfuric acid (17 ml). The whole was heated at 100°C for 2 h, cooled down, treated with magnesium oxide (1·5 g), stirred for 30 min, filtered, and the isobutyl alcohol from the filtrate removed by distillation through a 15 cm column. The residue (50 g) was heated with phthalic anhydride (50 g) in benzene (300 ml) for 4 h at 80 to 90°C, the acidic portion extracted with aqueous sodium carbonate, the extract treated with 40% aqueous sodium hydroxide (50 ml), and the whole refluxed for 1 h. The alcohol was isolated by extraction with ether. Yield, 25% of compound *IVa* distilling at 75—80°C/30 Torr. For $C_7H_{16}O_2$ (132·2) calculated: 63·60% C, 12·19% H; found: 63·41% C, 12·00% H.

Preparation of Ketones *I*—*IV*

At —15°C, acetyl chloride (4·0 g) was added dropwise with shaking into a solution of diazomethane (8·0 g) in ether (250 ml). After 1 h, the solution was concentrated under diminished pressure at —5°C to 0°C to the volume of about 20—30 ml. The appropriate alcohol (0·05 mol) and boron trifluoride etherate (0·1—0·2 g) was added to the concentrate and the reaction initiated by heating the mixture to 15—25°C. When the evolution of nitrogen ceased, the mixture was diluted with water, extracted with ether, and the extract worked up. The residue was subjected to fractional distillation. The ketonic fraction was purified by chromatography on 30—40 parts of silica gel with the use of 6 : 1 light petroleum–ether as eluant. The ketones were obtained in 20—25% yields.

In this manner, the alcohol *Ia* yielded 6,10,10-trimethyl-4,9-dioxa-2-undecanone (*I*) and the alcohol *IIa* afforded 10-ethyl-6-methyl-4,9-dioxa-2-dodecanone (*II*). The alcohols *IIIc* and *IVa* furnished 6,10-dimethyl-4,8-dioxa-2-undecanone (*III*) and 6,9-dimethyl-4,7-dioxa-2-decanone (*IV*), resp. (Table I).

Preparation of Esters *V*, *VI*, *IX*, *XI*, *XIII*, and *XIV*

Diethyl ethoxycarbonylmethanephosphonate or diisopropyl isopropoxycarbonylmethanephosphonate (1·75 mmol) was added dropwise with stirring at 20°C to a suspension of sodium hydride (40 mg) in 1,2-dimethoxyethane (8 ml) under nitrogen and the mixture was stirred for 1 h. The appropriate ketone (1·6 mmol) was then added dropwise and the stirring continued for 3 h at 20—40°C. The course of the reaction was checked by thin-layer chromatography. When the reaction was complete, the mixture was poured into water preacidified with acetic acid, the product extracted with light petroleum, the extract worked up, and the crude product purified by chromatography on 30—40 parts of silica gel with the use of 9 : 1 light petroleum–ether as eluant. The first chromatographic fractions contained the *cis*-isomer while the *trans*-isomer was isolated from back fractions. Yields, 80—90%. The ratio of *cis*-isomers to *trans*-isomers, 1 to 1·5—2·0.

In this manner, the ketone *I* afforded ethyl and isopropyl 3,7,11,11-tetramethyl-5,10-dioxa-2-dodecenoate (*V* and *VI*). The ketone *II* yielded ethyl 11-ethyl-3,7-dimethyl-5,10-dioxa-2-tridecenoate (*IX*) and from the ketone *III*, ethyl 3,7,11-trimethyl-5,9-dioxa-2-dodecenoate (*XI*)

was prepared. The ketone *IV* furnished ethyl and isopropyl 3,7,10-trimethyl-5,8-dioxa-2-undecenoate (*XIII* and *XIV*).

Preparation of Amides *VII*, *VIII*, *X*, *XII*, *XV*, and *XVI*

The amides were prepared analogously to the esters with the use of sodium hydride (40 mg), 1,2-dimethoxyethane (8 ml), diethyl diethylaminocarbonylmethanephosphonate or diethyl ethylaminocarbonylmethanephosphonate (1·75 mmol each), and the appropriate ketone (1·6 mmol). The crude amides were purified by chromatography on 30–40 parts of silica gel with the use of light petroleum–ether (4 : 1) as eluant. The first chromatographic fractions contained the *cis*-isomer while the *trans*-isomer was present in back fractions. Yields, 60–85%. The ratio of *cis*-isomers to *trans*-isomers, 1 to 1·5.

In this manner, the ketone *I* afforded the N,N-diethylamide and N-ethylamide of 3,7,11,11-tetramethyl-5,10-dioxa-2-dodecenoic acid (*VII* and *VIII*). The ketone *II* yielded the N,N-diethylamide of 11-ethyl-3,7-dimethyl-5,10-dioxa-2-tridecenoic acid (*X*). The ketone *III* furnished the N,N-diethylamide of 3,7,11-trimethyl-5,9-dioxa-2-dodecenoic acid (*XII*). From the ketone *IV*, the N,N-diethylamide and N-ethylamide of 3,7,10-trimethyl-5,8-dioxa-2-undecenoic acid (*XV* and *XVI*) resulted.

Compounds *V* and *VII*

A mixture of 6,10,10-trimethyl-4,9-dioxa-2-undecanone (190 mg), ethoxycarbonylmethylenetriphenylphosphorane (400 mg) or dimethylaminocarbonylmethylenetriphenylphosphorane (500 mg), benzoic acid (40 mg), and benzene (8 ml) was refluxed under nitrogen for 8–16 h, the benzene evaporated, and the residue repeatedly triturated with light petroleum. The extracts were combined and worked up. The crude products were purified by chromatography on silica gel. Yields, 50–55%.

Characterisation

Compounds *I*–*XVI* were characterised by elemental analysis and IR spectra. In some cases, the ^{1}H-NMR spectra or mass spectra were taken. The purity and the ratio of *cis*-isomers to *trans*-isomers was determined by gas chromatography. In the case of ketones *I*–*IV* and esters of dioxaalkenoic acids, Cellit impregnated with 10% of Apiezon L was used at 130–150°C (ketones) and 190–200°C (dioxa compounds). The amides of dioxaalkenoic acids were chromatographed on Gas Chrom Q impregnated with 3% SE 30 at 170–190°C.

The IR spectra of dioxa ketones *I*–*IV* contained absorption bands of the methly ketone (at about 1725 and 1355 cm^{-1}) and significant bands of the ethereal oxygen atom (1115–1125, 1090 cm^{-1}), indicating the presence of two ethereal groups in the molecule. The structures of ketones *I*–*III* were confirmed by ^{1}H-NMR spectra. 6,10,10-Trimethyl-4,9-dioxa-2-undecanone (*I*): $C_{(6)}$—CH_3 0·98, d, J = 6·9, 3 H; $C_{(10)}$—$(CH_3)_3$ 1·20, s, 9 H; 2 $H_{(7)}$ + $H_{(6)}$ 1·15–2·05, m, 3 H; $C_{(2)}$—CH_3 2·18, s, 3 H; 2 $H_{(8)}$ + 2 $H_{(5)}$ 3·38, m, 4 H; 2 $H_{(3)}$ 4·0, s, 2 H. 10-Ethyl-6-methyl-4,9-dioxa-2-dodecanone (*II*): $C_{(11)}$—CH_3 + $C_{(1')}$—CH_3 0·89, t, 6 H; $C_{(6)}$—CH_3 0·95, d, J = 6·8, 3 H; 2 $H_{(7)}$ + 2 $H_{(11)}$ + 2 $H_{(1')}$ 1·3–1·8, m, 6 H; $H_{(6)}$ 1·95, m, 1 H; $C_{(2)}$—CH_3, 2·16, s, 3 H; $H_{(10)}$ 3·08, m, 1 H; 2 $H_{(5)}$ + 2 $H_{(8)}$ 3·25–3·60, m, 4 H; 2 $H_{(3)}$ 3·98, s, 2 H. 6,10-Dimethyl-4,8-dioxa-2-undecanone (*III*): $C_{(10)}$—$(CH_3)_2$ 0·89, d, J = 7·0, 6 H; $C_{(6)}$—CH_3 0·98, d, J = 7·0, 3 H; $H_{(6)}$ + $H_{(10)}$ 1·50–2·30, m, 2 H; $C_{(2)}$—CH_3 2·17, s, 3 H; 2 $H_{(5)}$ + 2 $H_{(7)}$ + 2 $H_{(9)}$ 3·10–3·60, m, 6 H; 2 $H_{(3)}$ 3·98, s, 2 H. Mass spectrum of compound *III*

exhibited molecular peak M^+ 202 and the fragmentation M−43, M−57, *m/e* 43, 57, 73, 87, 129 was in accordance with the structure.

The IR spectra of esters *V*, *IX*, *XI*, and *XIII* exhibited absorption bands of the ester group in conjugation with a double bond (1 720, 1 715, 1 650–1 660, 1 225, and 1 150 cm^{-1}) and bands of the ethereal oxygen atom (1 115, 1 100 or 1 085 cm^{-1}). The structure of ethyl *cis*, *trans*-3,7,11,11-tetramethyl-5,10-dioxa-2-dodecenoate (*V*) was confirmed by ^{1}H-NMR spectrum: $C_{(7)}$—CH_3, 0·95, d, $J = 6·8$ (*cis*); $C_{(7)}$—CH_3 0·96, d, $J = 0·68$ (*trans*); $C_{(11)}$—$(CH_3)_3$ 1·19, s; 2 $H_{(8)}$ 1·20 to 1·80, m; $H_{(7)}$ 1·82, m; $C_{(3)}$—CH_3 1·95, q, $J(CH_3, H_2) = 1·3$, $J(CH_3, H_4) = J(CH_3, H_{4'}) = 0·75$ (*cis*); $C_{(3)}$—CH_3 2·09, m, $J(CH_3, H_2) = 1·3$, $J(CH_3, H_4) = J(CH_3, H_{4'}) = 1·2$ (*trans*); 2 $H_{(9)}$ + 2 $H_{(6)}$ 3·15–3·50, m (*cis*, *trans*); 2 $H_{(8)}$ 3·92, m (*trans*); 2 $H_{(8)}$ 4·55, m (*cis*); $H_{(2)}$ 5·72, m, $J(H_2, CH_3) = 1·3$, $J(H_2, H_4) + J(H_2, H_{4'}) = 1·5$ (*cis*); $H_{(2)}$ 5·93, m, $J(H_2, CH_3) = 1·3$, $J(H_2, H_4) + J(H_2, H_{4'}) = 1·65$ (*trans*); ethyl ester: CH_2 4·13, q, $J = 7·5$ (*cis*); CH_2 4·17, q, $J = 7·6$ (*trans*); —CH_3 1·27, t.

The IR spectra of N,N-diethylamides *VII*, *X*, *XII*, and *XV* contained absorption bands that were ascribed to a substituted amide group in conjugation with a double bond (1 660, 1 630 cm^{-1}) and bands of the ethereal oxygen atom (1 110, 1 100 cm^{-1}). The structure of amides *VII* and *X* was confirmed by ^{1}H-NMR spectra. N,N-Diethylamide of *trans*-3,7,11,11-tetramethyl-5,10-dioxa-2-dodecenoic acid (*VII*): $C_{(7)}$—CH_3 0·95, d, $J = 6·8$, 3 H; 2 CH_3 N,N-diethylamide 1·15, t, $J = 7·1$, 6 H; $C_{(11)}$—$CH_3)_3$ 1·18, s, 9 H; 2 $H_{(8)}$ + $H_{(7)}$ 1·20–2·00, m, 3 H; $C_{(3)}$—CH_3 1·98, m, $J = 1·3$, 3 H; 2 $H_{(9)}$ + 2 $H_{(6)}$ + 2 CH_2 N,N-diethylamide 3·15–3·55, cm, 8 H; 2 $H_{(4)}$ 3·92, m, 2 H; $H_{(2)}$ 6·11, m, $J = 1·3$, 1 H. t. N,N-Diethylamide of *cis*-11-ethyl-3,7-dimethyl-5,10-dioxa-2-tridecenoic acid (*X*): $C_{(11)}$—CH_3 + $C_{(1')}$—CH_3 0·87, t, 6 H; $C_{(7)}$—CH_3 0·93, d, $J = 7·1$, 3 H; 2 CH_3 N,N-diethylamide 1·12, t, 6 H; 2 $H_{(8)}$ + 2 $H_{(11)}$ + 2 $H_{(1')}$ 1·25–1·75, m, 6 H; $H_{(7)}$ 1·81, m, 1 H; $C_{(3)}$—CH_3 1·88, m, $J = 1·2$, 3 H; $H_{(10)}$ 3·07, m, $J = 5·8$, 1 H; 2 $H_{(9)}$ + + 2 $H_{(6)}$ + 2 CH_2 N,N-diethylamide, 3·20–3·60, cm, 8 H; 2 $H_{(4)}$ 4·25, s, 2 H; $H_{(2)}$ 5·91, m, 1 H. The *trans*-isomer differed in the following values: $C_{(7)}$—CH_3 0·94, d, $J = 6·8$, 3 H; $C_{(3)}$—CH_3 1·87, m, 3 H; 2 $H_{(4)}$ 3·88, m, 2 H; $H_{(2)}$ 6·20, m, 1 H.

The IR spectra of N-ethylamides *VIII* and *XVI* exhibited absorption bands due to a monosubstituted amide groups in conjugation with a double bond (3 460, 1 677, 1 650, 1 540, and 1 506 cm^{-1}) and an absorption band of the ethereal oxygen atom (1 115 cm^{-1}).

Biological Activity

The juvenile activity was expressed in ID-50 Morph. units designating such an amount of the test substance per specimen which when topically applied to the last instar larva brings about formation of a half-imaginal specimen. The esters of 5,10-dioxa and 5,9-dioxa acids exhibited juvenile activity on *Dysdercus cingulatus* (0·01–1·0 ID-50 Morph. units) and *Graphosoma italicum* (10 to 100 ID-50 Morph. units). The amides of 5,10-dioxa and 5,9-dioxa acids were active on *Tenebrio molitor* (5–30 ID-50 Morph. units). The 5,8-dioxa analogues were inactive.

Elemental analyses were performed in the Analytical Department (Dr J. Horáček, Head) of this Institute by Mrs V. Rusová, Mrs A. Froňková, Mrs Y. Černá, and Mrs E. Sýkorová. The IR spectra were measured by Mr P. Formánek and Mrs K. Matoušková and interpreted by Dr J. Smolíková. The ^{1}H-NMR *spectra were measured and interpreted by Dr M. Masojídková and Dr M. Synáčková. Technical assistance was supplied by Miss M. Tesařiková and Miss D. Stiborková. Biological assays were performed by Dr K. Sláma, Institute of Entomology, Czechoslovak Academy of Sciences, Prague.*

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Translated by J. Pliml.