

CYCLIC ANALOGUES OF THE INSECT JUVENILE HORMONE*

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Derivatives of 3,7-dimethyl-9-(2-oxolanyl)-2,6-nonadienoic acid (methyl, ethyl, isopropyl, cyclopropylmethyl, and propargyl ester, N-ethylamide, N,N-diethylamide, and nitrile), 3,7-dimethyl-9-(2-oxolanyl)-2-nonenic acid (methyl, ethyl, and isopropyl ester, N-ethylamide and N,N-diethylamide), and 3,7-dimethyl-9-(2-oxolanyl)-2,4-nonadienoic acid (methyl and isopropyl ester) have been prepared.

In connection with detailed investigations in the field of the insect juvenile hormone, particularly with respect to the relationship between chemical structure and biological activity, attention has been now paid to preparation** of bioanalogues in which the oxirane ring of the parent juvenile hormone had been replaced by the oxolane ring. The preparation of some of these analogues has been so far reported in patent applications only^{1,2}.

As the starting material in the synthesis of the present analogues, 4-(2-oxolanyl)-2-butanol (*I*) has been used. Compound *I* is readily accessible by the catalytic hydrogenation of furfurylideneacetone³. Oxidation of the alcohol *I* with the Jones reagent^{4,5} afforded 4-(2-oxolanyl)-2-butanone (*II*) which was converted to ethyl 3-methyl-5-(2-oxolanyl)-2-butenolate (*III*) by reaction with diethyl ethoxycarbonylmethanephosphonate⁶. The catalytic hydrogenation of compound *III* yielded ethyl 3-methyl-5-(2-oxolanyl)butanoate (*IV*) which was reduced with lithium aluminium hydride to afford 3-methyl-5-(2-oxolanyl)butanol (*VI*). A similar reduction of compound *III* gave 3-methyl-5-(2-oxolanyl)-2-butenol (*V*). The alcohols *V* and *VI* were converted to 1-bromo-3-methyl-5-(2-oxolanyl)-2-butene (*VII*) and 1-bromo-3-methyl-5-(2-oxolanyl)butane (*VIII*), resp. Alkylation of ethyl acetoacetate with bromides *VII* and *VIII* and ketonic hydrolysis of the resulting keto esters afforded 6-methyl-8-(2-oxolanyl)-5-octen-2-one (*IX*) and 6-methyl-8-(2-oxolanyl)-2-octanone (*X*), resp.

By reaction of ketones *IX* and *X* either with triphenylalkoxycarbonylmethylene-

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** The biological activity of the present substances will be reported elsewhere.

phosphoranes under acidic catalysis⁷ or with dialkyl esters of alkoxy-carbonyl-methane (or cyanomethane-, alkylaminocarbonylmethane-, and dialkylaminocarbonylmethane-)phosphonic acids^{6,8} there were prepared the corresponding derivatives of 3,7-dimethyl-9-(2-oxolanyl)-2,6-nonadienoic acid (derivatives *XIa–XIc*, *XIh*, *XIi*, *XV*) and of 3,7-dimethyl-9-(2-oxolanyl)-2-nonenoic acid (*XIIa–XIIe*), resp.

The propargyl ester *XIf* and the cyclopropylmethyl ester *XIg* were prepared from the ethyl ester *XIb* by saponification, conversion of the liberated acid *XId* to its chloride *XIe*, and the subsequent reaction with the appropriate primary alcohol^{9,10}.

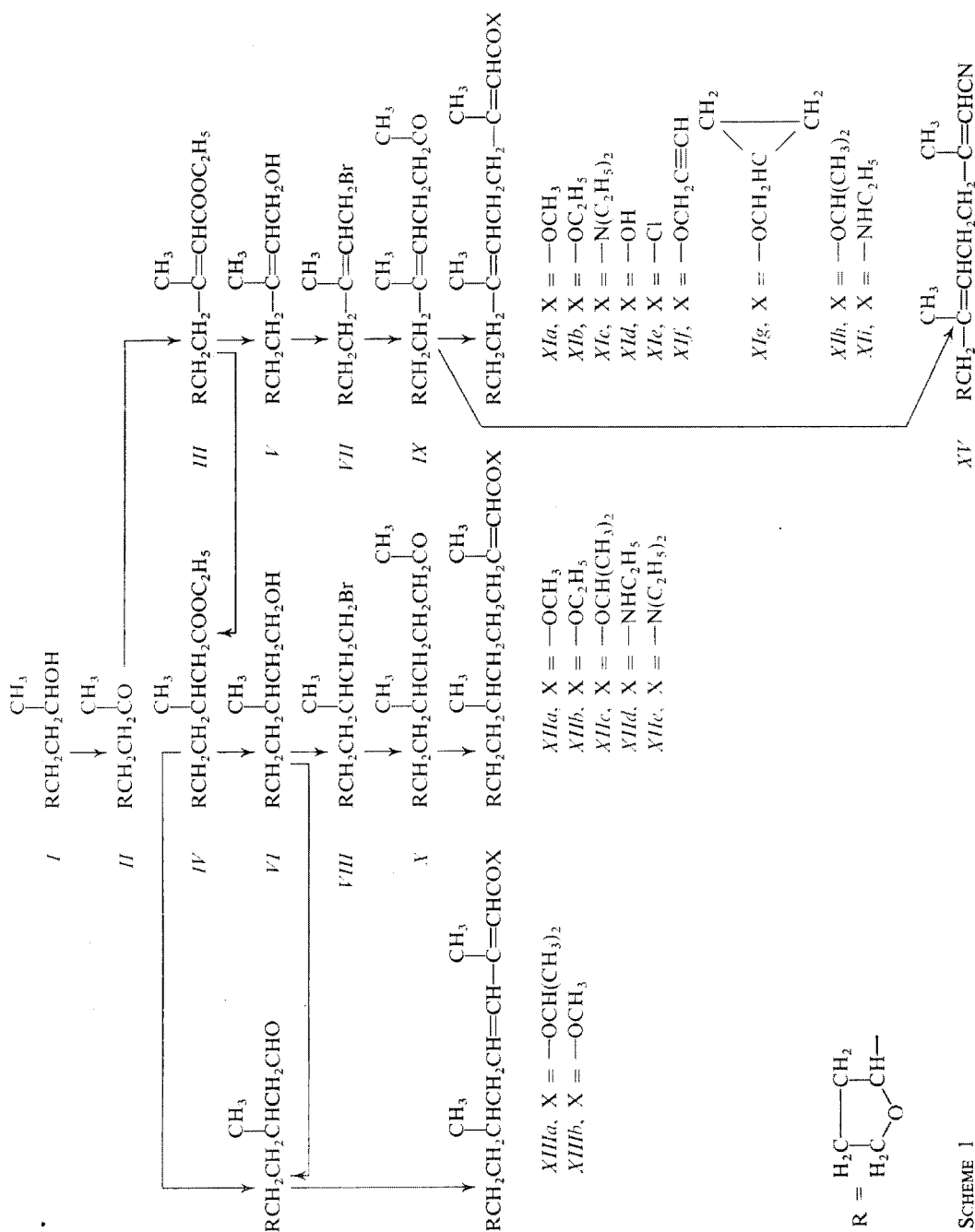
The esters *XIIIa* and *XIIIb* of 3,7-dimethyl-9-(2-oxolanyl)-2,4-nonadienoic acid were prepared from 3-methyl-5-(2-oxolanyl)pentanal (*XIV*) by reaction with the corresponding dialkyl 2-methyl-3-alkoxy-carbonyl-2-propenephosphonates. The aldehyde *XIV* is accessible either by reduction of ethyl 3-methyl-5-(2-oxolanyl)pentanoate (*IV*) with sodium dihydridobis(2-methoxyethoxy)aluminum¹¹ or by oxidation of 3-methyl-5-(2-oxolanyl)pentanol (*VI*) with the chromic trioxide-pyridine complex in dichloromethane¹². All the reaction steps are depicted in Scheme 1.

EXPERIMENTAL

Column chromatography was performed on the Pitra silica gel (particle size, 60–120 micron; produced by Service laboratories of this Institute), partially deactivated by the addition of 12% water. Thin-layer chromatography was carried out on the Merck silica gel G. The homogeneity of substances and the ratio of *cis/trans* isomers was determined by gas chromatography on a Pyc Argon Chromatograph with ionisation detection (⁹⁰Sr); the columns were packed with 10% butanediol succinate or QF 1 on Chromosorb W. The IR spectra were taken on a UR 10 or UR 20 spectrometer (Carl Zeiss, Jena, German Democratic Republic) in tetrachloromethane. The UV spectra were recorded in ethanol on an Optica Milano CF 4 spectrometer. The mass spectra were measured on an A.I.E. MS 902 apparatus combined with a Pyc Series 104 Model 64 gas chromatograph.

4-(2-Oxolanyl)-2-butanone (*II*)

4-(2-Oxolanyl)-2-butanol³ (*I*; 149.4 g; 1.036 mol) was dissolved in oxidation-stable acetone (600 ml) and the solution cooled down to +5°C. The precooled oxidant (77.8 g *i.e.* 0.8 mol of chromium trioxide, 341 ml of water, and 127.6 g *i.e.* 1.25 mol of conc. sulfuric acid) was then dropwise added with vigorous stirring over 30 min at such a rate to maintain the temperature at about 20°C. After stirring for 4 h at room temperature, the starting alcohol *I* practically disappeared (thin-layer chromatography, 9 : 1 light petroleum-acetone). The excess oxidant was then decomposed by addition of the required amount of solid sodium metabisulfite (Na₂S₂O₅). The lower aqueous phase was separated and extracted with light petroleum (200 ml). The extract was combined with the original upper phase; two layers resulted; the lower phase was combined with the original lower phase and extracted with light petroleum (200 ml). This extract was combined with the original upper phase; if a lower layer separated, it was combined with the original lower phase. The whole process was repeated twice more. The thus-obtained extract was successively washed with two 50 ml portions of saturated aqueous sodium chloride, two 50 ml portions of saturated aqueous sodium hydrogen carbonate, and saturated aqueous sodium chloride (50 ml)



SCHEME 1

again, dried over anhydrous magnesium sulfate, and distilled under diminished pressure to afford 7.03 g (4.8%) of the forerun, b.p. up to 91.5°C/13.5 Torr, and 109.6 g (74.4%) of the ketone *II*, b.p. 91.5–98.5°C/13.5 Torr. For $C_8H_{14}O_2$ (142.2) calculated: 67.57% C, 9.93% H; found: 67.54% C, 9.78% H. IR spectrum (cm^{-1}): 1721, 1359, 1079, and 1033.

Ethyl 3-Methyl-5-(2-oxolanyl)butanoate (*IV*)

Ethyl 3-methyl-5-(2-oxolanyl)-2-butenolate⁶ (*III*; 96.8 g; 0.456 mol) was dissolved in 96% ethanol (150 ml) and hydrogenated over a 5% palladium on active charcoal catalyst to afford 88.2 g of a liquid, b.p. 72°C/0.2 Torr to 94.5°C/0.1 Torr. The purity of the product was not satisfactory as shown by thin-layer chromatography on silica gel in 9 : 1 light petroleum–acetone. The crude product was therefore subjected to column chromatography on silica gel (1700 g) in 96 : 4 light petroleum–acetone to afford 76.3 g (78%) of the ester *IV*, b.p. 80°C/0.03 Torr to 77.2°C/0.008 Torr. For $C_{12}H_{22}O_3$ (214.3) calculated: 67.25% C, 10.35% H; found: 67.28% C, 10.30% H. IR spectrum (cm^{-1}): 1734, 1185, 1160, 1096, and 1069.

3-Methyl-5-(2-oxolanyl)-2-butenol (*V*)

The ester⁶ *III* (21.3 g; 0.1 mol) in ether (100 ml) was added dropwise with stirring and cooling (–20°C) over 80 min into a solution of lithium aluminium hydride (2.47 g) in ether (300 ml). The mixture was stirred in the original freezing bath for 2.5 h (after this period of time the bath temperature was –10°C), allowed to warm to room temperature and decomposed¹³ by successive additions of water (2.5 ml), 15% aqueous sodium hydroxide (2.5 ml), and water (7.5 ml) again. The precipitate was filtered off and washed with ether. The filtrate and washings were processed as usual, dried over Drierite and distilled to afford 0.47 g of the forerun, b.p. up to 100°C/0.25 Torr, and 13.7 g (80.4%) of the alcohol *V*, b.p. 100–106°C/0.25 Torr. For $C_{10}H_{18}O_2$ (170.2) calculated: 70.54% C, 10.66% H; found: 70.41% C, 10.38% H. IR spectrum (cm^{-1}): 3615, 1665, 1089, 1069, 1024, and 1006.

3-Methyl-5-(2-oxolanyl)butanol (*VI*)

The ester *IV* (67.85 g; 0.316 mol) in ether (70 ml) was added dropwise with stirring over 1 h into a solution of lithium aluminium hydride (7.21 g; 0.19 mol) in ether (430 ml), the mixture refluxed for 2 h, decomposed¹³ by the successive additions of water (7.3 ml), 15% aqueous sodium hydroxide (7.3 ml), and water (21.9 ml) again, and processed as usual to afford 51.9 g (95.2%) of compound *VI*, b.p. 102.1–103.0°C/0.43 Torr. For $C_{10}H_{20}O_2$ (172.3) calculated: 69.72% C, 11.70% H; found: 69.74% C, 11.96% H.

1-Bromo-3-methyl-5-(2-oxolanyl)-2-butene (*VII*)

Into a solution containing the alcohol *V* (67.3 g; 0.395 mol), light petroleum (115 ml), and dry pyridine (9.5 ml) there was added dropwise with stirring and cooling to –15°C over 90 min a solution of phosphorus tribromide (48.1 g; 0.178 mol) in light petroleum (40 ml). The mixture was stirred at –14°C for additional 30 min, poured into a mixture of ice and water, and extracted with light petroleum. The extract was successively washed with water, 0.5M potassium hydrogen carbonate, and water again, dried over Drierite, and taken down under diminished pressure on a rotatory evaporator at the bath temperature of 20°C to afford 74.5 g (81%) of the crude bromide *VII* which was used in the next step without delay because of its instability.

1-Bromo-3-methyl-5-(2-oxolanyl)butane (*VIII*)

The title compound *VIII* was prepared according to ref.¹⁴ from the alcohol *VI* (45.0 g; 0.261 mol), triphenylphosphine (75.4 g; 0.287 mol), dimethylformamide (260 ml), and dry bromine (45.9 g; 0.287 mol). The light petroleum extract was cooled down, the solid triphenylphosphine oxide filtered off, and the filtrate processed as usual. In the attempted distillation under diminished pressure, the crude bromide began to decompose. The content of the distillation flask was therefore cooled down, poured into water, and the bromide extracted into light petroleum. The extract was successively washed with water, 0.5M potassium hydrogen carbonate, and water again until neutral, dried over magnesium sulfate, evaporated, and the residue chromatographed on silica gel (440 g) in 96 : 4 light petroleum–ether. Yield, 39.2 g (64%) of the bromide *VIII*. For $C_{10}H_{19}BrO$ (235.2) calculated: 51.07% C, 8.15% H, 33.98% Br; found: 51.02% C, 8.11% H, 33.90% Br.

6-Methyl-8-(2-oxolanyl)-5-octen-2-one (*IX*)

A mixture of the crude bromide *VII* (74.5 g; 0.319 mol) and ethyl acetoacetate (54.1 g; 0.415 mol) was cooled down to $-20^{\circ}C$ and treated dropwise with stirring over 1 h with ethanolic sodium ethoxide (from 8.1 g of sodium and 180 ml of ethanol) at such a rate to keep the temperature between $-12^{\circ}C$ and $-7^{\circ}C$. The stirring was continued for 3 h at the same temperature. The mixture was then allowed to stand for 48 h, heated to $80^{\circ}C$, and treated dropwise at this temperature over 1 h with 10% aqueous sodium hydroxide (507 ml). The whole mixture was then heated at $80^{\circ}C$ for additional 4 h, cooled down, extracted with light petroleum, and the extract processed as usual to afford 2.7 g of a forerun, b.p. up to $107^{\circ}C/0.45$ Torr, and 57.8 g (86%) of the required ketone *IX*, b.p. $107^{\circ}C/0.45$ Torr to $116^{\circ}C/0.3$ Torr. The analytical sample was redistilled. For $C_{13}H_{22}O_2$ (210.3) calculated: 74.24% C, 10.54% H; found: 74.54% C, 10.51% H. IR spectrum (cm^{-1}): 1720, 1670, 1360, and 1070.

6-Methyl-8-(2-oxolanyl)-2-octanone (*X*)

Into a stirred ethanolic sodium ethoxide solution (from 4.4 g of sodium and 95 ml of ethanol) there was added dropwise over 15 min ethyl acetoacetate (26.0 g; 0.2 mol) and then over 1 h the bromide *VIII* (39.2 g; 0.167 mol). The mixture was kept at room temperature overnight and heated at $90^{\circ}C$ for 9 h. Aqueous 10% sodium hydroxide (245 ml) was then added dropwise at $90^{\circ}C$ over 30 min and the heating at $90^{\circ}C$ continued for additional 4 h. The mixture was then cooled down, extracted with light petroleum, and the extract processed as usual to afford 5.97 g of a forerun, b.p. up to $99^{\circ}C/0.008$ Torr, and 21.0 g (59%) of the ketone *X*, b.p. $99.5-106.0^{\circ}C$: 0.008 Torr. The analytical sample was chromatographed on silica gel in 95 : 5 light petroleum–acetone and redistilled. For $C_{13}H_{24}O_2$ (212.3) calculated: 73.53% C, 11.40% H; found: 73.55% C, 11.36% H. IR spectrum (cm^{-1}): 1720, 1360, 1080, 1069, and 1051.

Methyl 3,7-Dimethyl-9-(2-oxolanyl)-2-nonenoate (*XIIa*)

A mixture of the ketone *X* (2.17 g; 0.01 mol), methoxycarbonylmethylenetriphenylphosphorane (5.02 g; 0.015 mol) dry benzene (30 ml), and benzoic acid (0.99 g) was refluxed under argon for 24 h. A further portion of the phosphorane (1.67 g; 0.005 mol), benzene (10 ml), and benzoic acid (0.3 g) was then added and the reflux continued for additional 24 h. This procedure was repeated once more. The benzene was then evaporated under diminished pressure and the oily viscous residue extracted by repeated triturations with light petroleum. The extracts were combined and processed as usual. The resulting crude ester *XIIa* was chromatographed on silica gel

(175 g) in 93 : 7 light petroleum–methyl acetate and the fractions checked by thin-layer chromatography on silica gel in 85 : 15 light petroleum–methyl acetate. The appropriate fractions were pooled and distilled to afford 1.42 g (53%) of the ester *XIIa*, boiling at 120–130°C (bath temperature) and 0.004 Torr. As shown by gas–liquid chromatography, the *cis/trans* ratio of the main fraction was 41 : 59. For $C_{16}H_{28}O_3$ (268.4) calculated: 71.60% C, 10.52% H; found: 71.95% C, 10.63% H. IR spectrum (cm^{-1}): 1720, 1649, 1225, 1152, 1068.

Ethyl 3,7-Dimethyl-9-(2-oxolanyl)-2-nonenoate (*XIIb*)

A. The title ethyl ester *XIIb* was prepared analogously to the methyl ester *XIIa* from the ketone *X* (2.17 g; 0.01 mol). The crude product was chromatographed on a column of silica gel (175 g) in 96 : 4 light petroleum–ethyl acetate. The fractions were checked by thin-layer chromatography on silica gel in 9 : 1 light petroleum–ethyl acetate. The appropriate fractions were pooled and processed as usual to afford 1.60 g (57%) of the ester *XIIb* boiling at the bath temperature of 125°C : 0.004 Torr to 135°C/0.003 Torr. As shown by gas–liquid chromatography, the middle fraction of the product contained the *cis/trans* isomers in the ratio 42 : 58. For $C_{17}H_{30}O_3$ (282.4) calculated: 72.30% C, 10.71% H; found: 72.59% C, 10.92% H. IR spectrum (cm^{-1}): 1715, 1223, 1150, and 1047.

B. From the ketone *X* (2.17 g; 0.01 mol) and diethyl ethoxycarbonylmethanephosphonate (2.47 g; 11 mmol) there was obtained 2.36 g (84%) of the ester *XIIb* boiling at the bath temperature of 130°C/0.007 Torr to 140°C/0.005 Torr. As indicated by gas–liquid chromatography, the distillate contained three isomers. For $C_{17}H_{30}O_3$ (282.4) calculated: 72.30% C, 10.71% H; found: 72.12% C, 10.65% H. IR spectrum (cm^{-1}): 1749, 1715, 1223, 1150, 1048. The shoulder at 1735 cm^{-1} indicates the presence of a small amount of a non-conjugated compound. As determined by mass spectroscopy, all the three isomers exhibit the molecular ion 282. The mass spectra of two major isomers were identical while the spectrum of the third isomer differed in intensity of some fragment ions (this observation suggests localisation of the double bond in some other position).

Methyl 3,7-dimethyl-9-(2-oxolanyl)-2,6-nonadienoate (*XIa*) was prepared from the ketone *IX* (2.14 g; 0.01 mol) and dimethyl methoxycarbonylmethanephosphonate in the usual manner. Chromatography and distillation afforded fractions boiling at the bath temperatures of 108°C : 0.005 Torr to 115°C/0.004 Torr (0.66 g; 24.6%) and 108–120°C/0.004 Torr (1.38 g; 51.8%). As indicated by gas–liquid chromatography, the two fractions differed by the ratio of isomers only. For $C_{16}H_{26}O_3$ (266.4) calculated: 72.14% C, 9.84% H; found: 72.18% C, 9.77% H. IR spectrum (cm^{-1}): 1719, 1650, 1222, 1150, and 1070.

Ethyl 3,7-dimethyl-9-(2-oxolanyl)-2,6-nonadienoate (*XIb*) was prepared analogously from the ketone *IX* (2.14 g; 0.01 mol) and diethyl ethoxycarbonylmethanephosphonate in the usual manner. Chromatography and distillation afforded fractions boiling at the bath temperatures of 108 to 120°C/0.005 Torr (0.32 g; 11.4%) and 123–145°C/0.004 Torr (2.09 g; 74.5%). For $C_{17}H_{28}O_3$ (280.4) calculated: 72.81% C, 10.07% H; found: 73.09%, 10.20% H. IR spectrum (cm^{-1}): 1715, 1222, 1150, and 1070. As indicated by gas–liquid chromatography, the two fractions differed by the content of *cis/trans* isomers only.

N,N-Diethylamide of 3,7-dimethyl-9-(2-oxolanyl)-2,6-nonadienoic acid (*XIc*) was prepared from the ketone *IX* (2.14 g; 0.01 mol) and diethyl diethylaminocarbonylmethanephosphonate. Fractions obtained by column chromatography on silica gel (140 g) in 9 : 1 light petroleum–acetone were checked by thin-layer chromatography on silica gel in 8 : 2 light petroleum–acetone. The appropriate fractions were pooled and taken down under diminished pressure on a rotatory

evaporator. Three portions were obtained, differing in the content of isomers (as determined by gas-liquid chromatography: 0.50 g (16.3%), 1.32 g (42.9%), and 1.21 g (39.3%). For $C_{19}H_{30}NO_2$ (307.5) calculated: 74.22% C, 10.82% H, 4.55% N; found: 73.87% C, 10.82% H, 4.33% N. IR spectrum (cm^{-1}): 1652, 1630, and 1070. Mass spectra of four major isomers were measured and found to be almost identical (M^+ equal to 307 in all cases).

3,7-Dimethyl-9-(2-oxolanyl)-2,6-nonadienoic Acid (*XId*)

The ester *XIb* (8.35 g; 29.7 mmol) was saponified by standing at room temperature for four days with potassium hydroxide (5 g) in water (5 ml) and methanol (50 ml). Usual work-up yielded 7.4 g (98.5%) of the crude acid *XId*.

Propargyl 3,7-Dimethyl-9-(2-oxolanyl)-2,6-nonadienoate (*XIf*)

Into a stirred solution containing the acid *XId* (3.17 g; 12.5 mmol), dry ether (33 ml), and dry pyridine (0.99 g; 12.5 mmol) there was added dropwise under cooling thionyl chloride (1.49 g; 12.5 mmol) and the mixture stirred at room temperature for 1 h. Propargyl alcohol (0.7 g; 12.5 mmol) in pyridine (0.99 g; 12.5 mmol) was then added dropwise over 10 min, the stirring continued for 2 h, the mixture kept at room temperature overnight, decomposed with water, extracted with ether, and the extract processed as usual. The crude ester *XIf* was chromatographed on silica gel (140 g) in 92 : 8 light petroleum-acetone and the content of fractions checked by thin-layer chromatography on silica gel in 9 : 1 light petroleum-acetone. The appropriate fractions were pooled and distilled to afford 2.38 g (65%) of the ester *XIf* boiling at the bath temperature of 130–142°C at 0.008 Torr. For $C_{18}H_{26}O_3$ (290.4) calculated: 74.44% C, 9.03% H; found: 73.29% C, 9.00% H. IR spectrum (cm^{-1}): 3310, 1744, 1728, 1705, 1648, 1640, 1139, and 1070. Mass spectra: M^+ 290 with four major isomers; the spectra of two and two isomers were almost identical.

Cyclopropylmethyl 3,7-dimethyl-9-(2-oxolanyl)nonadienoate (*XIg*) was prepared analogously to the preceding paragraph from the acid *XId* (4.1 g; 16.2 mmol) and cyclopropylmethanol. Column chromatography was performed on silica gel (140 g) in 93 : 7 light petroleum-acetone and the fractions checked by thin-layer chromatography on silica gel in 9 : 1 light petroleum-acetone. The appropriate fractions were pooled and evaporated to afford two portions differing in the content of isomers: 1.48 g (29.8%) and 2.35 g (47.3%). For $C_{19}H_{30}O_3$ (306.4) calculated: 74.46% C, 9.82% H; found: 72.52% C, 9.53% H. IR spectrum (cm^{-1}): 3080, 3005, 1714, 1734, 1650, 1222, 1154, and 1072. Mass spectra: M^+ 306 with the predominating isomers; the spectra were almost identical.

3-Methyl-5-(2-oxolanyl)pentanal (*XIV*)

A. Into a solution of the ester *IV* (13.19 g; 61.5 mmol) in ether (65 ml) there was added dropwise under argon with stirring and cooling ($-75^\circ C$) over 80 min a 70% benzene solution (9.23 ml) of sodium dihydridobis(2-methoxyethoxy)aluminate¹¹ diluted with ether (15 ml). The mixture was stirred at -75° for 24 h and the freezing bath was then removed. The $-75^\circ C$ cold mixture was decomposed over 30 min with 20% aqueous sulfuric acid (62 ml). As soon as the temperature was $10^\circ C$, the mixture was worked up as usual. As indicated by thin-layer chromatography on silica gel in 85 : 15 light petroleum-acetone, the crude product (13.11 g) contained the required aldehyde *XIV*, the unreacted starting ester *IV*, and the corresponding alcohol. The residue was therefore dissolved in ether (100 ml), the solution treated with sodium metabisulfite ($Na_2S_2O_5$; 16 g) in lukewarm water (30 ml), and the whole mixture stirred under argon for 16 h. The

precipitate of the aldehyde bisulfite was collected with suction, washed with ice-cold water and ether, dissolved in water, and the aldehyde liberated by the addition of a solution of sodium carbonate (7.0 g) in water (70 ml). The aldehyde was extracted with ether, the extract washed, dried over anhydrous magnesium sulfate, and distilled to afford 3.58 g (34%) of compound *XIV* boiling at the bath temperature of 120–125°C/10.75 Torr. For $C_{10}H_{18}O_2$ (170.2) calculated: 70.54% C, 10.66% H; found: 70.45% C, 10.42% H. IR spectrum (cm^{-1}): 1726 and 1070.

B. Into a mixture of dry pyridine (20.78 g; 0.26 mol) and dichloromethane (330 ml), chromium trioxide (13.14 g; 0.13 mol) was added, under argon with stirring. The mixture was stirred for 30 min and then the alcohol *VI* (3.78 g; 21.9 mmol) in dichloromethane (4 ml) was added. The stirring at room temperature was continued for 15 min. The upper dichloromethane solution was decanted and the remaining dark precipitate washed with three 145 ml portions of ether. The dichloromethane solution was combined with ethereal washings, washed successively with three 220 ml portions of 5% aqueous sodium hydroxide, water, 5% aqueous HCl (220 ml), water, 5% aqueous sodium hydrogen carbonate (220 ml), and water again till neutral, dried over anhydrous magnesium sulfate, and distilled. Yield, 2.96 g (79%) of the aldehyde *XIV* boiling at the bath temperature of 120–125°C/11 Torr.

Preparation of Esters, Amides, and Nitriles *XIh*, *XIi*, *XIic–XIie*, *XIIIa*, *XIIIb*, and *XV* (general procedure)

To a stirred suspension of sodium hydride (10 mmol) in dry and peroxide-free 1,2-dimethoxyethane (20 ml) there were added dropwise at room temperature under argon over 5–10 min the appropriate substituted esters of phosphonic acids (11–13 mmol) and the mixture stirred for 1 h at room temperature or at 50°C depending on the formation of the ylide. The carbonyl compound (10 mmol) was then added dropwise at room temperature and the mixture stirred for 1 h at room temperature and for 0.5 to 19 h at 50–60°C. The reaction course was checked by thin-layer chromatography on silica gel. When the starting carbonyl compound disappeared or when the composition of the reaction mixture remained constant, the mixture was poured into water (500 ml) acidified with acetic acid or sulfuric acid, the product extracted with light petroleum, the extract washed as usual, dried over anhydrous magnesium sulfate, evaporated, and the residue chromatographed as specified below.

Isopropyl 3,7-dimethyl-9-(2-oxolanyl)-2,6-nonadienoate (XIh), obtained from the ketone *IX* (2.14 g; 10 mmol) and diisopropyl isopropoxycarbonylmethanephosphonate (3.46 g; 13 mmol) was chromatographed on a column of silica gel in 96 : 4 light petroleum–acetone. The appropriate fractions (as determined by thin-layer chromatography on silica gel in 9 : 1 light petroleum–acetone) yielded 0.40 g (13.6%) of a liquid boiling at the bath temperature of 118–135°C/0.004 Torr and 2.37 g (80.5%) of a liquid boiling at the bath temperature of 132–137°C/0.004 Torr, differing by the ratio of isomers, as indicated by gas–liquid chromatography. For $C_{18}H_{30}O_3$ (294.4) calculated: 73.43% C, 10.27% H; found: 73.14% C, 10.07% H. IR spectrum (cm^{-1}): 1710, 1648, 1242, 1150, 1112, and 1070.

Nitrile of 3,7-dimethyl-9-(2-oxolanyl)-2,6-nonadienoic acid (XV) prepared from the ketone *IX* (2.14 g; 10 mmol) and diethyl cyanomethylphosphonate (2.90 g; 13 mmol) was chromatographed on a column of silica gel (140 g) in 88 : 12 light petroleum–ethyl acetate. The appropriate fractions (as determined by thin-layer chromatography on silica gel in 8 : 2 light petroleum–ethyl acetate) were pooled and distilled to yield 2.08 g (89%) of the nitrile *XV* boiling at the bath temperature of 120°C/0.008 Torr to 130°C/0.004 Torr. For $C_{15}H_{23}NO$ (233.9) calculated: 77.20% C, 9.94% H, 6.00% N; found: 77.50% C, 9.97% H, 5.77% N. IR spectrum (cm^{-1}): 2220, 1663, 1630, and 1070.

N-Ethylamide of 3,7-dimethyl-9-(2-oxolanyl)-2,6-nonadienoic acid (XII), prepared from the ketone *IX* (2.14 g; 10 mmol) and diethyl ethylaminocarbonylmethanephosphonate (13 mmol) was chromatographed on a column of silica gel (140 g) in 85 : 15 light petroleum–acetone. The appropriate fractions (as determined by thin-layer chromatography on silica gel in 8 : 2 light petroleum–acetone) were pooled and evaporated to afford residues differing in the ratio of isomers only (as determined by gas–liquid chromatography): 2.32 g (83.0%) and 0.31 g (11.1%). For $C_{17}H_{29}NO_2$ (279.4) calculated: 73.07% C, 10.46% H, 5.01% N; found: 73.08% C, 10.55% H, 5.16% N. IR spectrum (cm^{-1}): 3450, 1667, 1640, 1630, 1545, 1533, 1512, 1503, and 1070.

Isopropyl 3,7-dimethyl-9-(2-oxolanyl)-2-nonenoate (XIIC), prepared from the ketone *X* (2.17 g; 10 mmol) and diisopropyl isopropoxycarbonylmethanephosphonate (3.46 g; 13 mmol) was chromatographed on a column of silica gel (165 g) in 88 : 12 light petroleum–ether. The appropriate fractions (as determined by thin-layer chromatography on silica gel in 7 : 3 light petroleum–ether) were pooled and evaporated to yield 1.41 g (47.6%) of the ester *XIIC* boiling at the bath temperature of 130°C/0.006 Torr to 140°C/0.005 Torr. For $C_{18}H_{32}O_3$ (296.4) calculated: 72.93% C, 10.88% H; found: 73.22% C, 10.99% H. IR spectrum (cm^{-1}): 1711, 1649, 1224, 1152, and 1112.

N-Ethylamide of 3,7-dimethyl-9-(2-oxolanyl)-2-nonenoic acid (XIId), prepared from the ketone *X* (2.17 g; 10 mmol) and diethyl ethylaminocarbonylmethanephosphonate (2.90 g; 13 mmol) was chromatographed on a column of silica gel (180 g) in 9 : 1 light petroleum–acetone. The appropriate fractions (as determined by thin-layer chromatography on silica gel in 8 : 2 light petroleum–acetone) were pooled and distilled to yield 1.70 g (60.4%) of the amide *XIId* boiling at the bath temperature of 175–185°C/0.004 Torr. For $C_{14}H_{31}NO_2$ (281.4) calculated: 72.55% C, 11.10% H, 4.98% N; found: 72.38% C, 11.02% H, 5.16% N. IR spectrum (cm^{-1}): 3458, 3330, 1666, 1640, 1533, and 1070.

N,N-Diethylamide of 3,7-dimethyl-9-(2-oxolanyl)-2-nonenoic acid (XIIe), prepared from the ketone *X* (2.17 g; 10 mmol) and diethyl diethylaminocarbonylmethanephosphonate (3.27 g; 13 mmol) was chromatographed on a column of silica gel (170 g) in light petroleum–acetone 92 : 8. The appropriate fractions (as determined by thin-layer chromatography on silica gel in 8 : 2 light petroleum–acetone) were pooled and distilled to afford 2.03 g (65.6%) of the amide *XIIe* boiling at the bath temperature of 175°C/0.004 Torr to 185°C/0.003 Torr. For $C_{19}H_{35}NO_2$ (309.5) calculated: 73.73% C, 11.40% H, 4.53% N; found: 73.79% C, 10.98% H, 4.90% N. Mass spectrum: M^+ 309 with the corresponding fragmentation. IR spectrum (cm^{-1}): 1640, 1630, 1098, 1080, and 1070.

Isopropyl 3,7-dimethyl-9-(2-oxolanyl)-2,4-nonadienoate (XIIIa), prepared from the aldehyde *XIV* (1.70 g; 10 mmol) and diisopropyl 2-methyl-3-isopropoxycarbonyl-2-propenephosphonate (3.37 g, 11 mmol) was chromatographed on a column of silica gel (133 g) in 96 : 4 light petroleum–acetone. The appropriate fractions (as determined by thin-layer chromatography on silica gel in 9 : 1 light petroleum–acetone) were pooled and distilled to afford 1.21 g (41.1%) of the ester *XIIIa* boiling at the bath temperature of 139–148°C/0.004 Torr, consisting of two isomers, probably *trans-trans* and *trans-cis*, as determined by gas–liquid chromatography. For $C_{18}H_{30}O_3$ (294.4) calculated: 73.43% C, 10.27% H; found: 73.44% C, 10.21% H. IR spectrum (cm^{-1}): 1708, 1635, 1611, 1161, 1114. UV spectrum: λ_{max} 264 nm, $\log \epsilon$ 4.27 (ethanol).

Methyl 3,7-dimethyl-9-(2-oxolanyl)-2,4-nonadienoate (XIIIb), prepared from the aldehyde *XIV* (1.70 g; 10 mmol) and dimethyl 2-methyl-3-methoxycarbonyl-2-propenephosphonate (2.78 g; 12.5 mmol) was chromatographed on a column of silica gel (140 g) in 98 : 2 light petroleum–acetone. The appropriate fractions (as determined by thin-layer chromatography on silica gel in 9 : 1 light petroleum–acetone) were pooled and distilled to afford a liquid boiling at the bath temperatures of 142°C/0.007 Torr to 155°C/0.005 Torr (2.06 g; 77.4%) and 140°C/0.006 Torr to 150°C :

: 0.005 Torr (0.35 g; 13.0%). For $C_{16}H_{26}O_3$ (266.4) calculated: 72.14% C, 9.84% H; found: 72.27% C, 10.00% H. IR spectrum (cm^{-1}): 1720, 1638, 1613, 1436, 1240, 1159, 1067, and 1045.

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