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Floyd, Jr. et al.

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[54] **1-ALKOXY-9-KETO-PROSTENOIC ACID DERIVATIVES**

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[52] **U.S. Cl.**..... **260/514 D;** 260/345.8; 260/395; 260/410.9 R; 260/413; 260/468 J; 260/468 K; 260/468 D; 260/473; 260/501.1; 260/501.17; 260/514 K; 260/514 J; 424/305; 424/317

[51] **Int. Cl.**..... **C07c 61/36;** C07c 69/74

[58] **Field of Search**..... 260/468 D, 514 D, 395

[56] **References Cited**

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Primary Examiner—Robert Gerstl

Attorney, Agent, or Firm—Edward A. Conroy, Jr.

[57] **ABSTRACT**

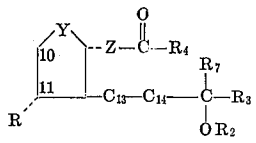
This disclosure describes certain 11-alkoxy-9-keto-(or hydroxy)-prostenoic acid derivatives useful as antimicrobial agents, hypotensive agents, anti-ulcer agents, or as intermediates.

13 Claims, No Drawings

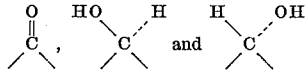
1-ALKOXY-9-KETO-PROSTENOIC ACID DERIVATIVES

BRIEF SUMMARY OF THE INVENTION

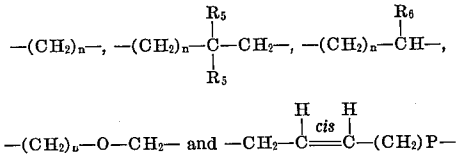
This invention relates to novel 11-alkoxy substituted prostanoic acids and derivatives as well as to intermediates and methods for their preparation. The novel compounds of this invention may be represented by the following general formula:



wherein R_1 is lower alkoxy, ω-hydroxy-substituted lower alkoxy, or ω-tetrahydropyranyloxy-substituted lower alkoxy; R_2 is hydrogen, lower alkyl, or triphenylmethyl; R_3 is a straight chain alkyl group having from 2 to 10 carbon atoms, a straight chain alkyl group having from 2 to 10 carbon atoms and substituted with one or two lower alkyl groups, a straight chain alkenyl methyl group having from 3 to 10 carbon atoms, a straight chain alkenyl methyl group having from 3 to 10 carbon atoms and substituted with one or two lower alkyl groups, a cycloalkyl group having from 4 to 9 carbon atoms, lower alkyl substituted cycloalkyl group having from 5 to 10 carbon atoms, a cycloalkyl-substituted lower alkyl group having from 6 to 12 carbon atoms and in which the cycloalkyl group is optionally substituted with a lower alkyl group, a cycloalkenyl group having from 5 to 9 carbon atoms, a lower alkyl substituted cycloalkenyl group having 6 to 10 carbon atoms, a cycloalkenyl substituted lower alkyl group having from 6 to 12 carbon atoms and in which are cycloalkenyl group is optionally substituted with a lower alkyl group, admantyl, or an adamantyl substituted lower alkyl group; R_4 is hydroxy, an alkoxy group having from 1 to 12 carbon atoms, or tetrahydropyranyloxy; R_7 is hydrogen or a lower alkyl group having up to 3 carbon atoms; Y is a divalent radical selected from the group consisting of those of the formulae:



and Z is a divalent radical selected from the group consisting of those of the formulae:



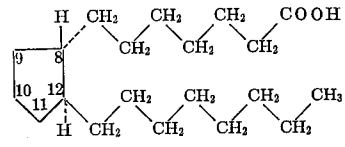
wherein *n* is an integer from 3 to 8, inclusive, p is an integer from 2 to 6 inclusive, R_5 is an alkyl group having up to 3 carbon atoms, and R_6 is an alkyl group having up to 3 carbon atoms, a fluorine atom or a phenyl group; and the moiety $-C_{13}-C_{14}-$ is ethylene or trans-vinylene; with the proviso that when R_7 is a lower alkyl group then R_2 is hydrogen; and all optical isomers thereof.

Also embraced within the scope of the present invention are the non-toxic, pharmaceutically acceptable salts of the novel compounds of the present invention when R_4 is hydroxy. The cations comprised in these salts include, for example, the non-toxic metal cations such as the sodium ion, potassium ion, calcium ion, and magnesium ion as well as the organic amine cations such as the tri(lower alkyl)amine cations (e.g., triethylamine, triethanolamine, procaine, and the like).

The novel compounds of the present invention are obtainable as yellow oils having characteristic absorption spectra. They are relatively insoluble in water but are relatively soluble in common organic solvents such as ethanol, ethyl acetate, dimethylformamide, and the like. The cationic salts of the compounds when R_4 is hydroxy are, in general, white to yellow crystalline solids having characteristic melting points and absorption spectra. They are relatively soluble in water, methanol, and ethanol but are relatively insoluble in benzene, diethyl ether, and petroleum ether.

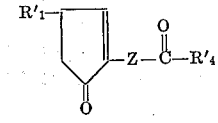
DETAILED DESCRIPTION OF THE INVENTION

The prostaglandins are a family of closely related compounds which have been obtained from various animal tissues, and which stimulate smooth muscle, lower arterial blood pressure, antagonize epinephrine-induced mobilization of free fatty acids, and have other pharmacological and autopharmacological effects in mammals. See Bergström et al., J. Biol. Chem. 238, 3555 (1963) and Horton, Experientia 21, 113 (1965) and references cited therein. All of the so called natural prostaglandins are derivatives of prostanoic acid:



The hydrogen atoms attached to C-8 and C-12 are in trans-configuration. The natural prostaglandins represent only one of the possible optical isomers. The compounds of this invention include all possible optical isomers.

The novel compounds of the present invention may be readily prepared from certain 4-substituted cyclopentenone intermediates which may be represented by the following general formula:



wherein R'_1 is lower alkoxy or ω-tetrahydropyranyloxy-substituted lower alkoxy; R'_4 is tetrahydropyranyloxy

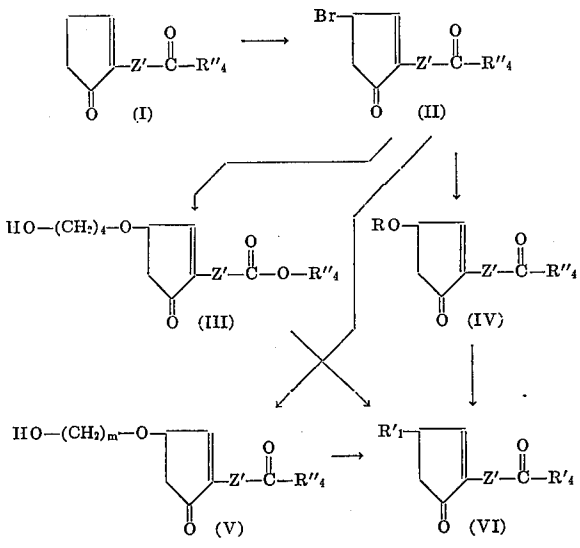
or an alkoxy group having from 1 to 12 carbon atoms; and Z is as hereinabove defined.

Certain of the 4-oxycylopentenone intermediates may be prepared from the corresponding 4-unsubstituted cyclopentenones (I) in accordance with the reaction scheme of Flowsheet A, wherein Z' embraces all of Z, but not cis $-CH_2-CH=CH-(CH_2)_p-$.

The requisite cyclopentenones are described in Belgium Pat. No. 786,215 (granted and laid open to inspection on Jan. 15, 1973) or can be obtained by analogous procedures to those described in the aforesaid patent.

In Flowsheet A which follows, Z', R'_1 and R'_4 are as hereinabove defined; R is a lower alkyl group, R''_4 is hydroxy or an alkoxy group having from one to 12 carbon atoms, and *m* is an integer from two to five inclusive.

FLOWSHEET A

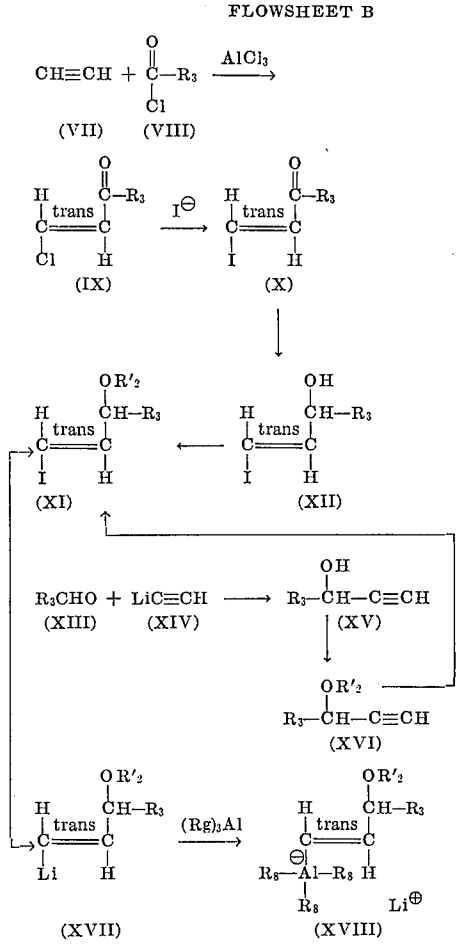


Introduction of the 4-oxy function into the 4-unsubstituted cyclopentenones (I) is accomplished by first halogenating the 4-position with an allylic halogenating reagent, preferably N-bromosuccinimide. The resulting 4-bromocyclopentenones (II) is then solvolyzed for the introduction of the oxy function. This step is preferably carried out in the presence of a silver salt to facilitate the displacement of the halide ion. The particular 4-oxy derivative that is formed is determined by the nature of the solvent system. Treatment of the 4-bromocyclopentenone with silver fluoroborate in water-acetone (for solubility) provides the 4-hydroxycyclopentenone. When the solvent system is water-tetrahydrofuran, in addition to the 4-hydroxy derivative there is also obtained the 4'-hydroxybutyloxy derivative (III), formed by solvolysis with tetrahydrofuran. When the solvent is only tetrahydrofuran then only the latter compound is formed. Substitution of tetrahydrofuran with alcohols, e.g., methanol, ethanol, isopropanol, butanol and the like, provides the 4-alkoxycyclopentenones (IV). With ethylene glycol or propylene glycol etc. the corresponding 4-(ω-substituted hydroxy alkoxy)-cyclopentenone (V) is obtained. In the latter three procedures it is preferably to add a proton acceptor which will not react with (II), for example, sym-collidine.

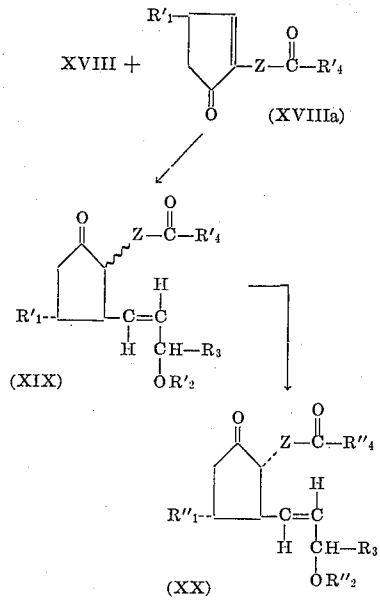
In general these procedures are operable with either the free carboxylic acid or alkyl carboxylate, as desired. A particular alkyl carboxylate not provided by formula (I) can be obtained by hydrolysis to the acid and esterification in the usual way, for example with the appropriate alcohol, or for a t-butyl ester with isobutylene. However, for the subsequent alanate conjugate addition process it is necessary to utilize a cyclopentenone wherein the carboxylic acid as well as all free hydroxyl groups are blocked. A particularly useful blocking group for both functions is the tetrahydropyranyl group since the group can easily be cleaved with weak acid under conditions which do not disrupt the subsequently-prepared, relatively-unstable 11-oxy-9-keto system (β-oxy-ketone). Thus, it is not possible to effect a satisfactory chemical hydrolysis of an alkyl ester or of an O-alkanoyl group in an 11-oxy-9-keto prostanoic acid derivative under conditions to which this system is stable (enzymatic hydrolysis is possible). Of course these stability considerations do not apply in the "F" (9-hydroxy) series.

The 9-keto-13-trans-prostenoic acids and esters of this invention nay be prepared via the novel conjugate addition processed outlined in the Flowsheet B which follows. In Flowhseet B, R_3, R'_1, R'_4, R''_4, and Z are as defined hereinabove; R_8 is a lower alkyl group (each of three R_8 radicals bonded to a aluminum does not necessarily have to be the same), R'_2 is lower alkyl or triphenylmethyl, R' is hydrogen or lower alkyl and R''_2 is lower alkoxy or ω-hydroxy-substituted lower alkoxy.

FLOWSHEET B



FLOWSHEET B—Continued

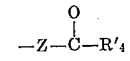


In accordance with the reaction scheme of Flowsheet B, acetylene (VII) is treated with an appropriate acid chloride (VIII) in the presence of aluminum trichloride to provide the 1-chloro-3-keto-trans-1-alkene (IX). Interchange with sodium iodide, preferably in a ketone solvent such as acetone, provides the corresponding trans-vinyl iodide (X). Reduction of the keto function in (X) with sodium borohydride furnishes the alcohol (XII), which is then blocked with the triphenylmethyl group or a triphenylmethyl group substitued with one or two methoxy groups or an O-lower alkyl group is introduced. Blocking the hdyroxy function can also be accomplished with a trialkylsilyl group.

The blocked trans-vinyl iodide can also be obtained by treatment of the appropriate aldehyde (XIII) with lithium acetylide (XIV) in the usual manner, blocking the product 3-hydroxy-1-alkyne (XV) and then, in one operation, treating the resulting (XVI) successively with disiamylborane, trimethylamine N-oxide, and iodine and auqeous sodium hydroxide. to give (XI). This latter procedure is preferred when R_3 is adamatyl, contains a center of unsaturation, a cyclopropyl ring or other relatively sensitive feature.

The blocked vinyl iodide (XI) is then submitted to metal interchange with an alkyl lithium, e.g. n-butyl lithium, at very low temperatures, e.g. −78°c., which provides the vinyl lithium derivative (XVII), the trans-configuration of the double bond being retained. After 1 to 4 hours, addition of a trialkyl aluminum [$(R_8)_3Al$], preferably trimethyl aluminum, to the solution of the lithio derivative (XVII) furnishes the lithio alanate intermediate (XVIII), also with retention of the trans-configuration of the double bond. The cycloalkenone (XVIII), dissolved in ether or other non-prototropic solvent, is then added to the alanate solution. The resulting solution is allowed to warm to room temperature and is kept for about 6 to 18 hours at ambient temperatures. Potential hydroxy or carboxylic acid groups in cycloalkenone (XVIII*a*) are blocked as ethers or esters, preferably, with tetrahydropyranyl and/or trialkylsilyl groups. Interchange of alanate (XVIII) with cycloalkenone (XVIII*a*) results in the transfer of the trans-1-alkenyl ligand in (XVIII) with retention of the

trans-configuration in a 1,4-conjugate manner to the cycloalkneone (XVIII*a*) furnishing, after quenching the reaction solution, the 1,4-conjugate addition product (XIX). It is important to note too that the trans-alkenyl ligand from (XVIII) adds trans to the 4-substituent in (XVIII*a*). In (XIX) we are however not certain of the relative configuration of the side chains to each other. The situation is indicated in structure (XIX) by the ~ bond between the ring and the

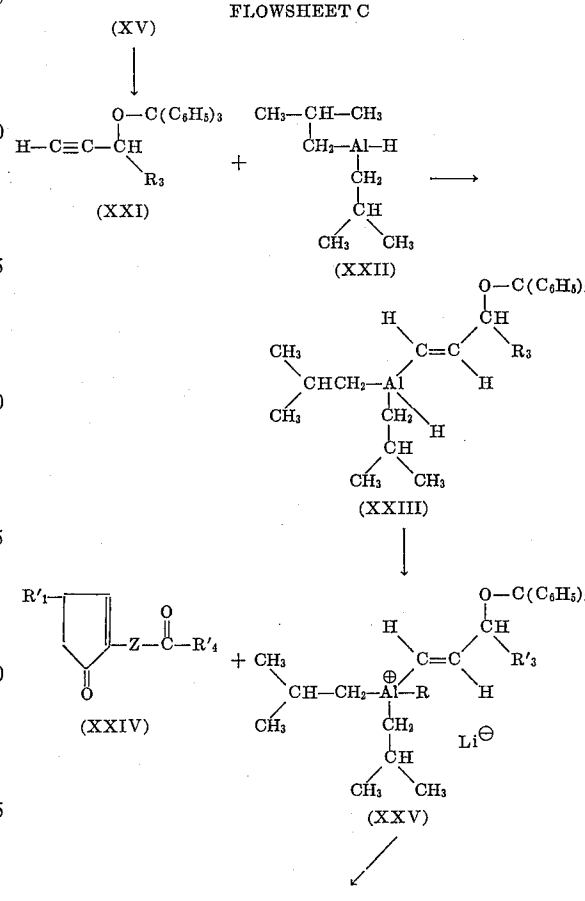


chain and is indicated in the nomenclature of the compounds involved by the designation 8ξ. In any event deblocking to (XX) with acid, e.g. treatment with acetic acid: tetrahydrofuran: water in the ratio of 3:1:1 at 35°–45°C. for from 3 to 48 hours, results in the trans-relationship between the chains. This procedure results in de-O-tritylation as well as hydrolysis of tetrahydropyranyl and trialkylsilyl groups. Alkyl esters are not cleaved by this procedure, however these esters can be hydrolized by enzymatic or microbiological techniques known to the art.

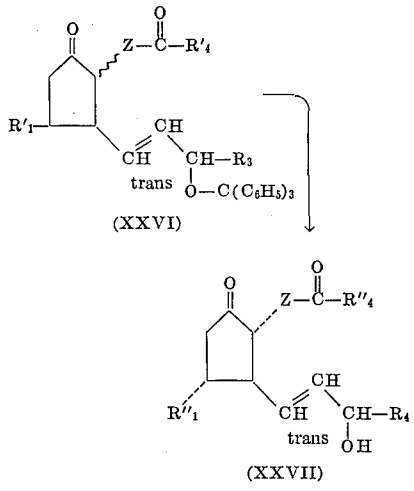
In order to ensure a trans-relationship in (XIX) these products can be submitted to conditions known in the literature to equilibrate the 8-iso PGE_1 to a mixture containing about 90% of the trans product. These conditions involve treatment with potassium acetate in aqueous methanol for 96 hours at room temperature.

An alternative route, also involving conjugate addition of an alanate to a cycloalkenone, is outlined in Flowsheet C, which follows. In Flowsheet C R_3, R_8, Z, R'_1, R'_4, and R'_4 are as hereinabove defined.

FLOWSHEET C



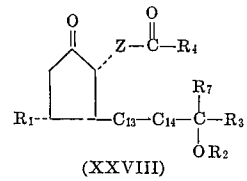
FLOWSHEET C—Continued



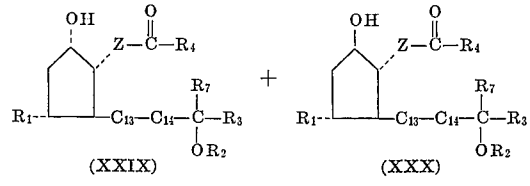
(XXVI)

(XXVII)

FLOWSHEET D



(XXVIII)



(XXIX) (XXX)

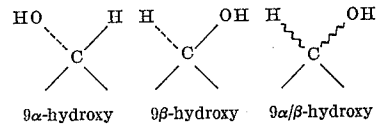
In accordance with the reaction scheme of Flowsheet C, the triphenylmethoxy substituted 1-alkyne (XXI), prepared by O-triphenylmethylation of the corresponding 1-alkyne-3-ol (XV, Flowsheet B), is treated with diisobutylaluminum hydride (XXII), which provides the alane (XXIII) containing the trans-double bond and is carried out in an inert solvent such as benzene, toluene, and the like at temperatures in the range of 40°–60°C. for several hours. It can also be carried out in a solvent such as tetrahydrofuran, usually in an approximate 2:1 mixture with benzene or hexane; in which case the reaction requires somewhat more vigorous conditions, usually heating at about 70°C–75°C. for about eighteen hours. The subsequent reaction with methyl or n-butyl lithium (R_8–Li) is preferably carried out in a mixture of the above solvents with an ether-type solvent such as diethyl ether, dibutyl ether, tetrahydrofuran and the like. This reaction is rapid and is preferably carried out at 0°C–10°C. with cooling. The conjugate 1,4-addition of the resulting alanate salt (XXV) to the 4-oxy-cyclopent-2 -en-1-one (XXIV) is preferably carried out at ambient temperatures for a period of 12 to 24 hours. This reaction is also best carried out in an ether-type solvent such as diethyl ether, dibutyl ether, tetrahydofuran, and the like. The intermediate alanate-enolate adduct is then carefully hydrolzed in situ, with dilute hydrochloric acid with cooling, and the product (XXVI) is isolated in the usual manner, well known in the art. Removal of tetrahydropryanyl blocking groups and of the triphenylmethyl blocking group can then be accomplished by treating with weak acid. A preferred procedure involves heating at 45°C. for 3.5 hours in a solvent system consisting of acetic acid:tetrahydrofuran:water in the proportion of 4:2:1. If (XXVI) is a tetrahydropyranyl ester, there is then obtained the prostenoic acid (XXVII,R''_4=hydroxy).

The 9-keto derivatives (XXVIII) of this invention can be converted to the corresponding 9-hydroxy derivatives. If this conversion is effected with sodium borohydride, the product is a mixture of 9α- and 9β-hydroxy derivatives (XXIX) and (XXX) as set forth in the following reaction scheme:

In Flowsheet D R_1, R_2, R_3, R_4, R_7, Z and $-C_{13}$–C_{14}— are as hereinabove defined. When the reaction is carried out with lithium perhydro-9b-boraphenylyl hydride [H. C. Brown and W. C. Dickason, Journ. Amer. Chem. Soc., 92, 709 (1970)] the product is at least predominantly the 9α-hydroxy derivative (XXIX), wherein the 9-hydroxy group is cis to the side-chain attached to C_8 and to the 11-oxy function.

Those compounds of this invention embodying the $-CH_2-CH_2-$ lingage at $-C_{13}$–C_{14}— may be prepared from the corresponding Δ^{13} derivatives, obtained via the alanate process, by catalytic reduction, preferably at low pressure with a noble metal catalyst in an inert solvent at ambient temperatures.

In accordance with accepted convention, an α-substituent at the 8-, 9-, 11- or 12-positions is behind the plane of the paper whereas a β-substituent at these positions is in front of the plane of paper. This is usually represented by a - - - bond for an α-substituent, a — bond for a β-substituent, and a ∿ bond where both are indicated. Thus, the 9-hydroxy derivatives may be variously represented as follows:



9α-hydroxy 9β-hydroxy 9α/β-hydroxy

The novel compounds of the present invention have utility as hypotensive agents, anti-ulcer agents, agents for the treatment of gastric hypersecretion and gastric crosion, bronchodilators, antimicrobial agents, anticonvulsants, abortifacients, agents for the induction of labor, agents for the induction of menses, fertility-controlling agents, central Nervous system regulatory agents, analgesic agents, salt and water-retention regulatory agents, diuretics, fat metabolic regulatory agents, serum-cholesterol lowering agents, anti-inflammatory agents and as agents for the inhibition of platelet aggregation, and for the treatment of periodontal disease, glucoma, uveitis, sickle cell anemia and

psoriasis. Certain of the novel commpounds of this invention possess utility as intermediates for the preparation of other of the novel compounds of this invention.

The compounds of this invention also provide protection against the ulcerogenic properties of certain nonsteroidal anti-inflammatory agents, e.g., indomethacin, aspirin, and phenylbutazone.

The novel compounds of the present invention are useful as hypotensive agents and their hypotensive activity was demonstrated in the following test procedure. This procedure is a modification of the technique described by Pike et al., *Prostaglandins, Nobel Symposium* 2, Stockholm, June, 1966; p. 165.

Male Wistar strain rats (Royal Hart Farms) averaging approximately 250 grams in weight were fastened to rat boards in a supine position by means of canvas vests and limb ties. The femoral area was infiltrated subcutaneously with lidocaine and the iliac artery and vein were exposed and cannulated. Arterial blood pressure (systolic/diastolic) was recorded using a Statham P_{23} Db pressure, the animals were anethetized before use with pentobarbital, 30 mg./kg. of body weight intravenously, and also were given hexamethoxium bitartrate, 2 mg./kg. of body weight intravenously. The test compounds were prepared by ultrasonic dispersion in a saline-Tween 80 vehicle. A constant intravenous dose volume of 0.5 ml. was administered and test doses ranged from 0.1 to 10.0 mg./kg. of body weight. Increasing or decreasing doses were selected depending on the dose response obtained. In Table I below are set forth doses at which at least a decrease of about 10 mm. in diastolic blood pressure was observed for typical compounds of the present invention.

TABLE I

Compound	Effective dose (mg./kg. of body weight)
9-oxo-11α-methoxy-15-hydroxy--13-trans-prostenoic acid	1.0
9-oxo-11α-methoxy-15-hydroxy--15-methyl-13-trans-prostenoic acid	0.5
9-oxo-11α-methoxy-15-hydroxy--16,16-dimethyl-13-trans-prostenoic acid	<1.0
9-oxo-11α-methoxy-15-hydroxy--13-trans,17-cis-prostadienoic acid	1.0
9-oxo-3-oxa-11α-methoxy-15-hydroxy-16,16-dimethyl-13-trans--prostenoic acid	2.0
9-oxo-11α-methoxy-15-hydroxy--15-methyl-17,18-cis-methano--13-trans-prostenoic acid	<2.0
9-oxo-11α-methoxy-15-hydroxy-15--hydroxy-16,19-trans-ethano-13--trans-prostenoic acid	<1.0
9-oxo-11α-(2-hydroxyethoxy)-15--hydroxy-13-trans-prostenoic acid	1.0
9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-13-trans--prostenoic acid	0.5
9-oxo-11α-(2-hydroxyethoxy)-15--hydroxy-13-trans,17-cis-prostadienoic acid	1.0

This invention will be described in greater detail in conjunction with the following specific examples.

In the following examples, unless otherwise specified, the products obtained include all possible optical isomers.

EXAMPLE 1

Preparation of
2-(6-carboxy-6-fluorohexyl)cyclpent-2-en-1-one

This cyclopentenone is prepared by the procedure described in Belgium Pat. No. 786,215 (Jan. 15, 1973) for the preparation of 2-(6-carboxyoctyl)cyclopent-2-en-1-one by substituting diethyl fluoromalonate for diethyl ethylmalonate.

EXAMPLE 2

Preparation of
2-(6-carboxy-6-phenylhexyl)cyclopent-2-en-1-one

This cyclopentenone is prepared by the procedure described in Belgium Pat. No. 786,215 (Jan. 15, 1973) for the preparation of 2-(6-carboxyoctyl)cyclopent-2-en-1-one by substituting diethyl phenylmalonate for diethyl ethylmalonate.

EXAMPLE 3

Preparation of
2-(6-carboxyheptyl)cyclopent-2-en-1-one

This cyclopentenone is prepared by the procedure described in Belgium Pat. No. 786,215 (Jan. 15, 1973) for the preparation of 2-(6-carboxyheptyl)cyclopent-2-en-1-one by substituting diethyl methyl malonate for diethyl ethylmalonate.

EXAMPLE 4

Preparation of
2-(6-carbo-n-butoxyhexyl)cyclopent-2-en-1-one

A solution of 50 g. of 2-(6-carboxyhexyl)cyclopent-2-en-1-one [Bagli et al., *Tetrahedron Letters*, No. 5, 465 (1966)] in 1400 ml. of n-butanol containing 2.7 g. of p-toluenesulfonic acid monohydrate is allowed to stand at room temperature in a stoppered flask for about 24 hours. The solution is taken to dryness. The residue is taken up in ether and the ethereal solution is washed several times with saline solution, dried with anhydrous magnesium sulfate, and taken to dryness to afford the subject butyl ester.

EXAMPLES 5–7

Treatment of 2-(6-carboxyhexyl)cyclopent-2-en-1-one by the procedure of Example 4 with the appropriate alcohol affords the esters of the following table.

TABLE I

Example	Alcohol	Product Ester
5	isopropanol	2-(6-carboisopropoxyhexyl)cyclopent-2-en--1-one
6	methanol	2-(6-carbomethoxyhexyl)-cyclopent-2-en-1-one
7	1-hydroxy--n-decane	2-(6-carbo-n-decyloxyhexyl)cyclopent-2-en--1-one

EXAMPLE 8

Preparation of 4-bromo-2-(6-carboxyhexyl)cyclopent-2-en-1-one

A stirred mixture of 35.9 g. (0.171 moles) of 2-(6-carboxyhexyl)cyclopent-2-en-1-one [Bagli et al., Tetrahedron Letters, No. 5, 465 (1966)], 35.0 g. (0.197 moles) of N-bromosuccinimide, and 600 ml. of carbon tetrachloride is refluxed for 35 minutes. The mixture is cooled to 5°C. and filtered. The filtrate is washed with cold water, dried over magnesium sulfate, and taken to dryness to give an oil, $\lambda_{max.}^{MeOH} = 225$ mμ (8850); ν max. = 1705 (carbonyl groups) and 1625 cm^{-1} (olefin group).

EXAMPLES 9–32

In the manner of the preceding Example 8, the various cyclopentenones of Table 1A, which follows, are converted to the corresponding 4-bromo derivatives.

Table 1A

Example	Starting cyclopent-2-en-1-one	Product 4-Bromocyclopentenones
9	2-(6-carbethoxyhexyl)-cyclopent-2-en-1-one*	4-bromo-2-(6-carbethoxyhexyl)-cyclopent-2-en-1-one
10	2-(6-carbomethoxyhexyl)cyclopent-2-en-1-one (Example 6)	4-bromo-2-(6-carbomethoxyhexyl)cyclopent-2-en-1-one
11	2-(4-carbethoxybutyl)cyclopent-2-en-1-one*	4-bromo-2-(4-carbethoxybutyl)cyclopent-2-en-1-one
12	2-(3-carbethoxypropyl)cyclopent-2-en-1-one*	4-bromo-2-(3-carbethoxypropyl)cyclopent-2-en-1-one
13	2-(4-carboxybutyl)cyclopent-2-en-1-one*	4-bromo-2-(4-carboxybutyl)cyclopent-2-en-1-one
14	2-(3-carboxypropyl)cyclopent-2-en-1-one*	4-bromo-2-(3-carboxypropyl)cyclopent-2-en-1-one
15	2-(8-carboxyoctyl)cyclopent-2-en-1-one*	4-bromo-2-(8-carboxyoctyl)cyclopent-2-en-1-one
16	2-(8-carbethoxyoctyl)cyclopent-2-en-1-one*	4-bromo-2-(8-carbethoxyoctyl)cyclopent-2-en-1-one
17	2-(6-carboxyoctyl)cyclopent-2-en-1-one*	4-bromo-2-(6-carboxyoctyl)cyclopent-2-en-1-one
18	2-(6-carbethoxyoctyl)cyclopent-2-en-1-one*	4-bromo-2-(6-carbethoxyoctyl)cyclopent-2-en-1-one
19	2-(6-carboxy-5,5-dimethylhexyl)cyclopent-2-en-1-one*	4-bromo-2-(6-carboxy-5,5-dimethylhexyl)-cyclopent-2-en-1-one
20	2-(6-carbethoxy-5,5-dimethylhexyl)cyclopent-2-en-1-one*	4-bromo-2-(6-carbethoxy-5,5-dimethylhexyl)-cyclopent-2-en-1-one
21	2-(6-carboxy-5-oxahexyl)cyclopent-2-en-1-one*	4-bromo-2-(6-carboxy-5-oxahexyl)cyclopent-2-en-1-one
22	2-(6-carbethoxy-5-oxahexyl)-cyclopent-2-en-1-one*	4-bromo-2-(6-carbethoxy-5-oxahexyl)cyclopent-2-en-1-one
23	2-(6-carboxy-6-fluorohexyl)-cyclopent-2-en-1-one (Example 1)	4-bromo-2-(6-carboxy-6-fluorohexyl)cyclopent-2-en-1-one
24	2-(5-carboxypentyl)cyclopent-2-en-1-one*	4-bromo-2-(5-carboxypentyl)cyclopent-2-en-1-one
25	2-(5-carbethoxypentyl)cyclopent-2-en-1-one*	4-bromo-2-(5-carbethoxypentyl)cyclopent-2-en-1-one
26	2-(7-carboxyheptyl)cyclopent-2-en-1-one*	4-bromo-2-(7-carboxyheptyl)cyclopent-2-en-1-one
27	2-(7-carbethoxyheptyl)cyclopent-2-en-1-one*	4-bromo-2-(7-carbethoxyheptyl)cyclopent-2-en-1-one
28	2-(6-carboxy-6-phenylhexyl)-cyclopent-2-en-1-one (Example 2)	4-bromo-2-(6-carboxy-6-phenylhexyl)cyclopent-2-en-1-one
29	2-(6-carbo-n-butoxyhexyl)-cyclpent-2-en-1-one (Example 4)	4-bromo-2-(6-carbo-n-butoxyhexyl)cyclopent-2-en-1-one
30	2-(6-carbo-isopropoxyhexyl)-cyclo ent-2-en-1-one (Example 5)	4-bromo-2-(6-carbo-isopropoxyhexyl)-cyclopent-2-en-1-one
31	2-(6-carbo-n-decyloxyhexyl)-cyclopent-2-en-1-one (Example 7)	4-bromo-2-(6-carbo-n-decyloxyhexyl)cyclopent-2-en-1-one
32	2-(6-carboxyheptyl)cyclopent-2-en-1-one Example 3)	4-bromo-2-(6-carboxyheptyl)-cyclopent-2-en-1-one

*Belgium Pat. No. 786,215 (January 15, 1973).

EXAMPLE 33

Preparation of 4-methoxy-2-(6-carboxyhexyl)cyclopent-2-en-1-one

To a stirred solution of 5.30 g. of crude 4-bromo-2-(6-carboxyhexyl)cyclopent-2-en-1-one (Example 8) in 85 ml. of methanol at 0°–3°C. is added 4.40 g. (22.6 mmole) of silver fluoborate in one portion. After 2 minutes, the mixture is treated with 2.66 g. (24.8 mmones) of 2,6-lutidine. After stirring for 30 minutes at 0°–3°C. the mixture is stirred at ambient temperature for 45 minutes. Silver bromide is removed by filtration, and the filtrate is concentrated to a volume of 40 ml. The solution is treated with saturated sodium chloride solution and extracted with ether. The extract is washed successively with 0.5N hydrochloric acid solution, water, and saturated sodium chloride solution; dried over magnesium sulfate; and concentrated. Partition chromatography of the residue on Celite gives an oil, $\lambda_{max.}^{MeOh} = 220$ mμ (7450): $\nu_{max.}$ — 1715 (carbonyl groups) and 1095 cm^{-1} (methoxy group).

EXAMPLES 34–61

Alcoholysis with the appropriate alcohol of the 4-bromocyclopentenones listed in Table 2, directly following, in the manner of Example 33 provides the 4-alkoxycyclopentenones of the Table.

Table 2

Example	Starting bromocyclopentenone of example	Product 4-alkoxycyclopent-2-en-1-one
34	9	4-ethoxy-2-(6-carbethoxyhexyl)-cyclopent-2-en-1-one
35	10	4-methoxy-2-(6-carbomethoxyhexyl)cyclopent-2-en-1-one

Table 2-Continued

Example	Starting bromocyclopentenone of example	Product 4-alkoxycyclopent-2-en-1-one
36	11	4-propoxy-2-(4-carbethoxybutyl)-cyclopent-2-en-1-one
37	12	4-isopropoxy-2-(3-carbethoxypropyl)cyclopent-2-en-1-one
38	13	4-methoxy-2-(4-carboxybutyl)cyclopent-2-en-1-one
39	14	4-ethoxy-2-(3-carboxypropyl)cyclopent-2-en-1-one
40	15	4-methoxy-2-(8-carboxyoctyl)cyclopent-2-en-1-one
41	16	4-isopropoxy-2-(8-carbethoxyoctyl)cyclopent-2-en-1-one
42	17	4-methoxy-2-(6-carboxyoctyl)cyclopent-2-en-1-one
43	18	4-n-butoxy-2-(6-carboxyoctyl)cyclopent-2-en-1-one
44	19	4-methoxy-2-(6-carboxy-5,5-dimethylhexyl)-cyclopent-2-en-1-one
45	20	4-methoxy-2-(6-carbethoxy-5,5-dimethylhexyl)cyclopent-2-en-1-one
46	21	4-methoxy-2-(6-carboxy-5-oxahexyl)cyclopent-2-en-1-one
47	22	4-ethoxy-2-(6-carbethoxy-5-oxahexyl)cyclopent-2-en-1-one
48	23	4-methoxy-2-(6-carboxy-6-fluorohexyl)cyclopent-2-en-1-one
49	24	4-methoxy-2-(5-carboxypentyl)cyclopent-2-en-1-one
50	25	4-sec-butoxy-2-(5-carbethoxypentyl)cyclopent-2-en-1-one
51	26	4-methoxy-2-(7-carboxyheptyl)cyclopent-2-en-1-one
52	27	4-methoxy-2-(7-carbethoxyheptyl)cyclopent-2-en-1-one
53	28	4-methoxy-2-(6-carboxy-6-phenylhexyl)cyclopent-2-en-1-one
54	32	4-methoxy-2-(6-carboxyheptyl)-cyclopent-2-en-1-one
55	29	4-methoxy-2-(6-carbo-n-butoxyhexyl)cyclopent-2-en-1-one
56	30	4-methoxy-2-(6-carbo-isopropoxyhexyl)cyclopent-2-en-1-one
57	31	4-methoxy-2-(6-carbo-n-decyloxyhexyl)cyclopent-2-en-1-one
58	8	4-ethoxy-2-(6-carboxyhexyl)cyclopent-2-en-1-one
59	8	4-propoxy-2-(6-carboxyhexyl)cyclopent-2-en-1-one
60	8	4-isopropoxy-2-(6-carboxyhexyl)cyclopent-2-en-1-one
61	8	4-n-butoxy-2-(6-carboxyhexyl)cyclopent-2-en-1-one

EXAMPLE 62

Preparation of 4-tert-butoxy-2-(6-carbethoxyhexyl)cyclopent-2-en-1-one

A stirred mixture of 6.35 g. (20 mmoles) of 4-bromo-2-(carbethoxyhexyl)cyclopent-2-en-1-one (Example 9), 3.01 g. (11 moles) of silver carbonate, and 40 ml. of t-butanol is heated at 70°C. for 17 hours. The mixture is cooled and filtered. After evaporation of t-butanol the residue is treated with aqueous sodium chloride and extracted with 3:1 ether-hexane. The extract is washed with saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. The crude product is purified by chromatography on silica gel to give in order of elution: the subject compound as an oil; λmax. MeOH = 219 mμ (8860); νmax. = 1735 (ester carbonyl group), 1725 ketone carbonyl group), and 1365 cm^{-1} (tert.-butyl group); and 4-hydroxy-2-(6-carbethoxyhexyl)cyclopent-2-en-1-one also as an oil

EXAMPLE 63

Preparation of 4-(2-hydroxyethoxy)-2-(6-carboxyhexyl)cyclopent-2-en-1-one

To a stirred solution of 19.1 g. of crude 4-bromo-2-(6-carboxyhexyl)cyclopent-2-en-one (Example 8) in 310 ml. of ethylene glycol is added 15.6 g. (80 mmole) of silver fluoborate during 2 minutes. The exothermic reaction is controlled to give a temperature of 29°C., and after 1 minute the mixture is treated during 1 minute with 8.6 g. (80 mmole) of 2,6-lutidine. The mixture is stirred at ambient temperature for 2 hours, diluted with water, and filtered. The filtrate is diluted with saturated sodium chloride solution and extracted with ether. The extract is washed with half-saturated sodium chloride solution containing a little hydrochloric acid and saturated sodium chloride solution. The extract is dried over magnesium sulfate and concentrated. Column chromatography of the residue on silica gel gives an oil, λ max. MeOH = 216 mμ (8350); ν max. = 3340 (hydroxyl groups), 1700 (carbonyl groups), and 1620 cm^{-1} (olefin group).

EXAMPLES 64–85

By the procedure described in Example 63, treatment with the appropriate diol of the various 4-bromocyclopentenones listed in Table 3, which follows, are converted to the corresponding 4-(ω-hydroxyalkyl)cyclopenteneones of the Table.

TABLE 3

Example	Starting 4-bromo-cyclopentenone of Example	Product 4-(ω-hydroxyalkoxy)cyclopent-2-en-1-one
64	9	4-β-hydroxyethoxy-2-(6-carbethoxyhexyl)cyclopent-2-en-1-one
65	10	4-β-hydroxyethoxy-2-(6-carbomethoxyhexyl)cyclopent-2-en-1-one
66	11	4-γ-hydroxypropoxy-2-(4-carbethoxybutyl)-cyclopent-2-en-1-one
67	12	4-β-hydroxyethoxy-2-(3-carbethoxypropyl)cyclopent-2-en-1-one
68	13	4-β-hydroxyethoxy-2-(4-carboxybutyl)cyclopent-2-en-1-one
69	14	4-β-hydroxyethoxy-2-(3-carboxypropyl)cyclopent-2-en-1-one
70	15	4-β-hydroxyethoxy-2-(8-carboxyoctyl)cyclopent-2-en-1-one

TABLE 3—Continued

Example	Starting 4-bromo--cyclopentenone of Example	Product 4-(ω-hydroxy-alkoxy)cyclopent-2-en--1-one
71	16	4-β-hydroxyethoxy-2-(8--carbethoxyoctyl)cyclo-pent-2-en-1-one
72	17	4-β-hydroxyethoxy-2-(6--carboxyoctyl)cyclo-pent-2-en-1-one
73	18	4-γ-hydroxypropoxy-2--(6-carbethoxyoctyl)-cyclopent-2-en-1-one
74	19	4-β-hydroxyethoxy-2-(6--carboxy-5,5-dimethyl-hexyl)cyclopent-2-en-1--one
75	20	4-β-hydroxyethoxy-2-(6--carbethoxy-5,5-dimeth-ylhexyl)cyclopent-2-en--1-one
76	21	4-β-hydroxyethoxy-2-(6--carboxy-5-oxahexyl)-cyclopent-2-en-1-one
77	22	4-γ-hydroxypropoxy-2-(6--carbethoxy-5-oxahexyl)-cyclopent-2-en-1-one
78	23	4-β-hydroxyethoxy-2-(6--carboxy-6-fluorohexyl)-cyclopent-2-en-1-one
79	24	4-β-hydroxyethoxy-2-(5--carboxypentyl)cyclo-pent-2-en-1-one
80	26	4-β-hydroxyethoxy-2-(7--carboxyheptyl)cyclo-pent-2-en-1-one
81	28	4-β-hydroxyethoxy-2-(6--carboxy-6-phenylhexyl)-cyclopent-2-en-1-one
82	29	4-β-hydroxyethoxy-2-(6--carbo-n-butoxyhexyl)-cyclopent-2-en-1-one
83	30	4-β-hydroxyethoxy-2--(carboisopropoxyhexyl)-cyclopent-2-en-1-one
84	31	4-β-hydroxyethoxy-2-(6--carbo-n-decyloxyhexyl)-cyclopent-2-en-1-one
85	8	4-β-hydroxypropoxy-2--(6-carboxyhexyl)cyclo-pent-2-en-1-one

EXAMPLE 86

Preparation of 4-β-tetrahydropyran-2′-yloxyethoxy-2-(6-carbotetrahydropyran-2′-yloxyhexyl)cyclopent-2-en-1-one

To a stirred solution of 5.59 g. of 4-(2-hydroxyethoxy)-2-(6-carboxyhexyl)cyclopent-2-en-1-one (Example 63) and 20.7 g. (246 mmoles) of dihydropyran in 100 ml. of methylene chloride at 20°C. is added 47 mg. (0.246 mmoles) of p-toluenesulfonic acid monohydrate in 1 portion. The temperature is maintained at 20°-25°C. by cooling and is stirred for one hour at that temperature. The solution is diluted with 200 ml. of ether and poured into a mixture of 40 ml. of saturated sodium bicarbonate solution, 40 ml. of saturated sodium chloride solution, and 80 ml. of water. The phases are separated, and the aqueous phase is extracted with additional ether. The total extract is washed successively with water and saturated sodium chloride solution, dried over potassium carbonate, and freed of volatile matter by concentration at reduced pressure to give an oil, λ max. MeOH = 223 mμ (9500); ν max. 1730 (ester carbonyl group), 1705 (ketone carbonyl group), and 1030 cm^{-1} (tetrahydropyranyloxy groups).

EXAMPLES 87–102

By the procedure described in Example 86 the 4-alkoxycyclopentenone carboxylic acids listed in Table 4 were converted to the corresponding tetrahydropyran-2′-yl esters of the table.

TABLE 4

Example	Starting 4-alkoxycyclopentenone carboxylic acid of Example	Product Tetrahydropyran--2′yl ester 4-alkoxycyclopent-2-en-1-one
87	38	4-methoxy-2-(4-carbotetrahydropyran-2′-yloxybutyl)cyclopent-2-en-1--one
88	39	4-ethoxy-2-(3-carbotetrahydropyran-2′-yloxypropyl)cyclopent-2-en-1-one
89	40	4-methoxy-2-(8-carbotetrahydropyran-2′-yloxyoctyl)cyclopent-2-en-1-one
90	42	4-methoxy-2-(6-carbotetrahydropyran-2′-yloxyoctyl)cyclopent-2-en-1-one
91	44	4-methoxy-2-(6-carbotetrahydropyran-2′-yloxy-5,5-dimethylhexyl)cyclopent-2-en-1-one
92	46	4-methoxy-2-(6-carbotetrahydroxypyran-2′-yloxy-5-oxahexyl)cyclopent-2-en-1-one
93	48	4-methoxy-2-(6-carbotetrahydropyran-2′-yloxy-6-fluorohexyl)cyclopent-2-en-1-one
94	49	4-methoxy-2-(5-carbotetrahydropyran-2′-yloxypentyl)cyclopent-2-en-1-one
95	51	4-methoxy-2-(7-carbotetrahydropyran-2′-yloxyheptyl)cyclopent-2-en-1-one
96	53	4-methoxy-2-(6-carbotetrahydropyran-2′-yloxy-6-phenylhexyl)cyclopent-2-en-1-one
97	58	4-ethoxy-2-(6-carbotetrahydropyran-2′-yloxyhexyl)cyclopent-2-en-1-one
98	59	4-propoxy-2-(6-carbotetrahydropyran-2′-yloxyhexyl)cyclopent-2-en-1-one
99	60	4-isopropoxy-2-(6-carbotetrahydropyran-2′-yloxyhexyl)cyclopent-2-en-1-one
100	61	4-n-butoxy-2-(6-carbotetrahydropyran-2′-yloxyhexyl)cyclopent-2-en-1-one
101	33	4-methoxy-2-(6-carbotetrahydropyran-2′-yloxy-

TABLE 4-Continued

Example	Starting 4-alkoxycyclopentenone carboxylic acid of Example	Product Tetrahydropyran-2'yl ester 4-alkoxycyclopent-2-en-1-one
		hexyl)cyclopent-2-en-1-one
102	54	4-methoxy-2-(6-carbotetrahydropyran-2'-yloxyheptyl)cyclopent-2-en-1-one

EXAMPLES 103–124

Treatment of the 4-(ω-hydroxyalkoxy)cyclopentenones of Table 5 below with dihydropyran in the manner of Example 86 provides the 4-(ω-tetrahydropyranyloxyalkoxy)cyclopentenone esters listed in the table.

TABLE 5

Example	Starting 4-(ω-hydroxyalkoxy)-cyclopentenone of Example	Product 4-(ω-tetrahydropyran-2'-yloxyalkoxy)-cyclopent-2-en-1-one ester
103	64	4-β-tetrahydropyrany-2'-yloxyethoxy-2-(6-carbethoxyhexyl)cyclopent-2-en-1-one
104	65	4-β-tetrahydropyrany-2'-yloxyethoxy-2-(6-carbomethoxyhexyl)cyclopent-2-en-1-one
105	66	4-γ-tetrahydropyran-2'-yloxypropoxy-2-(4-carbethoxybutyl)cyclopent-2-en-1-one
106	67	4-β-tetrahydropyran-2'-yloxyethoxy-2-(3-carbethoxypropyl)cyclopent-2-en-1-one
107	68	4-β-tetrahydropyran-2'-yloxyethoxy-2-(4-carbotetrahydropyran-2'-yloxybutyl)cyclopent-2-en-1-one
108	69	4-β-tetrahydropyran-2'yloxyethoxy-2-(3-carbotetrahydropyran-2'-yloxypropyl)cyclopent-2-en-1-one
109	71	4-β-tetrahydropyran-2'-yloxyethoxy-2-(8-carbethoxyoctyl)cyclopent-2-en-1-one
110	70	4-β-tetrahydropyran-2'-yloxyethoxy-2-(8-carbotetrahydropyran-2'-yloxyoctyl)cyclopent-2-en-1-one
111	72	4-β-tetrahydropyran-2'-yloxyethoxy-2-(6-carbotetrahydropyran-2'-yloxyoctyl)cyclopent-2-en-1-one
112	73	4-γ-tetrahydropyran-2'-yloxypropoxy-2-(6-carbethoxyoctyl)cyclopent-2-en-1-one
113	74	4-β-tetrahydropyran-2'-yloxyethoxy-2-(6-carbotetrahydropyran-2'-yloxy-5,5-dimethylhexyl)-cyclopent-2-en-1-one
114	75	4-β-tetrahydropyran-2'-yloxyethoxy-2-(6-carbethoxy-5,5-dimethylhexyl)cyclopent-2-en-1-one
115	76	4-β-tetrahydropyran-2'-yloxyethoxy-2-(6-carbotetrahydropyran-2'-yloxy-5-oxahexyl)cyclopent-2-en-1-one
116	77	4-γ-tetrahydropyran-2'-yloxypropoxy-2-(6-carbethoxy-5-oxahexyl)cyclopent-2-en-1-one
117	78	4-β-tetrahydropyran-2'-yloxyethoxy-2-(6-carbotetrahydropyran-2'-yloxy-6-fluorohexyl)cyclopent-2-en-1-one
118	79	4-β-tetrahydropyran-2'-yloxyethoxy-2-(5-carbotetrahydropyran-2'-yloxypentyl)cyclopent-2-en-1-one
119	80	4-β-tetrahydropyran-2'-yloxyethoxy-2-(7-carbotetrahydropyran-2'-yloxyheptyl)cyclopent-2-en-1-one
120	81	4-β-tetrahydropyran-2'-yloxyethoxy-2-(6-carbotetrahydropyran-2'-yloxy-6-phenylhexyl)cyclopent-2-en-1-one
121	82	4-β-tetrahydropyran-2'-yloxyethoxy-2-(6-carbon-butoxyhexyl)cyclopent-2-en-1-one
122	83	4-β-tetrahydropyran-2'-yloxyethoxy-2-(6-carboisopropoxyhexyl)cyclopent-2-en-1-one
123	84	4-β-tetrahydropyran-2'-yloxyethoxy-2-(6-carbon-decyloxyhexyl)cyclopent-2-en-1-one
124	85	4-β-tetrahydropyran-2'-yloxypropoxy-2-(6-carbotetrahydropyran-2'-yloxyhexyl)cyclopent-2-en-1-one

EXAMPLE 125

Preparation of 4-(4-hydroxybutoxy)-2-(6-carboxyhexyl)cyclopent-2-en-1-one

To a stirred solution of 56.0 g. of crude 4-bromo-2-(6-carboxyhexyl)cyclopent-2-en-1-one (Example 8) in 400 ml. of tetrahydrofuran and 133 ml. of water at 3°C. is added 44.1 g. (0.226 moles) of silver fluoborate during 25 minutes. The mixture is stirred at 0°–5°C. for 60 minutes, diluted with water and ether, and filtered. The aqueous portion of the filtrate is saturated with solid sodium chloride and extracted with additional ether. The combined organic phases are washed successively with water and saturated sodium chloride solution, dried over magnesium sulfate, and concentrated. Column chromatography of the residue gives the subject compound as a mixture with 4-hydroxy-2-(6-carboxyhexyl)cyclopent-2-en-1-one, NMR ($CDCl_3$) 3.60 (multiplet, O-methylene hydrogens) and 4.60 ν (multiplet, O-methine hydrogen).

EXAMPLE 126

Preparation of 4-(4-tetrahydropyranyloxybutoxy)-2-(6-tetrahydropyranylcarboxyhexyl)cyclopent-2-en-1-one

In the manner of Example 86 the mixture of 4-hydroxy-2-(6-carboxyhexyl)cyclopent-2-en-1-one and 4-(4-hydroxybutoxy)-2-(6-carboxyhexyl)cyclopent-2-en-1-one (Example 125) is converted to a mixture of the subject compound and 4-tetrahydropyranyloxy-2-

(6-tetrahydropyranylcarboxyhexyl)-cyclopent-2-en-1-one with dihydropyran and p-toluenesulfonic acid monohydrate in methylene chloride.

EXAMPLE 127

Preparation of 3-triphenylmethoxy-1-octyne

A mixture of 1.26 g. (10.0 mmoles) of 1-octyn-3-ol, 4.85 g. (15.0 mmoles) of triphenylmethyl bromide, and 50 ml. of dry pyridine is heated at 95°C. for 60 minutes with occasional swirling. The solution is cooled, treated with water, and extracted with ether. The extract is washed successively with water and saturated sodium chloride, dried over magnesium sulfate, and concentrated. The crude product is purified by chromatography on Florisil and recrystallization from petroleum ether to give white crystals, m.p. 65°–66°C. λ max. (KBr) 3280 (acetylenic hydrogen), 1605, 1030, and 702 cm^{-1} (triphenylmethoxy group).

EXAMPLE 128

Preparation of 1-iodo-3-triphenylmethoxy-trans-1-octene

To a mixture of 0.650 g. (16.91 mmole) of sodium borohydride and 3.17 g. (45.2 mmoles) of 2-methyl-2-butene in 40 ml. of diglyme cooled to −5°C. under an inert atmosphere is added over 15 minutes 3.24 g. (22.6 mmoles) of boron trifluoride etherate and the resulting mixture is stirred at 0°C. for 2 hours. To this mixture is then added over 5 minutes 8.32 g. (22.6 mmoles) of 3-triphenylmethoxy-1-octyne (Example 127) in 10 ml. diglyme, the cooling bath is removed, and the mixture is stirred at ambient temperature for 1.5 hours. The mixture is cooled to 0°C. and 6.0 g. of finely divided anhydrous trimethylamine oxide is added over 10 minutes. The cooling bath is removed and the mixture is stirred at ambient temperatures for 0.5 hour. The mixture is then poured into 200 ml. of 15% sodium hydrooxide solution, a solution of 16 g. (63 mmoles) of iodine in 20 ml. of tetrahydrofuran is added immediately, and the resulting mixture is stirred for 0.5 hour. The organic phase is separated and the aqueous phase is washed with ether. The combined organic phase and washings are decolorized with 5% sodium thiosulfate solution, washed with saturated brine, dried (Na_2SO_4), and evaporated. The residue is dry-columned chromatographed upon alumina using hexane is eluent and the title compound is isolated as an oil.

EXAMPLES 129–138

In accordance with the method described in Example 127, the various 3-hydroxy-1-alkylenes listed in Table 6 below are converted to the corresponding 3-triphenylmethoxy-1-alkynes by treatment with triphenylmethyl bromide.

Table 6

Example	Starting 3-hydroxy-1-alkyne	Product 3-triphenylmethoxy-1-alkyne
129	1-heptyn-3-ol	3-triphenylmethoxyheptyne-1
130	1-hexyn-3-ol	3-triphenylmethoxyhexyne-1
131	1-pentyn-3-ol	3-triphenylmethoxypentyne-1
132	1-nonyne-3-ol[a]	3-triphenylmethoxynonyne-1
133	1-decyne-3-ol[b]	3-triphenylmethoxydecyne-1

Table 6-Continued

Example	Starting 3-hydroxy-1-alkyne	Product 3-triphenylmethoxy-1-alkyne
134	4-ethyl-1-octyne-3-ol	3-triphenylmethoxy-4-ethyl-octyne-1
135	4-methyl-1-heptyne-3-ol	3-triphenylmethoxy-4-methylheptyne-1
136	7-methyl-6-en-1-octyne-3-ol	3-triphenylmethoxy-7-methyl-6-en-octyne-1
137	5,9-dimethyl-9-en-1-decyne-3-ol[d]	3-triphenylmethoxy-5,9-dimethyl-9-en-decyne-1
138	cis-5-en-1-octyne-3-ol[e]	3-triphenylmethoxy-cis-5-en-octyne-1

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[a] M. Bertrand, Bull. Soc. Chim. France, 461 (1956).
[b] F. Bohlmann and D. Ratz, Chem. Ber., 90, 2265 (1957).
[c] U.S. Pat. 3,452,105 (June 24, 1969); Chem. Abs., 71, 60678 (1969).
[d] Sequin, Bull. Soc. Chim. France, 12, 948 (1945).
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EXAMPLE 138A

Preparation of 3-methoxy-1-octyne

To an ice-cooled solution of 63 g. of 1-octyn-3-ol in 300 ml. of dimethoxyethane is added under an inert atmosphere 312 ml. of 1.6 M n-butyllithium in hexane dropwise over 1 hour. To the mixture is then added 145 g. of methyl iodide and the resulting mixture is stirred at ambient temperatures for 24 hours and then heated to 60°C. for 1 hour. The mixture is cooled and poured into cold dilute hydrochloric acid. The organic phase is separated, washed with water and saturated brine, dried (Na_2SO_4), and evaporated to an oil, dried (Na_2SO_4), and evaporated to an oil. Fractional distillation of the oil in vacuo yields the product as a colorless oil.

EXAMPLES 139–148

Treatment of the 1-alkynes listed in Table 7 below with disiamylborane (prepared in situ from 2-methyl-2-butene, sodium borohydride and boron trifluoride), trimethylamine oxide, iodine and aqueous sodium hydroxide by the procedure described in Example 128 furnishes the product 3-triphenylmethoxy-1-iodo-trans-1-alkenes of the Table.

Table 7

Example	Starting 1-alkyne of Example	Product 1-iodo-trans-1-alkene
139	129	1-iodo-3-triphenylmethoxy-trans-heptene
140	130	1-iodo-3-triphenylmethoxy-trans-1-hexene
141	131	1-iodo-3-triphenylmethoxy-trans-1-pentene
142	132	1-iodo-3-triphenylmethoxy-trans-1-nonene
143	133	1-iodo-3-triphenylmethoxy-trans-1-decene
144	134	1-iodo-3-triphenylmethoxy-4-ethyl-trans-1-octene
145	135	1-iodo-3-triphenylmethoxy-4-methyl-trans-1-heptene
146	136	1-iodo-3-triphenylmethoxy-7-methyl-trans-1,6-octadiene
147	137	1-iodo-3-triphenylmethoxy-5,9-dimethyl-trans-1,9-decadiene
148	138	1-iodo-3-triphenylmethoxy-trans-1,cis-5-octadiene
148A	138A	1-iodo-3-methoxy-trans-1-octene

EXAMPLE 149

Preparation of 4,4-dimethyl-1-octyn-3-ol

To a solution of 20.2 g. (0.220 mole) of lithium acetylide-ethylenediamine complex in 100 ml. of dry dimethylsulfoxide is added 25.6 g. (0.200 mole) of 2,2-dimethyl-1-hexanal, prepared according to the procedure of G. Stork and S. R. Dowd, *J. Amer. Chem. Soc.*, 85, 2178 (1963), in 25 ml. of dimethylsulfoxide at a rate to maintain a temperature of 25°C. (cooling). The mixture is then maintained at 25°C. for 2 hours and is poured onto ice and excess hydrochloric acid. The mixture is extracted with ether and the organic phase is washed with water and saturated brine, dried (Na_2SO_4), and evaporated to an oil. Distillation in vacuo yields the product as a colorless oil.

EXAMPLE 150

Preparation of 4,4-dimethyl-3-tetrahydropyranyloxy-1-octyne

To a solution of 23.1 g. (0.150 mole) of 4,4-dimethyl-1-octyn-3-ol (Example 149) in 126 g. of freshly distilled dihydropyran is added 1 drop of phosphorous oxychloride and the solution is maintained at ambient temperature in a tightly stoppered flask for 20 hours. Five drops of triethylamine are then added and the mixture is evaporated in vacuo to an oil. The oil is chromatographed on 600 g. of silica gel and the product is eluted with 5% ethyl acetate in benzene yielding a colorless oil.

EXAMPLE 151

Preparation of 4,4-dimethyl-1-iodo-trans-1-octen-3-ol

To 233 ml. of a 0.43N solution of disiamylborane in diglyme cooled to 0°C. under an inert atmosphere is added 23.8 g. (0.100 mole) 4,4-dimethyl-3-tetrahydropyranyloxy-1-octyne (Example 150). The mixture is allowed to come to room temperature and is stirred at ambient temperature for 3 hours. The solution is cooled to 0°C. and 22.5 g. (0.30 mole) of triethylamine oxide is added portionwise such that the temperature is maintained at 0°–5°C. The mixture is stirred at 0°C. for 1 hour and is then poured into 150 ml. of 1 N sodium hydroxide followed immediately by a solution of 25.4 g. (0.100 mole) of iodine in 60 ml. of tetrahydrofuran. The mixture is stirred at ambient temperatures for 0.5 hour and poured into 500 ml. of water. The mixture is decolorized by addition of sodium thiosulfate and is extracted into ether. The organic phase is washed with water and the solvent is removed in vacuo. The residue is stirred at room temperature for 20 hours with 900 ml. 3:1:1 tetrahydrofuran-acetic acid-water. The solution is evaporated in vacuo and the residue is chromatographed on silica gel in benzene using 10–20% ethylacetate in benzene.

EXAMPLE 152

Preparation of 4,4-dimethyl-1-iodo-3-triphenylmethoxy-trans-1-octene

Treatment of 11.2 g. (0.396 mole) of 4,4-dimethyl-1-iodo-trans-1-octen-3-ol (Example 151) with 12.8 g. of triphenylmethyl bromide in 50 ml. of pyridine and purification on Florisil, all as described in Example 127 gives the title compound.

EXAMPLE 153

Preparation of 5,5-dimethyl-1-octyn-3-ol

Treatment of 20.2 g. (0.220 mole) of lithium acetylide-ethylenediame complex in 100 ml. of dimethylsulfoxide with 25.6 g. (0.200 mole) of 3,3-dimethylhexanol [prepared according to the procedure of A. W. Burgstahler, *J. Amer. Chem. Soc.*, 82, 4681 (1960)] and distillation of the product, all as described in Example 149 yields the title compound.

EXAMPLE 154

Preparation of 5,5-dimethyl-3-tetrahydropyranyloxy-1-octyne

Treatment of 23.1 g. (0.150 mole) of 5,5-dimethyl-1-octyne-3-ol (Example 153) with 126 g. of dihydropyran and 1 drop of phosphorus oxychloride as described in Example 150 gives the title compound.

EXAMPLE 155

Preparation of 5,5-dimethyl-1-iodo-trans-1-octen-3-ol

Treatment of 23.8 g. (0.100 mole) of 5,5-dimethyl-3-tetrahydropyranyloxy-1-octyne (Example 154) successively with 233 mg. of 0.43 M disiamylborane in diglyme, 22.5 g. of trimethylamine oxide, 150 ml. of 1 N sodium hydroxide, 25.4 g. of iodine, and 900 ml. of 3:1:1 tetrahydrofuran-acetic acid-water as described in Example 151 gives the title compound.

EXAMPLE 156

Preparation of 5,5-dimethyl-1-iodo-3-triphenylmethoxy-trans-1-octene

Treatment of 6.0 g. of 5.5-dimethyl-1-iodo-trans-1-octen-3-ol (Example 155) with 6.9 g. of triphenylmethyl bromide in 30 ml. of pyridine and purification on Florisil all as described in Example 127 gives the title compound.

EXAMPLE 157

Preparation of 1,1-dimethoxy-cis-3,4-methanohexane (cis-1-ethyl-2-(2,2-dimethoxyethyl)-cyclopropane)

To an ethereal suspension of zinc-silver couple, prepared according to the procedure of J. M. Danis, C. Girand, and J. M. Conia, *Synthesis*, 1972, 549, from 0.400 g. of silver acetate, 400 ml. of acetic acid, 68 g. of granular zinc, silver wool, and 600 ml. of ether, is added dropwise 136 g. of diiodomethane at a rate to maintain a gentle reflux. The mixture is then stirred at room temperature for 1 hour and and to it is then added 57.7 g. of 1,1-dimethoxy-cis-3-hexene (M. Winter, *Helvetica Chimica Acta*, 46, 1792 (1963)) over a period of 20 minutes and the mixture is refluxed for 5 hours. The mixture is cooled to 0°C., 600 ml. of ether is added followed by 50.5 g. of pyridine dropwise over a period of 1 hour. The resulting precipitate is filtered and washed with ether. The filtrate and washings are combined and evaporated and the residue is fractionally distilled at 12 torr. to yield the title compound as a colorless oil.

EXAMPLE 158

Preparation of cis-3,4-methano-1-hexanol

To a vigorously stirred solution of 31.6 g. of 1,1-dimethoxy-cis-3,4-methano-hexane (Example 157), 75

mg. of hydroquinone, 6 g. of oxalic acid in 150 ml. of acetone heated at 45°C. under an inert atmosphere is added 700 ml. of water over a period of 0.5 hour. The mixture is cooled and extracted well with ether. The organic phase is separated, washed with saturated sodium bocarbonate solution and saturated brine, dried (Na_2SO_4) and evaporated. The residue is distilled at 30 torr. to yield the title compound.

EXAMPLE 159

Preparation of cis-5,6-methano-1-octyn-3-ol

To a solution of 15.2 g. (0.165 mole) of lithium acetylide-ethylenediamine complex in 100 ml. of dry dimethylsulfoxide is added 16.8 g. (0.150 mole) of cis-3,4-methano-1-hexanol (Example 158) in 25 ml. of dimethylsulfoxide at a rate to maintain a temperature of 25°C. (cooling). The mixture is then maintained at 25°C. for 2 hours and is poured onto ice and excess hydrochloric acid. The mixture is extracted with ether and the organic phase is washed with water and saturated brine, dried (Na_2SO_4), and evaporated to an oil. Distillation in vacuo yields the title compound as a colorless oil.

EXAMPLE 160

Preparation of 3-triphenylmethoxy-cis-5,6-methano-1-octyne

A mixture of 13.8 g. of cis-5,6-methano-1-octyn-3-ol (Example 159) and 33.0 g. of triphenylmethyl bromide in 100 ml. of pyridine is heated to 100°C. for 1.5 hours under an inert atmosphere. The mixture is cooled and filtered. The filtrate is partioned between ice water and ether. The organic phase is washed with cold dilute hydrochloric acid, saturated sodium bicarbonate solution, and saturated brine, dried ($NaSO_4$), and evaporated to an oil. The latter is dissolved in hexane and passed to an oil. The latter is dissolved in hexane and passed through 400 g. of Florisil to yield after evaporation the title compound as a colorless oil.

EXAMPLE 161

Preparation of 1-iodo-3-triphenylmethoxy-cis-5,6-methano-trans-1-octene

To 160 ml. of a 0.50M solution of disiamylborane in diglyme cooled to 0°C. under an inert atmosphere is added 28.6 g. (0.075 mole) 3-triphenylmethoxy-cis-5,6-methano-1-octyne (Example 160). The mixture is allowed to come to room temperature and is stirred at ambient temperature for 3 hours. The solution is cooled to 0°C, and 16.9 g. (0.225 mole) of triethylamine oxide is added portionwise such that the temperature is maintained at 0–5°C. The mixture is stirred at 0°C. for 1 hour and is then poured into 300 ml. of 1 N sodium hydroxide followed immediately be a solution of 57 g. (0.225 mole) of iodine in 150 ml. of tetrahydrofuran. The mixture is stirred at ambient temperatures for 0.5 hour and poured into 1000 ml. of water. The mixture is decolorized by addition of sodium thiosulfate solution and is extracted into ether. The organic phase is washed with water and the solvent is removed in vacuo. The residue is purified by dry-column chromatography upon 1.5 kg. of alumina using hexane as eluent. The title compound is obtained as an oil.

EXAMPLES 162–168

Treatment of the carboxaldehydes listed in Table 8 below with lithium acetylide by the procedure described in Example 159 followed by treatment of the resulting 3-hydroxy-1-alkyne with triphenylmethyl bromide by the procedure of Example 160 furnishes the product 3-triphenylmethoxy-1-alkynes of the table.

TABLE 8

Example	Starting carboxaldehyde	Product 3-triphenylmethoxy-1-alkyne
162	(2-cyclohexenyl)-acetaldehyde[1]	4-(2-cyclohexenyl)-3-triphenylmethoxy-1-butyne
163	(3-cyclohexenyl)-acetaldehyde[1]	4-(3-cyclohexenyl)-3-triphenylmethoxy-1-butyne
164	adamantane-1-carboxaldehyde	3-(1-adamantyl)-3-triphenylmethoxy-1-propyne
165	2-cyclohexene-carboxaldehyde	3-(2-cyclohexenyl)-3-triphenylmethoxy-1-propyne
166	3-cyclohexene-carboxaldehyde	3-(3-cyclohexenyl)-3-triphenylmethoxy-1-propyne
167	adamantane-2-carboxaldehyde[2]	3-(2-adamantyl)-3-triphenylmethoxy-1-propyne
168	(adamantyl-1)acetaldehyde	4-(1-adamantyl)-1-butyne

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EXAMPLES 169–175

Treatment of the 3-triphenylmethoxy-1-alkynes listed in Table 9 below with disiamylborane, trimethylamine oxide; iodine and aqueous sodium hydroxide by the procedure described in Example 161 furnishes the product 3-triphenylmethoxy-1-iodo-1-trans-alkenes of the table.

Table 9

Example	Starting 3-triphenylmethoxy-1-alkynes of Example	Product 3-triphenylmethoxy-1-iodo-1-trans-alkene
169	162	4-(2-cyclohexenyl)-3-triphenylmethoxy-1-iodo-1-trans-butene
170	163	4-(3-cyclohexenyl)-3-triphenylmethoxy-1-iodo-1-trans-butene
171	164	3-(1-adamantyl)-3-triphenylmethoxy-1-iodo-1-trans-propene
172	165	3-(2-cyclohexenyl)-3-triphenylmethoxy-1-iodo-1-trans-propene
173	166	3-(3-cyclohexenyl)-3-triphenylmethoxy-1-iodo-1-trans-propene
174	167	3-(2-adamantyl)-3-triphenylmethoxy-1-iodo-1-trans-propene
175	168	4-(1-adamantyl)-3-triphenylmethoxy-1-iodo-1-trans-butene

EXAMPLE 176

Preparation of cyclopentylacetyl chloride

To a solution of 50 g. of cyclopentaneacetic acid containing 2.9 ml. of N,N-dimethylformamide is added dropwise, with stirring, 51 g. of thionyl chloride over a period of 15 minutes. After stirring for an additional 60

minutes excess thionyl chloride is removed in vacuo and the residual oil as distilled to give 55.4 g. (94%) of product, b.p. 57°–58°C. (10 mm.)

EXAMPLE 177

Preparation of 1-chloro-4-cyclopentyl-1-trans-buten-3-one

A three-necked flask filtered with a stirrer, a gas inlet tube and a gas outlet tube protected with a calcium chloride tube is surrounded by an ice-water bath. The system is flushed with acetylene for 3 minutes. Carbon tetrachloride (150 ml.) is added to the flask and acetylene is bubbled through at a fast rate for 3 minutes. Aluminium chloride (59 g.) is added and acetylene is bubbled through the mixture for 5 minutes. The gas inlet tube is replaced by a dropping funnel protected by a calcium chloride drying tube. Cyclopentaneacetyl chloride (55.4 g., Example 176) is added to the reaction mixture with stirring over a period of about 20 minutes. The dropping funnel is replaced by the gas inlet tube and with stirring, acetylene gas is bubbled through at a rate in excess of the saturation rate. After about 15 minutes the rate of absorption of acetylene suddenly becomes very rapid, and the acetylene is passed through as rapidly as it is absorbed. The introduction of acetylene is continued for 45 minutes after rapid absorption (which lasts about 1 hour) has subsided.

The reaction mixture is poured with stirring onto 430 g. of ice + 180 ml. of saturated sodium chloride solution. The aqueous phase is extracted three times more with ether. The combined extracts are dried with anhydrous magnesium sulfate and evaporated to dryness in vacuo. After addition of 1.5 g. of hydroquinone the residual oil is distilled to give 57 g. (89%) of oil, b.p. 67°–69°C. (0.14 mm.).

EXAMPLE 178

Preparation of 4-cyclopentyl-1-iodo-1-trans-buten-3-one

A solution of 57 g. of 1-chloro-4-cyclopentyl-1-trans-butene-3-one (Example 177) in 36 0 ml. of acetone containing 55 g. of sodium iodide is stirred at the reflux temperature for 18 hours. The resulting mixture is cooled, filtered and the mother liquor is taken to dryness. The residual oil is dissolved in ether washed successively with water, dilute sodium thiodulfate solution, and saturated sodium chloride solution, dried with anhydrous magnesium sulfate and taken to dryness to give 87 g. (99%) of orange oil. Vapor phase chromatography shows one peak.

EXAMPLE 179

Preparation of 4-cyclopentyl-1-iodo-1-trans-buten-3-ol

To a solution of 7.1 g. of sodium borohydride in 60 ml. of absolute alcohol, stirred in an ice bath under nitrogen atmosphere, is added dropwise, over a period of about 2 hours, a solution containing 87 g. of 4-cyclopentyl-1-iodo-trans-buten-3-one (Example 178) in 160 ml. of absolute alcohol. The temperature is maintained at 5°–10°C. The solution is poured into 850 ml. of iced water and the resulting mixture is extracted 3 times with ether. The combined extracts are washed with dilute sodium bisulfite solution, saturated sodium chloride solution, dried with anhydrous magnesium sulfate and taken to dryness to give 81 g. of yellow oil. Column chromatography on a column of 1 kg. of silica gel using benzene as eluent gives 75 g. (88%) of oily product.

Examples 180–199

Treatment of the listed carboxylic acids on Table 10 below with thionyl chloride by the procedure described in Example 176 followed by treatment of the resulting acid chloride with acetylene by the procedure described in Example 177, and thence by treatment of the resulting 1-chloro-1-trans-alkene-3-one with sodium iodide by the procedure described in Example 178, and then by treatment of the resulting 1-iodo-1-trans-alkene-3-one with sodium borohydride by the procedure described in Example 179 is productive of the product 3-hydroxy-1-iodo-1-trans-alkenes of the table.

Table 10

Example	Starting carboxylic acid	Product 3-hydroxy-1-iodo-1-trans-alkene
180	cyclobutylacetic acid[1]	4-cyclobutyl-3-hydroxy-1-iodo-1-trans-butene
181	3-cyclopentylpropionic acid	5-cyclopentyl-3-hydroxy-1-iodo-1-trans-pentene
182	4-cyclopentylbutyric acid[2]	6-cyclopentyl-3-hydroxy-1-iodo-1-trans-hexene
183	5-cyclopentylpentanoic acid[2]	7-cyclopentyl-3-hydroxy-1-iodo-1-trans-heptene
184	6-cyclopentylhexanoic acid[2]	8-cyclopentyl-3-hydroxy-1-iodo-1-trans-octene
185	2-methyl-3-cyclopentylpropanoic acid[3]	5-cyclopentyl-4-methyl-3-hydroxy-1-iodo-1-trans-pentene
186	2-ethyl-4-cyclopentylbutyric acid[4]	6-cyclopentyl-4-ethyl-3-hydroxy-1-iodo-1-trans-hexene
187	(2-trans-methylcyclopentyl)-acetic acid[5]	4-(2-trans-methylcyclopentyl)-3-hydroxy-1-iodo-1-trans-butene
188	cyclohexylacetic acid	4-cyclohexyl-3-hydroxy-1-iodo-1-trans-butene
189	3-cyclohexylpropionic acid	5-cyclohexyl-3-hydroxy-1-iodo-1-trans-pentene
190	4-cyclohexylbutyric acid[6]	6-cyclohexyl-3-hydroxy-1-iodo-1-trans-hexene
191	cycloheptylacetic acid[7]	4-cycloheptyl-3-hydroxy-1-iodo-1-trans-butene
192	cyclooctylacetic acid[8,9]	4-cyclooctyl-3-hydroxy-1-iodo-1-trans-butene
193	(4-methylcyclohexyl)acetic acid[10]	4-(4-methylcyclohexyl)-3-hydroxy-1-iodo-1-trans-butene
194	(3-methylcyclohexyl)acetic acid[11]	4-(3-methylcyclohexyl)-3-hydroxy-1-iodo-1-trans-butene
195	trans-2-methylcyclopentane carboxylic acid[12]	3-(trans-2-methylcyclopentyl)-3-hydroxy-1-iodo-1-trans-propene
196	cyclohexane carboxylic acid	3-cyclohexyl-3-hydroxy-1-iodo-1-trans-propene
197	trans-4-methylcyclohexane carboxylic acid[13]	3-(trans-4-methylcyclohexyl)-3-hydroxy-1-iodo-1-trans-propene
198	cyclooctane carboxylic acid[14]	3-cyclooctyl-3-hydroxy-1-iodo-1-trans-propene
199	cycloheptane carboxylic acid	3-cycloheptyl-3-hydroxy-1-iodo-1-trans-propene

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Table 10-Continued

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EXAMPLE 200

Preparation of 4-cyclopentyl-1-iodo-3-triphenylmethoxy-1-trans-butene

A mixture of 21.4 g. of 4-cyclopentyl-1-iodo-1-trans-buten-3-ol (Example 179) in 170 ml. of dry pyridine containing 31 g. of triphenylmethyl bromide is heated on the steam-bath for 2 hours. The dark mixture is poured into 850 ml. of iced water and the resulting solution is extracted three times with ether. The combined extracts are washed with ice cold 2% hydrochloric acid until the washings are acidic, saturated sodium chloride solution, dried with anhydrous magnesium sulfate and taken to dryness. Trituration of the residue followed by filtration removes triphenylcarbinol. The mother liquor is taken to dryness and the residual syrup is chromatographed on 400 g. of florisil using hexane gives 32 g. (78%) of syrup which solidifies on standing. Recrystallization from hexane affords white crystals, m.p. 87°–88°C.

EXAMPLE 201

Preparation of 4-cyclopentyl-1-iodo-3-(p-methoxyphenyldiphenyl)methoxy-1-trans-butene

A solution of 20 g. of 4-cyclopentyl-1-iodo-1-trans-buten-3-ol (Example 179) and 25 g. of p-anisylchlorodiphenylmethane in 170 ml. of dry pyridine is kept at 60°C. for 18 hours, then at 70°C. for 3 hours. The cooled solution is poured into 850 ml. of iced water. The resulting solution is partitioned between ether and water. The ether layer is washed with water, dried with anhydrous magnesium sulfate and taken to dryness. Further evaporation with toluene gets rid of residual pyridine. The resulting oil is chromatographed on 300 g. of florisil with hexanes to give 22.3 g. of product. The material is homogeneous according to thin layer chromatography.

EXAMPLES 202 – 221

Treatment of the listed 3-hydroxy-1-iodo-trans-1-alkenes of Table 11 below with triphenylmethylbromide by the procedure described in Example 200 above is productive of the product 3-triphenylmethoxy-1-iodo-trans-1-alkenes of the table.

Table 11

Example	Starting 1-iodo-1 trans-alkene of Example	Product 3-triphenylmethoxy-1-iodo--trans-1-alkene
202	180	4-cyclobutyl-3-triphenylmethoxy-1-iodo-1-trans-butene
203	181	5-cyclopentyl-3-triphenylmethoxy-1-iodo--1-trans-pentene
204	182	6-cyclopentyl-3-triphenylmethoxy-1-iodo--1-trans-hexene
205	183	7-cyclopentyl-3-triphenylmethoxy-1-iodo--1-trans-heptene
206	184	8-cyclopentyl-3-triphenylmethoxy-1-iodo--1-trans-octene
207	185	5-cyclopenyl-4-methyl--3-triphenylmethoxy-1--iodo-1-trans-pentene
208	186	6-cyclopentyl-4-ethyl--3-triphenylmethoxy-1--iodo-1-trans-hexene
209	187	4-(2-trans-methylcyclopentyl)-3-triphenylmethoxy-1-iodo-1-trans--butene
210	188	4-cyclohexyl-3-triphenylmethoxy-1-iodo--1-trans-butene
211	189	5-cyclohexyl-3-triphenylmethoxy-1-iodo-1--trans-pentene
212	190	6-cyclohexyl-3-triphenylmethoxy-1-iodo-1--trans-hexene
213	191	4-cycloheptyl-3-triphenylmethoxy-1-iodo-1--trans-butene
214	192	4-cyclooctyl-3-triphenylmethoxy-1-iodo-1--trans-butene
215	193	4-(4-methylcyclohexyl)--3-triphenylmethoxy-1--iodo-1-trans-butene
216	194	4-(3-methylcyclohexyl)--3-triphenylmethoxy-1--iodo-1-trans-butene
217	195	3-(trans-2-methylcyclopentyl)-3-triphenylmethoxy-1-iodo-trans--propene
218	196	3-cyclohexyl-3-triphenylmethoxy-1-iodo-1--trans-propene
219	197	3-(trans-4-methylcyclohexyl)-3-triphenyl--methoxy-1-iodo-1-trans--propene
220	198	3-cyclooctyl-3-triphenylmethoxy-1-iodo-1--trans-propene
221	199	3-cycloheptyl-3-triphenylmethoxy-1-iodo--1-trans-propene

EXAMPLE 222

Preparation of 1-chloro-trans-1-octen-3-one

To a slurry of 233.5 g. (1.75 moles) of aluminum chloride in 390 ml. of carbon tetrachloride, saturated with acetylene and cooled in an ice bath, is added over 20 minutes 201.9 g. (1.50 moles) of hexanoyl chloride. After the addition is complete, acetylene is bubbled into the mixture as rapidly as it is absorbed and for 1 hour after absorption becomes slow. The mixture is poured onto 1700 g. of ice and 720 ml. of saturated brine. The organic phase is separated and the aqueous phase is washed with ether. The combined organic phase and washings are washed with saturated brine, dried (Na_2SO_4) and evaporated. The residual oil is combined with 10 g. of hydroquinone and distilled to yield a colorless oil, b.p. 51°–52°C. (0.10 torr.).

EXAMPLE 224

Preparation of 1-iodo-trans-1-octen-3-one

A mixture of 54.5 g. (0.364 mole) of sodium iodide and 40 g. (0.249 mole) of 1-chloro-trans-1-octen-3-one (Example 222) in 360 ml. of acetone is stirred and refluxed for 24 hours. The reaction mixture is cooled, filtered and concentrated. The residue is partitioned between water and ether. The organic phase is washed with dilute sodium bicarbonate solution, brine, dried ($MgSO_4$) and evaporated to an oil. This material is used directly without purification.

EXAMPLE 225

Preparation of 1-iodo-trans-1-octen-3-ol

A solution of 78.2 g. (0.310 moles) of 1-iodo-trans-1-octen-3-one (Example 224) in 150 ml. of absolute ethanol is added dropwise over 2 hours to a slurry of 6.49 g. (0.172 moles) of sodium borohydride in 50 ml. of absolute ethanol cooled in an ice bath. After the addition is complete, the mixture is stirred for 2 hours with ice cooling and is then poured into 1 l. of water. The mixture is extracted into benzene and the organic phase is washed with saturated brine, dried (Na_2SO_4) and evaporated. The resulting oil is dissolved into 400 ml. of absolute ethanol and treated with 5 mole percent of p-carboxyphenylhydrazine at 70°C. for 1.5 hours to remove residual ketone. The mixture is cooled and evaporated and the residue is dissolved into 400 ml. of ether and is filtered. The filtrate is washed with dilute sodium bicarbonate solution and saturated brine, dried (Na_2SO_4), and evaporated to an oil. This oil is chromatographed upon 2 kg. of Florisil packed in hexane and the product is obtained upon elution with benzene. Distillation of the product yields a colorless oil, b.p. 74°–76°C. (0.005 torr.)

EXAMPLE 226

Preparation of 1-iodo-3-(p-anisyldiphenylmethoxy)-trans-1-octene

A mixture of 14.92 g. (0.0588 mole) of 1-iodo-trans-1-octen-3-ol (Example 225) and 18.2 g. (0.0588 mole) of p-anisyldiphenylmethyl chloride in 165 ml. of dry pyridine is heated at 60°C. for 18 hours under an inert atmosphere. The mixture is cooled and the solvent is evaporated in vacuo. The residue is partiioned between ether and water, and the organic phase is washed with water and saturated brine, dried ($MgSO_4$), and evaporated. The residue is chromatpgraphed upon 300 g. of Florisil packed in hexane and the product is eluted with hexane and 4:1 hexane-benzene the yield a colorelss oil.

EXAMPLE 227

Preparation of 9-oxo-11α-methoxy-15-hydroxy-13-trans-prostenoic acid

To a solution of 6.030 g. (0.01215 mole) of 1-iodo-3-triphenylmethoxy-trans-1-octene (Example 128) in 8 ml. of toluene cooled to −78°C. under an inert atmosphere is added 5.2 ml. of 2.34 M solution of n-butyllithium in hexane, The resulting solution is allowed to warm to −40°C. and is maintained at this temperature for 1 hour. To the solution containing 3-triphenylmethoxy-trans-1-octenyllithium is then added 5.0 ml. of a 2.44 M (0.0122 mole) solution of trimethylaluminum in heptane and the mixture is allowed to warm to −10°C. The mixture containing lithium trimethyl(3-triphenylmethoxy-trans-1-octenyl)alanate is then cooled to −78°C. and to it is added a solution of 3.94 g. (0.01215 mole) of 4-methoxy-2-(4-carbotetrahydropyran-2'-yloxyhexyl)cyclopent-2-en-1-one (Example 101) dissolved in 10 ml. of diethyl ether. The mixture is allowed to warm to room temperature and is stirred at ambient temperature for 18 hours. The mixture is then poured onto ice and diluted hydrochloric acid and is extracted into ether. The organic phase is washed with water and saturated brine, dried (Na_2SO_4), and evaporated to yield a colorless oil.

The resulting crude 9-oxo-11α-methoxy-15-triphenylmethoxy-8ξ-13-trans-prostenoic acid is dissolved in 100 ml. of glacial acetic acid:tetrahydrofuran:water (4:2:1) and is heated at 45°C. for 7 hours. The mixture is cooled, diluted with aqueous sodium chloride solution and extracted with ether. The extract is washed with water and concentrated using toluene for azeotropic removal of aqueous acetic acid. The residue is chromatographed on silica gel to yield the title product and its 15-epimer.

EXAMPLE 228–393

Treatment of 1-iodo-3-triphenylmethoxy (or 3-methoxy)-trans-1-alkene listed in Table 12 below with n-butyl lithium followed by treatment of the resulting trans-1-alkenyl lithium derivative with trimethylaluminum and then treatment of the resulting lithio (trans-1-alkenyl)trimethyl alanate with the blocked 4-oxy-cyclopent-2-en-1-ones also listed in Table 12 below all by the procedure described in Example 227 gives, with the exception of the 15-methoxy derivative, the 15-O-triphenylmethyl-8-ξ-derivatives corresponding to the products of the table. Further treatment of these intermediates with acetic acid:tetrahydrofuran:-water as described in Example 227 gives the products of the table.

TABLE 12

Example	Starting 4-oxycyclopent--2-en-1-one of Example	Starting 1-iodo-1--trans alkene of Example	Product 9-oxo-11-oxy-15-hydroxy(methoxy)-13-trans--prostenoic acid
228	101	143	9-oxo-11α-methioxy-15-hydroxy-20-ethyl-13-trans--prostenoic acid
229	101	144	9-oxo-11α-methoxy-15-hydroxy-16-ethyl-13-trans--prostenoic acid
230	101	148A	9-oxo-11α-methoxy-15-methoxy-13-trans-prostenoic acid
231	101	148	9-oxo-11α-methoxy-15-hydroxy-13-trans,17-cis-prostadienoic acid
232	101	152	9-oxo-11α-methoxy-15-hydroxy-16,16-dimethyl-13--trans-prostenoic acid
233	101	156	9-oxo-11α-methoxy-15-hydroxy-17,17-dimethyl-13--trans-prostenoic acid
234	101	161	9-oxo-11α-methoxy-15-hydroxy-17,18-cis-methano-13--trans-prostenoic acid

TABLE 12 —Continued

Example	Starting 4-oxycyclopent--2-en-1-one of Example	Starting 1-iodo-1--trans alkene of Example	Product 9-oxo-11-oxy-15-hydroxy(methoxy)-13-trans--prostenoic acid
235	101	171	9-oxo-11α-methoxy-15-hydroxy-16,17,18,19,20-pentanor-15-(1-adamantyl)-trans-prostenoic acid
236	101	172	9-oxo-11α-methoxy-15-hydroxy-16,20-methano-13--trans,17-prostadienoic acid
237	101	221	9-oxo-11α-methoxy-15-hydroxy-16,20-ethano-13--trans-prostenoic acid
238	101	219	9-oxo-11α-methoxy-15-hydroxy-16,19-trans-ethano--13-trans-prostenoic acid
239	87	140	9-oxo-11α-methoxy-15-hydroxy-6,7,19,20-tetranor--13-trans-prostenoic acid
240	87	210	9-oxo-11α-methoxy-15-hydroxy-6,7-dinor-17,20-ethano-13-trans-prostenoic acid
241	88	202	9-oxo-11α-ethoxy-15-hydroxy-5,6,7,20-tetranor-17,-19-methano-13-trans-prostenoic acid
242	88	141	9-oxo-11α-ethoxy-15-hydroxy-5,6,7,18,19,20-hexanor-13-trans-prostenoic acid
243	89	143	9-oxo-11α-methoxy-15-hydroxy-7a,7b-bishomo-20--ethyl-13-trans-prostenoic acid
244	89	152	9-oxo-11α-methoxy-15-hydroxy-7a,7b-bishomo-16,16--dimethyl-13-trans-prostenoic acid
245	89	220	9-oxo-11α-methoxy-15-hydroxy-7a,7b-bishomo-16,20--(1,3-propano)-13-trans-prostenoic acid
246	90	139	9-oxo-11α-methoxy-15-hydroxy-2-ethyl-20-nor-13--trans-prostenoic acid
247	90	173	9-oxo-11α-methoxy-15-hydroxy-2-ethyl-16,20-methano-13-trans,18-prostadienoic acid
248	91	175	9-oxo-11α-methoxy-15-hydroxy-3,3-dimethyl-16-(1-adamantyl)-17,18,19,20-tetranor-13-trans-prostenoic acid
249	91	142	9-oxo-11α-methoxy-15-hydroxy-3,3,20-trimethyl-13-trans-prostenoic acid
250	92	128	9-oxo-11α-methoxy-15-hydroxy-3-oxa-13-trans-prostenoic acid
251	92	148A	9-oxo-11α,15-dimethoxy-3-oxa-13-trans-prostenoic acid
252	92	152	9-oxo-11α-methoxy-15-hydroxy-3-oxa-16,16-dimethyl-13-trans-prostenoic acid
253	92	169	9-oxo-11α-methoxy-15-hydroxy-3-oxa-17,20-ethano-13-trans,18-prostadienoic acid
254	92	218	9-oxo-11α-methoxy-15-hydroxy-3-oxa-16,20,methano-13-trans-prostenoic acid
255	93	203	9-oxo-11α-methoxy-15-hydroxy-2-fluoro-18,20-ethano-13-trans-prostenoic acid
256	93	145	9-oxo-11α-methoxy-15-hydroxy-2-fluoro-16-methyl-20-nor-13-trans-prostenoic acid
257	94	139	9-oxo-11α-methoxy-15-hydroxy-7,20-dinor-13-trans-prostenoic acid
258	94	214	9-oxo-11α-methoxy-15-hydroxy-7-nor-17,20-(1,4-butano)-13-trans-prostenoic acid
259	95	142	9-oxo-11α-methoxy-15-hydroxy-7a-homo-20-methyl-13-trans-prostenoic acid
260	95	161	9-oxo-11α-methoxy-15-hydroxy-7a-homo-17,18-cis-methano-13-trans-prostenoic acid
261	95	206	9-oxo-11α-methoxy-15-hydroxy-7a-homo-20-cyclopentyl-13-trans-prostenoic acid
262	96	156	9-oxo-11α-methoxy-15-hydroxy-2-phenyl-17,17-dimethyl-13-trans-prostenoic acid
263	96	211	9-oxo-11α-methoxy-15-hydroxy-2-phenyl-18,20-(1,3-propano(-13-trans-prostenoic acid
264	97	152	9-oxo-11α -ethoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoic acid
265	97	207	9-oxo-11α-ethoxy-15-hydroxy-16-methyl-18,20-ethano-13-trans-prostenoic acid
266	97	146	9-oxo-11α-ethoxy-15-hydroxy-19-methyl-13-trans,18-prostadienoic acid
267	97	148	9-oxo-11α-ethoxy-15-hydroxy-13-trans,17-cis-prostadienoic acid
268	98	152	9-oxo-11α-propoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoic acid
269	98	139	9-oxo-11α-propoxy-15-hydroxy-20-nor-13-trans-prostenoic acid
270	98	128	9-oxo-11α-propoxy-15-hydroxy-13-trans-prostenoic acid
271	98	174	9-oxo-11α-propoxy-15-hydroxy-16,17,18,19,20-pentanor-15-(2-adamantyl)-13-trans-prostenoic acid
272	98	170	9-oxo-11α-propoxy-15-hydroxy-17,20-ethano-13-trans,19-prostadienoic acid
273	99	148	9-oxo-11α-isopropoxy-15-hydroxy-13-trans,17-cis-prostadienoic acid
274	99	148A	9-oxo-11α-isopropoxy-15-methoxy-13-trans-prostenoic acid
275	99	152	9-oxo-11α-isopropoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoic acid
276	99	200	9-oxo-11α-isopropoxy-15-hydroxy-17,20-methano-13-trans-prostenoic acid
277	99	226	9-oxo-11α-isopropoxy-15-hydroxy-13-trans-prostenoic acid
278	100	152	9-oxo-4-n-butoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoic acid

TABLE 12 —Continued

Example	Starting 4-oxycyclopent--2-en-1-one of Example	Starting 1-iodo-1--trans alkene of Example	Product 9-oxo-11-oxy-15-hydroxy(methoxy)-13-trans--prostenoic acid
279	100	128	9-oxo-4-n-butoxy-15-hydroxy-13-trans-prostenoic acid
280	100	145	9-oxo-4-n-butoxy-15-hydroxy-16-methyl-20-nor-13-trans-prostenoic acid
281	100	208	9-oxo-4-n-butoxy-15-hydroxy-16-ethyl-19,20-(1,3-propano)-13-trans-prostenoic acid
282	100	221	9-oxo-4-n-butoxy-15-hydroxyy-16,20-ethano-13-trans-prostenoic acid
283	102	217	9-oxo-11α-methoxy-15-hydroxy-2,17-dimethyl-20-nor-16,19-trans-methano-13-trans-prostenoic acid
284	102	152	9-oxo-11α-methoxy-15-hydroxy-2,16,16-trimethyl-13-trans-prostenoic acid
285	102	128	9-oxo-11α-methoxy-15-hydroxy-2-methyl-13-trans-prostenoic acid
286	34	128	ethyl 9-oxo-11α-ethoxy-15-hydroxy-13-trans-prostenoate
287	34	215	ethyl 9-oxo-11α-ethoxy-15-hydroxy-20-methyl-17,20-ethano-13-trans-prostenoate
288	35	152	methyl 9-oxo-11α-methoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoate
289	35	174	methyl 9-oxo-11α-methoxy-15-hydroxy-16,17,18,19,-20-pentanor-15-(2-adamantyl)-13-trans-prostenoate
290	36	226	ethyl 9-oxo-11α-propoxy-15-hydroxy-6,7-dinor-13-trans-prostenoate
291	37	128	ethyl 9-oxo-11α-isopropoxy-15-hydroxy-5,6,7-trinor-13-trans-prostenoate
292	41	147	ethyl 9-oxo-11α-isopropoxy-15-hydroxy-7a,7b-bis-homo-17-methyl-20-(2-propenyl)-13-trans-prostenoate
293	41	148	ethyl 9-oxo-11α-isopropoxy-15-hydroxy-7a,7b-bis-homo-13-trans,17-prostadienoate
294	43	148A	ethyl 9-oxo-11α-butoxy-15-methoxy-2-ethyl-13-trans-prostenoate
295	43	152	ethyl 9-oxo-11α-butoxy-15-hydroxy-2-ethyl-16,16-dimethyl-13-trans-prostenoate
296	45	128	ethyl 9-oxo-11α-methoxy-15-hydroxy-3,3-dimethyl-13-trans-prostenoate
297	45	152	ethyl 9-oxo-11α-methoxy-15-hydroxy-3,3,16,16-tetramethyl-13-trans-prostenoate
298	47	143	ethyl 9-oxo-11α-ethoxy-15-hydroxy-3-oxa-20-ethyl-13-trans-prostenoate
299	47	204	ethyl 9-oxo-11α-ethoxy-15-hydroxy-3-oxa-19,20-(1,3-propano)-13-trans-prostenoate
300	50	142	ethyl 9-oxo-11α-sec-butoxy-15-hydroxy-7-nor-20-methyl-13-trans-prostenoate
301	50	212	ethyl 9-oxo-11α-sec-butoxy-15-hydroxy-7-nor-19,20-(1,4-butano)-13-trans-prostenoate
302	52	213	ethyl 9-oxo-11α-methoxy-15-hydroxy-7α-homo-17,20-(1,3-propano)-13-trans-prostenoate
303	52	148	ethyl 9-oxo-11α-methoxy-15-hydroxy-7α-homo-13-trans,17-prostadienoate
304	55	205	butyl 9-oxo-11α-methoxy-15-hydroxy-20,20-(1,4-butano)-13-trans-prostenoate
305	55	152	butyl 9-oxo-11α-methoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoate
306	55	128	butyl 9-oxo-11α-methoxy-15-hydroxy-13-trans-prostenoate
307	56	152	isopropyl 9-oxo-11α-methoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoate
308	56	128	isopropyl 9-oxo-11α-methoxy-15-hydroxy-13-trans-prostenoate
309	56	216	isopropyl 9-oxo-11α-methoxy-15-hydroxy-17,19-(1,3-propano)-13-trans-prostenoate
310	56	161	isopropyl 9-oxo-11α-methoxy-15-hydroxy-17,18-cis-methano-13-trans-prostenoate
311	57	128	decyl 9-oxo-11α-methoxy-15-hydroxy-13-trans-prostenoate
312	57	152	decyl 9-oxo-11α-methoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoate
313	57	143	decyl 9-oxo-11α-methoxy-15-hydroxy-20-ethyl-13-trans-prostenoate
314	57	213	decyl 9-oxo-11α-methoxy-15-hydroxy-17,20-(1,3-propano)-13-trans-prostenoate
315	57	201	decyl 9-oxo-11α-methoxy-15-hydroxy-17,20-methano-13-trans-prostenoate
316	62	128	ethyl 9-oxo-11α-t-butoxy-15-hydroxy-13-trans-prostenoate
317	62	152	ethyl 9-oxo-11α-t-butoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoate
318	62	209	ethyl 9-oxo-11α-t-butoxy-15-hydroxy-20-nor-17,18-trans-(1,3-propano)-13-trans-prostenoate
319	86	128	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-13-trans-prostenoic acid
320	86	152	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-13-trans-prostenoic acid
321	86	161	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-17,18-cis-methano-13-trans-prostenoic acid

TABLE 12 — Continued

Example	Starting 4-oxycyclopent--2-en-1-one of Example	Starting 1-iodo-1--trans alkene of Example	Product 9-oxo-11-oxy-15-hydroxy(methoxy)-13-trans--prostenoic acid
322	86	171	9-oxo-11α-(2-hydroxyethyl)-15-hydroxy-16,17,18,-19,20-pentanor-15-(1-adamantyl)-13-trans-prosten-oic acid
323	86	143	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-20-ethyl-13-trans-prostenoic acid
324	86	144	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16-ethyl-13-trans-prostenoic acid
325	86	221	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,20-eth-ano-13-trans-prostenoic acid
326	86	148A	9-oxo-11α-(2-hydroxyethoxy)-15-methoxy-13-trans-prostenoic acid
327	86	148	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-13-trans-17-cis-prostadienoic acid
328	107	140	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-6,7,19,20-tetranor-13-trans-prostenoic acid
329	107	210	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-6,7-dinor-17,20-ethano-13-trans-prostenoic acid
330	108	141	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-5,6,7,18,-19,20-hexanor-13-trans-prostenoic acid
331	108	221	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-5,6,7-tri-nor-16,20-ethano-13-trans-prostenoic acid
332	110	143	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bis-homo-20-ethyl-13-trans-prostenoic acid
333	110	152	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bis-homo-16,16-dimethyl-13-trans-prostenoic acid
334	110	128	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bis-homo-13-trans-prostenoic acid
335	110	220	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bis-homo-16,20-(1,3-propano)-13-trans-prostenoic acid
336	111	206	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-2-ethyl-20-cyclopentyl-13-trans-prostenoic acid
337	111	148	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-2-ethyl-13-trans,17-cis-prostadienoic acid
338	113	128	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3,3-dimeth-yl-13-trans-prostenoic acid
339	113	144	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3,3-dimeth-yl-16-ethyl-13-trans-prostenoic acid
340	113	213	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3,3-dimeth-yl-17,20-(1,3-propano)-13-trans-prostenoic acid
341	115	128	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-13-trans-prostenoic acid
342	115	152	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-16,-16-dimethyl-13-trans-prostenoic acid
343	115	219	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-16,-19-trans-ethano-13-trans-prostenoic acid
344	115	148A	9-oxo-11α -(2-hydroxyethoxy)-15-methoxy-3-oxa-13-trans-prostenoic acid
345	115	148	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-13-trans,17-prostadienoic acid
346	115	172	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-16,-20-methano-13-trans,17-cis-prostadienoic acid
347	117	152	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-2-fluoro-16,16-dimethyl-13-trans-prostenoic acid
348	117	128	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-2-fluoro-13-trans-prostenoic acid
349	117	214	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-2-fluoro-17,20(1,4-butano)-13-trans-prostenoic acid
350	118	139	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7,20-bis-nor-13-trans-prostenoic acid
351	118	145	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7,20-bis-nor- 16-methyl-13-trans-prostenoic acid
352	119	142	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a-homo-20-methyl-13-trans-prostenoic acid
353	119	152	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a-homo-16,16-dimethyl-13-trans-prostenoic acid
354	119	174	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a-homo-16,17,18,19,20-pentanor-15-(2-adamantyl)-13-trans-prostenoic acid
355	120	128	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-2-phenyl-13-trans-prostenoic acid
356	124	128	9-oxo-11α-(2-hydroxypropyl)-15-hydroxy-13-trans-prostenoic acid
357	124	152	9-oxo-11α-(2-hydroxypropoxy)15-hydroxy-16,16-di-methyl-13-trans-prostenoic acid
358	124	207	9-oxo-11α-(2-hydroxypropoxy)-15-hydroxy-16-meth-yl-18,20-ethano-13-trans-prostenoic acid
359	124	148	9-oxo-11α-(2-hydroxypropoxy)-15-hydroxy-13-trans,-17-cis-prostadienoic acid
360	126	128	9-oxo-11α-(4-hydroxybutoxy)-15-hydroxy-13-trans-prostenoic acid
361	126	152	9-oxo-11α-(4-hydroxybutoxy)-15-hydroxy-16,16-di-methyl-13-trans-prostenoic acid
362	103	152	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,-16-dimethyl-13-trans-prostenoate
363	103	147	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-17-methyl-20-(2-propenyl)-13-trans-prostenoate
364	103	217	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-19,-20-dinor-16,17-(1,3-propano)-13-trans-prostenoate

TABLE 12—Continued

Example	Starting 4-oxycyclopent--2-en-1-one of Example	Starting 1-iodo-1--trans alkene of Example	Product 9-oxo-11-oxy-15-hydroxy(methoxy)-13-trans--prostenoic acid
365	103	212	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-19,-20-(1,4-butano)-13-trans-prostenoate
366	104	139	methyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-20-nor-13-trans-prostenoate
367	104	148A	methyl 9-oxo-11α-(2-hydroxyethoxy)-15-methoxy-13-trans-prostenoate
368	105	202	ethyl 9-oxo-11α-(3-hydroxypropoxy)-15-hydroxy-6,7,20-trinor-17,19-methano-13-trans-prostenoate
369	106	208	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-5,6,7-trinor-16-ethyl-19,20-(1,3-propano)-13-trans-prostenoate
370	109	161	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,-7b-bishomo-17,18-cis-methano-13-trans-prostenoate
371	109	148	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a-7b-bishomo-13-trans,17-cis-prostadienoate
372	109	169	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,-7b-bishomo-17,20-ethano-13-trans,18-prostadienoate
373	112	148	ethyl 9-oxo-11α-(3-hydroxypropoxy)-15-hydroxy-2-ethyl-13-trans,17-cis-prostadienoate
374	112	203	ethyl 9-oxo-11α-(3-hydroxypropoxy)-15-hydroxy-2-ethyl-18,20-ethano-13-trans-prostenoate
375	114	156	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3,3,17,17-tetramethyl-13-trans-prostenoate
376	114	215	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3,3,20-trimethyl-17,20-ethano-13-trans-prostenoate
377	116	152	ethyl 9-oxo-11α-(3-hydroxypropoxy)-15-hydroxy-3-oxa-16,16-dimethyl-13-trans-prostenoate
378	116	218	ethyl 9-oxo-11α-(3-hydroxypropoxy)-15-hydroxy-3-oxa-16,20-methano-13-trans-prostenoate
379	121	128	butyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-13-trans-prostenoate
380	121	152	butyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,-16-dimethyl-13-trans-prostenoate
381	121	161	butyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-17,-18-cis-methano-13-trans-prostenoate
382	121	216	butyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-17,-19-(1,3-propanol)-13-trans-prostenoate
383	121	173	butyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,-20-methano-13-trans,18-prostadienoate
384	121	148	butyl 9-oxo-11α-92-hydroxyethoxy)-15-hydroxy-13-trans,17-cis-prostadienoate
385	122	148	isopropyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-13-trans,17-cis-prostadienoate
386	122	146	isopropyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-19-methyl-13-trans,18-prostadienoate
387	122	152	isopropyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-13-trans-prostenoate
388	122	175	isopropyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-17,18,19,20-tetranor-16-(1-adamantyl)-13-trans-prostenoate
389	123	128	decyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-13-trans-prostenoate
390	123	152	decyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,-16-dimethyl-13-trans-prostenoate
391	123	148A	decyl 9-oxo-11α-(2-hydroxyethoxy)-15-methoxy-13-trans-prostenoate
392	123	209	decyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-20-nor-17,18-trans-)1,3-propano)-13-trans-prostenoate
393	123	148	decyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-13-trans,17-cis-prostadienoate

EXAMPLE 394

Preparation of 9α,15-dihydroxy-11α-methoxy-13-trans-prostenoic acid

To a solution of 433 mg. of 9-oxo-11α-methoxy-15-hydroxy-13-trans-prostenoic acid (Example 227) in 4.5 ml. of tetrahydrofuran, stirred in an ice bath under nitrogen atmosphere, is added dropwise 3.7 ml. of 0.76M lithium perhydro-9b-boraphenyalyl hydride. After 40 minutes at 0°C. there is added 1.62 ml. of 3N sodium hydroxide followed by 1.62 ml. of 30% hydrogen peroxide. Ether is added and the resulting solution is acidified with 2N hydrochloric acid. The ether layer is

washed several times with saturated sodium chloride solution, dried with anhydrous magnesium sulfate and taken to dryness to give the subject product as an oil.

EXAMPLES 395–560

Treatment of the 9-oxo derivatives listed in Table 13 below with lithium perhydro-9b-boraphenalyl hydride by the procedure described above in Example 394 furnishes the product 9α-hydroxy-11-oxy-15-hydroxy(or methoxy)-13-trans-prostenoic acids of the table.

Table 13

Example	Starting 9-oxo-derivative of Example	Product 9α-hydroxy--11-oxy-15--hydroxy(methoxy)-13--trans-prostenoic acid
395	228	9α-hydroxy-11α-methoxy--15-hydroxy-20-ethyl-13--trans-prostenoic acid
396	229	9α-hydroxy-11α-methoxy--15-hydroxy-16-ethyl--13-trans-prostenoic acid
397	230	9α-hydroxy-11α-methoxy--15-methoxy-13-trans--prostenoic acid
398	231	9α-hydroxy-11α-methoxy--15-hydroxy-13-trans,--17-cis-prostadienoic acid
399	232	9α-hydroxy-11α-methoxy--15-hydroxy-16,16--dimethyl-13-trans--prostenoic acid
400	233	9α-hydroxy-11α-methoxy--15-hydroxy-17,17-dimethyl-13-trans-prostenoic acid
401	234	9α-hydroxy-11α-methoxy--15-hydroxy-17,18-cis--methano-13-trans--prostenoic acid
402	235	9α-hydroxy-11α-methoxy--15-hydroxy-16,17,18,19,20-pentanor-15-(1--adamantyl)-13-trans-prostenoic acid
403	236	9α-hydroxy-11α-methoxy--15-hydroxy-16,20-methano-13-trans,17-prostadienoic acid
404	237	9α,15-dihydroxy-11α--methoxy-16,20-ethano--13-trans-prostenoic acid
405	238	9α-hydroxy-11α-methoxy-15-hydroxy-16,19-trans-ethano-13-trans-prostenoic acid
406	239	9α-hydroxy-11α-methoxy--15-hydroxy-6,7,19,20--tetranor-13-trans--prostenoic acid
407	240	9α-hydroxy-11α-methoxy--15-hydroxy-6,7-dinor--17,20-ethano-13-trans--prostenoic acid
408	241	9α-hydroxy-11α-ethoxy--15-hydroxy-5,6,7,20--tetranor-17,19-methano-13-trans-prostenoic acid
409	242	9α-hydroxy-11α-ethoxy--15-hydroxy-5,6,7,18,--19,20-hexanor-13--trans-prostenoic acid
410	243	9α-hydroxy-11α-methoxy--15-hydroxy-7a,7b-bis-homo-20-ethyl-13-trans--prostenoic acid
411	244	9α-hydroxy-11α-methoxy--15-hydroxy-7a,7b-bis-homo-16,16-dimethyl-13--trans-prostenoic acid
412	245	9α-hydroxy-11α-methoxy--15-hydroxy-7a,7b-bis-homo-16,20(1,3-propano)--13-trans-prostenoic acid
413	246	9α-hydroxy-11α-methoxy--15-hydroxy-2-ethyl-20--nor-13-trans-prostenoic acid
414	247	9α-hydroxy-11α-methoxy--15-hydroxy-2-ethyl--16,20-methano-13-trans,--18-prostadienoic acid
415	248	9α-hydroxy-11α-methoxy--3,3-dimethyl-16-(1--adamantyl)-17,18,19,--20-tetranor-13-trans--prostenoic acid
416	249	9α-hydroxy-11α-methoxy--15-hydroxy-3,3,20--trimethyl-13-trans-prostenoic acid
417	250	9α-hydroxy-11α-methoxy--15-hydroxy-3-oxa-13--trans-prostenoic acid
418	251	9α-hydroxy-11α,15--dimethoxy-3-oxa-13--trans-prostenoic acid
419	252	9α-hydroxy-11α-methoxy--15-hydroxy-3-oxa-16,--16-dimethyl-13-trans--prostenoic acid
420	253	9α-hydroxy-11α-methoxy--15-hydroxy-3-oxa-17,--20-ethano-13-trans--18-prostadienoic acid
421	254	9α-hydroxy-11α-methoxy--15-hydroxy-3-oxa-16,--20-methano-13-trans--prostenoic acid
422	255	9α-hydroxy-11α-methoxy--15-hydroxy-2-fluoro--18,20-ethano-13-trans--prostenoic acid
423	256	9α-hydroxy-11α-methoxy--15-hydroxy-2-fluoro--16-methyl-20-nor-13--trans-prostenoic acid
424	257	9α-hydroxy-11α-methoxy-15-hydroxy-7,20-dinor--13-trans-prostenoic acid
425	258	9α-hydroxy-11α-methoxy--15-hydroxy-7-nor-17,20-(1,4-butano)--13-trans-prostenoic acid
426	259	9α-hydroxy-11α-methoxy--15-hydroxy-7a-homo--20-methyl-13-trans--prostenoic acid
427	260	9α-hydroxy-11α-methoxy--15-hydroxy-7a-homo--17,18-cis-methano-13--trans-prostenoic acid
428	261	9α-hydroxy-11α-methoxy--15-hydroxy-7a-homo--20-cyclopentyl-13--trans-prostenoic acid
429	262	9α-hydroxy-11α-methoxy--15-hydroxy-2-phenyl--17,17-dimethyl-13--trans-prostenoic acid
430	263	9α-hydroxy-11α-methoxy--15-hydroxy-2-phenyl--18,20-(1,3-propano)--13-trans-prostenoic acid
431	264	9α-hydroxy-11α-ethoxy--15-hydroxy-16,16--dimethyl-13-trans-

Table 13-Continued

Example	Starting 9-oxo-derivative of Example	Product 9α-hydroxy--11-oxy-15--hydroxy(methoxy)-13--trans-prostenoic acid
		-prostenoic acid
432	265	9α-hydroxy-11α-ethoxy--15-hydroxy-16-methyl--18,20-ethano-13-trans--prostenoic acid
433	266	9α-hydroxy-11α-ethoxy--15-hydroxy-19-methyl--13-trans,18-prosta-dienoic acid
434	267	9α-hydroxy-11α-ethoxy--15-hydroxy-13-trans--17-prostadienoic acid
435	268	9α-hydroxy-11α-propoxy--16,16-dimethyl-13--trans-prostenoic acid
436	269	9α-hydroxy-11α-propoxy--15-hydroxy-20-nor--13-trans-prostenoic acid
437	270	9α-hydroxy-11α-propoxy--15-hydroxy-13-trans--prostenoic acid
438	271	9α-hydroxy-11α-propoxy--16,17,18,19,20-pentanor-15-(2-adamantyl)--13-trans-prostenoic acid
439	272	9α-hydroxy-11α-propoxy--15-hydroxy-17,20--ethano-13-trans,19--prostadienoic acid
440	273	9α-hydroxy-11α-iso--propoxy-15-hydroxy--13-trans,17-prosta--dienoic acid
441	274	9α-hydroxy-11α-iso--propoxy-15-methoxy--13-trans-prostenoic acid
442	275	9α-hydroxy-11α-iso--propoxy-15-hydroxy--16,16-dimethyl-13--trans-prostenoic acid
443	276	9α-hydroxy-11α-iso--propoxy-15-hydroxy--17,20-methano--13-trans-prostenoic acid
444	277	9α-hydroxy-11α-iso--propoxy-15-hydroxy--13-trans-prostenoic acid
445	278	9α-hydroxy-4-n-butoxy--15-hydroxy-16,16--dimethyl-13-trans--prostenoic acid
446	279	9α-hydroxy-4-n-butoxy--15-hydroxy-13-trans--prostenoic acid
447	280	9α-hydroxy-4-n-butoxy--16-methyl-20-nor-13--trans-prostenoic acid
448	281	9α-hydroxy-4-n-butoxy--16-ethyl-19,20-(1,3--propano)-13-trans--prostenoic acid
449	282	9α-hydroxy-4-n-butoxy--15-hydroxy-16,20--ethano-13-trans--prostenoic acid
450	283	9α-hydroxy-11α-methoxy--15-hydroxy-2,17-di-methyl-20-nor-16,19--trans-methano-13-trans--prostenoic acid
451	284	9α-hydroxy-11α-methoxy--15-hydroxy-2,16,16--trimethyl-13-trans--prostenoic acid
452	285	9α-hydroxy-11α-methoxy--15-hydroxy-2-methyl--13-trans-prostenoic acid
453	286	ethyl 9α-hydroxy-11α--ethoxy-15-hydroxy-13--trans-prostenoate
454	287	ethyl 9α-hydroxy-11α-

Table 13-Continued

Example	Starting 9-oxo-derivative of Example	Product 9α-hydroxy--11-oxy-15--hydroxy(methoxy)-13--trans-prostenoic acid
		-ethoxy-15-hydroxy--20-methyl-17,20-ethano--13-trans-prostenoate
455	288	methyl 9α-hydroxy-11α--methoxy-15-hydroxy--16,16-dimethyl-13--trans-prostenoate
456	289	methyl 9α-hydroxy-11α--methoxy-15-hydroxy-16,-17,18,19,20-pentanor--15-(2-adamantyl)-13--trans-prostenoate
457	290	ethyl 9α-hydroxy-11α--propoxy-15-hydroxy-6,7--dinor-13-trans-pros-tenoate
458	291	ethyl 9α-hydroxy-11α--isopropoxy-15-hydroxy--5,6,7-trinor-13-trans--prostenoate
459	292	ethyl 9α-hydroxy-11α--isopropoxy-15-hydroxy--7a,7b-bishomo-17--methyl-20-(2-propenyl)--13-trans-prostenoate
460	293	ethyl 9α-hydroxy-11α--isopropoxy-15-hydroxy--7a,7b-bishomo-13--trans,17-prostadienoate
461	294	ethyl 9α-hydroxy-11α--butoxy-15-methoxy-2--ethyl-13-trans-pros-tenoate
462	295	ethyl 9α-hydroxy-11α--butoxy-15-hydroxy-2--ethyl-16,16-dimethyl--13-trans-prostenoate
463	296	ethyl 9α-hydroxy-11α--methoxy-15-hydroxy--3,3-dimethyl-13--trans-prostenoate
464	297	ethyl 9α-hydroxy-11α--methoxy-15-hydroxy--3,3,16,16-tetramethyl--13-trans-prostenoate
465	298	ethyl 9α-hydroxy-11α--ethoxy-15-hydroxy-3--oxa-20-ethyl-13--trans-prostenoate
466	299	ethyl 9α-hydroxy-11α--ethoxy-15-hydroxy--3-oxa-19,20-(1,3-pro-pano)-13-trans-pros-tenoate
467	300	ethyl 9α-hydroxy-11α--sec-butoxy-15-hydroxy--7-nor-20-methyl-13--trans-prostenoate
468	301	ethyl 9α-hydroxy-11α-sec-butoxy-15-hydroxy--7-nor-19,20-(1,4-bu-tano)-13-trans-pros-tenoate
469	302	ethyl 9α-hydroxy-11α--methoxy-15-hydroxy--7a-homo-17,20-(1,3--propano)-13-trans--prostenoate
470	303	ethyl 9α-hydroxy-11α--methoxy-15-hydroxy--7α-homo-13-trans-17--prostadienoate
471	304	butyl 9α-hydroxy-11α-methoxy-15-hydroxy-20,--20-(1,4-butano)-13--trans-prostenoate
472	305	butyl 9α-hydroxy-11α--methoxy-15-hydroxy-16,--16-dimethyl-13-trans--prostenoate
473	306	butyl 9α-hydroxy-11α--methoxy-15-hydroxy--13-trans-prostenoate
474	307	isopropyl 9α-hydroxy--11α-methoxy-15-hydroxy-16,16-dimethyl-13--trans-prostenoate

Table 13-Continued

Example	Starting 9-oxo-derivative of Example	Product 9α-hydroxy--11-oxy-15--hydroxy(methoxy)-13--trans-prostenoic acid
475	308	isopropyl 9α-hydroxy--11α-methoxy-15-hydroxy--13-trans-prostenoate
476	309	isopropyl 9α-hydroxy--11α-methoxy-15-hydroxy-17,19-(1,3-propano)-13-trans-prostenoate
477	310	isopropyl 9α-hydroxy--11α-methoxy-15-hydroxy-17,18-cis-methano-13-trans-prostenoate
478	311	decyl 9α-hydroxy-11α--methoxy-15-hydroxy-13--trans-prostenoate
479	312	decyl 9α-hydroxy-11α--methoxy-15-hydroxy--16,16-dimethyl-13--trans-prostenoate
480	313	decyl 9α-hydroxy-11α--methoxy-15-hydroxy-20--ethyl-13-trans-prostenoate
481	314	decyl 9α-hydroxy-11α--methoxy-15-hydroxy--17,20-(1,3-propano)--13-trans-prostenoate
482	315	decyl 9α-hydroxy-11α--methoxy-15-hydroxy--17,20-methano--13-trans-prostenoate
483	316	ethyl 9α-hydroxy-11α-t--butoxy-15-hydroxy-13--trans-prostenoate
484	317	ethyl 9α-hydroxy-11α-t--butoxy-15-hydroxy--16,16-dimethyl-13--trans-prostenoate
485	318	ethyl 9α-hydroxy-11α-t--butoxy-20-nor--17,18-trans-1,3-propano-13-trans-prostenoate
486	319	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-13-trans-prostenoic acid
487	320	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy--16,16-dimethyl-13--trans-prostenoic acid
488	321	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy--17,18-cis-methano-13--trans-prostenoic acid
489	322	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16,17,18,19,20--pentanor-15-(1-adamantyl)-13-trans-prostenoic acid
490	323	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy--20-ethyl-13-trans--prostenoic acid
491	324	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16-ethyl-13-trans--prostenoic acid
492	325	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16,20-ethano-13--trans-prostenoic acid
493	326	9α-hydroxy-11α-(2-hydroxyethoxy)-15-methoxy-13-trans-prostenoic acid
494	327	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-13-trans,17-cis prostadienoic acid
495	328	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-6,7,19,20-tetranor-13-trans-prostenoic acid
496	329	9α-hydroxy-11α-(2-hydroxyethoxy)-6,7-dinor--17,20-ethano-13-trans--prostenoic acid
497	330	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-5,6,7,18,19,20--hexanor-13-trans--prostenoic acid
498	331	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-5,6,7-trinor--16,20-ethano-13-trans--prostenoic acid
499	332	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo-20--ethyl-13-trans-prostenoic acid
500	333	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo--16,16-dimethyl-13--trans-prostenoic acid
501	334	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo--13-trans-prostenoic acid
502	335	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo--16,20-(1,3-propano)--13-trans-prostenoic acid
503	336	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-2-ethyl-20-cyclopentyl-13-trans--prostenoic acid
504	337	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-2-ethyl-13-trans,-17-cis-prostadienoic acid
505	338	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3,3-dimethyl-13--trans-prostenoic acid
506	339	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3,3-dimethyl-16--ethyl-13-trans-prostenoic acid
507	340	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3,3-dimethyl-17,-20-(1,3-propano)-13--trans-prostenoic acid
508	341	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-13-trans--prostenoic acid
509	342	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-16,16-dimethyl-13-trans-prostenoic acid
510	343	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-16,19--trans-ethano-13-trans--prostenoic acid
511	344	9α-hydroxy-11α-(2-hydroxyethoxy)-15-methoxy-3-oxa-13-trans--prostenoic acid
512	345	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-13-trans,-17-cis-prostadienoic acid
513	346	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-16,20--methano-13-trans,17--prostadienoic acid

Table 13-Continued

Example	Starting 9-oxo-derivative of Example	Product 9α-hydroxy--11-oxy-15--hydroxy(methoxy)-13--trans-prostenoic acid
514	347	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-2-fluoro-16,16--dimethyl-13-trans--prostenoic acid
515	348	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-2-fluoro-13--trans-prostenoic acid
516	349	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy--2-fluoro-17,20-(1,4--butano-13-trans-prostenoic acid
517	350	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy--7,20-bisnor-13-trans--prostenoic acid
518	351	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy--7,20-bisnor-16-methyl--13-trans-prostenoic acid
519	352	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy--7a-homo-20-methyl-13--trans-prostenoic acid
520	353	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy--7a-homo-16,16-dimethyl-13-trans-prostenoic acid
521	354	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy--7a-homo-16,17,18,19,20-pentanor-15-(2-adamantyl)-13-trans-prostenoic acid
522	355	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy--2-phenyl-13-trans--prostenoic acid
523	356	9α-hydroxy-11α-(2--hydroxypropoxy)-15--hydroxy-13-trans--prostenoic acid
524	357	9α-hydroxy-11α-(2--hydroxypropoxy)-15--hydroxy-16,16-dimethyl-13-trans-prostenoic acid
525	358	9α-hydroxy-11α-(2--hydroxypropoxy)-15--hydroxy-16-methyl-18,20-ethano-13-trans--prostenoic acid
526	359	9α-hydroxy-11α-(2--hydroxypropoxy)-15--hydroxy-13-trans,17-cis--prostadienoic acid
527	360	9α-hydroxy-11α-(4--hydroxybutoxy)-15--hydroxy-13-trans--prostenoic acid
528	381	9α-hydroxy-11α-(4-hydroxybutoxy)-15-hydroxy--16,16-dimethyl-13--trans-prostenoic acid
529	362	ethyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-16,16-dimethyl-13-trans-prostenoate
530	363	ethyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15--hydroxy-17-methyl-20--(2-propenyl)-13-trans--prostenoate
531	364	ethyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-19,20-dinor--16,17-(1,3-propano)--13-trans-prostenoate
532	365	ethyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-19,20-(1,4--butano)-13-trans--prostenoate

Table 13-Continued

Example	Starting 9-oxo-derivative of Example	Product 9α-hydroxy--11-oxy-15--hydroxy(methoxy)-13--trans-prostenoic acid
533	366	methyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-20-nor-13--trans-prostenoate
534	367	methyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--methoxy-13-trans--prostenoate
535	368	ethyl 9α-hydroxy-11α--(3-hydroxypropoxy)--15-hydroxy-6,7,20--trinor-17,19-methano--13-trans-prostenoate
536	369	ethyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-5,6,7-trinor--16-ethyl-19,20-(1,3--propano-13-trans--prostenoate
537	370	ethyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-7a,7b-bishomo--17,18-cis-methano-13--trans-prostenoate
538	371	ethyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-7a,7b-bishomo--13-trans,17-cis--prostadienoate
539	372	ethyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-7a,7b-bishomo--17,20-ethano-13-trans--18-prostadienoate
540	373	ethyl 9α-hydroxy-11α--(3-hydroxypropoxy)--15-hydroxy-2-ethyl--13-trans,17-cis--prostadienoate
541	374	ethyl 9α-hydroxy-11α--(3-hydroxypropoxy-15--hydroxy-2-ethyl-18,20--ethano-13-trans-prostenoate
542	375	ethyl 9α-hydroxy-11α--(3-hydroxyethoxy)-3,3,17,17-tetramethyl-13--trans-prostenoate
543	376	ethyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-3,3,20-trimethyl-17,20-ethano--13-trans-prostenoate
544	377	ethyl 9α-hydroxy-11α--(3-hydroxypropoxy)--15-hydroxy-3-oxa-16,--16-dimethyl-13-trans--prostenoate
545	378	ethyl 9α-hydroxy-11α--(3-hydroxypropoxy)-15--hydroxy-3-oxa-16,20--methano-13-trans--prostenoate
546	379	butyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-13-trans--prostenoate
547	380	butyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-16,16-dimethyl-13-trans-prostenoate
548	381	butyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-17,18-cis--methano-13-trans-prostenoate
549	382	butyl 9α-hydroxy-11α--(2-hydroxyethoxy-15--hydroxy-17,19-(1,3--propano-13-trans-prostenoate
550	383	butyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-16,20-methano--13-trans,18-prostadienoate
551	384	butyl 9α-hydroxy-11α-

Table 13-Continued

Example	Starting 9-oxo-derivative of Example	Product 9α-hydroxy--11-oxy-15--hydroxy(methoxy)-13--trans-prostenoic acid
		-(2-hydroxyethoxy)-15--hydroxy-13-trans,17--cis-prostenoate
552	385	isopropyl 9α-hydroxy--11α-(2-hydroxyethoxy)--15-hydroxy-13-trans,-17-cis-prostadienoate
553	386	isopropyl-9α-hydroxy--11α-(2-hydroxyethoxy)--15-hydroxy-19-methyl--13-trans,18-prostadienoate
554	387	isopropyl 9α-hydroxy--11α-(2-hydroxyethoxy)--15-hydroxy-16,16-dimethyl-13-trans-prostenoate
555	388	isopropyl 9α-hydroxy--11α-(2-hydroxyethoxy)--15-hydroxy-17,18,19,-20-tetranor-16-(1-adamantyl)-13-trans-prostenoate
556	389	decyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-13-trans-prostenoate
557	390	decyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-16,16-dimethyl-13-trans-prostenoate
558	391	decyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--methoxy-13-trans--prostenoate
559	392	decyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-20-nor-17,18--trans(1,3-propano)-13--trans-prostenoate
560	393	decyl 9α-hydroxy-11α--(2-hydroxyethoxy)-15--hydroxy-13-trans,17--cis-prostadienoate

EXAMPLE 561

A solution of 9-oxo-11α-methoxy-15-hydroxy-13-trans-prostenoic acid (Example 227) in tetrahydrofuran is added to 2.2 equivalents of lithium perhydro-9b-boraphenyalyl hydride in tetrahydrofuran at −78°C. After 30 minutes the solution is diluted with water and extracted with ether. The aqueous phase is acidified, saturated with sodium chloride and extracted with ether. The combined ether extracts are dried (magnesium sulfate) and concentrated in vacuo to give 9α,15-α-dihydroxy-11α-methoxy-13-trans-prostenoic acid, contaminated with 9β,15α-dihydroxy-11α-methoxy-13-trans-prostenoic acid. The crude mixture is dissolved in methylene chloride and added to a refluxing solution of 1.2 equivalents of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in methylene chloride. After 5 hours, the solution is cooled and filtered. The filtrate is concentrated in vacuo and the residue is purified by column chromatography to give 9α-hydroxy-11α-methoxy-15-oxo-13-trans-prostenoic acid. This material is dissolved in benzene and 2.2 equivalents each of trimethylsilyl chloride and triethylamine; triethylamine hydrochloride is removed by filtration and the solution is concentrated in vacuo to give trimethylsilyl 9α-trimethylsiloxy-11α-methoxy-15-oxo-13-trans-prostenoate.

The siloxy derivative is dissolved in ether at 0°C. and 1.05 equivalents of methyl magnesium bromide in ether is added. After the reaction is complete, the solution is poured into saturated aqueous ammonium chloride and extracted with ether. The ether is dried and concentrated in vacuo to give an oil. The oil is dissolved in methanol:water:acetic acid (approximately 10:1:1). After three hours at ambient temperatures, the solution is dilated with water, saturated with sodium chloride and extracted with ether. The ether extracts are dried and concentrated in vacuo to give 9α,15α-dihydroxy-15β-methyl-11α-methoxy-13-trans-prostenoic acid and 9α,15β-dihydroxy-15α-methyl-11α-methoxy-13-trans-prostenoic acid, which are separated by dry column chromatography.

Treatment of a solution of 9α-15α-dihydroxy-15β-methyl-11α-methoxy-13-trans-prostenoic acid with chromic acid-pyridine in methylene chloride (Collins Reagent) followed by addition of dilute acid and extraction with ether gives 9-oxo-11α-methoxy-15α-hydroxy-15β-methyl-13-trans-prostenoic acid.

Similar treatment of the corresponding 15β-hydroxy acid gives 9-oxo-11α-methoxy-15β-hydroxy-15α-methyl-prostenoic acid.

EXAMPLES 562–605

Treatment of the 9-oxo-15-hydroxy prostenoic acids of Table 14 below by the sequence of reactions described in Example 561 is productive of the 9-oxo-15-hydroxy-15-methyl products of the table. Also prepared in the course of these reaction sequences are the 9α-hydroxy derivative corresponding to the products of the table and the 15-keto derivatives of the 9α- and 9β-hydroxy compounds corresponding to the 9-oxo starting compounds, and the 9α- or 9β-trimethylsilyloxy trimethylsilyl esters of the 15-keto and 15-hydroxy-15-methyl compounds. In the instances of the 11α-(ω-hydroxyalkoxy)-derivatives silylation is carried out with 3.3 equivalents each of trimethylsilyl chloride and triethylamine in order to provide silylation of the ω-hydroxy group. In all cases both the 15α-hydroxy-15β-methyl and the 15β-hydroxy-15α-methyl products and intermediates are obtained. The epimers are separable by chromatographic procedures.

TABLE 14

Example	Starting 9-oxo--11-oxy-15-hydroxy prostenoic acid of Example	Product 9-oxo-11-oxy--15-hydroxy-15-methyl--13-trans-prostenoic acid
562	228	9-oxo-11α-methoxy-15--hydroxy-15-methyl-20--ethyl-13-trans-prostenoic acid
563	231	9-oxo-11α-methoxy-15--hydroxy-15-methyl-13--trans,17-cis-prostadienoic acid
564	239	9-oxo-11α-methoxy-15--hydroxy-15-methyl-6,-7,19,20-tetranor-13--trans-prostenoic acid
565	242	9-oxo-11α-ethoxy-15--hydroxy-15-methyl-5,-6,7,18,19,20-hexanor--13-trans-prostenoic acid
566	243	9-oxo-11α-methoxy-15--hydroxy-15-methyl--7a,7b-bishomo-20--ethyl-13-trans-prostenoic acid
567	246	9-oxo-11α-methoxy-15--hydroxy-15-methyl-2--ethyl-20-nor-13-trans-prostenoic acid

TABLE 14-Continued

Example	Starting 9-oxo--11-oxy-15-hydroxy prostenoic acid of Example	Product 9-oxo-11-oxy--15-hydroxy-15-methyl--13-trans-prostenoic acid
568	249	9-oxo-11α-methoxy-15--hydroxy-15-methyl--3,3,20-trimethyl-13--trans-prostenoic acid
569	250	9-oxo-11α-methoxy-15--hydroxy-15-methyl-3--oxa-13-trans-prostenoic acid
570	253	9-oxo-11α-methoxy-15--hydroxy-15-methyl-3--oxa-17,20-ethano-13--trans,18-prostadienoic acid
571	255	9-oxo-11α-methoxy-15--hydroxy-15-methyl-2--fluoro-18,20-ethano--13-trans-prostenoic acid
572	257	9-oxo-11α-methoxy-15--hydroxy-15-methyl--7,20-dinor-13-trans--prostenoic acid
573	258	9-oxo-11α-methoxy-15--hydroxy-15-methyl-7--nor-17,20-(1,4-butano)--13-trans-prostenoic acid
574	259	9-oxo-11α-methoxy-15--hydroxy-15-methyl-7a--homo-20-methyl-13--trans-prostenoic acid
575	260	9-oxo-11α-methoxy-15--hydroxy-15-methyl-7a--homo-17,18-cis-methano--13-trans-prostenoic acid
576	261	9-oxo-11α-methoxy-15--hydroxy-15-methyl-20--cyclopentyl-7a-homo-13--trans-prostenoic acid
577	263	9-oxo-11α-methoxy-15--hydroxy-15-methyl-2--phenyl-18,20-(1,3-propano)-13-trans-prostenoic acid
578	266	9-oxo-11α-ethoxy-15--hydroxy-15-methyl-19--methyl-13-trans,18--prostadienoic acid
579	267	9-oxo-11α-ethoxy-15--hydroxy-15-methyl-13--trans,17-cis-prostadienoic acid
580	269	9-oxo-11α-propoxy-15--hydroxy-15-methyl-20--nor-13-trans-prostenoic acid
581	270	9-oxo-11α-propoxy-15--hydroxy-15-methyl-13--trans-prostenoic acid
582	273	9-oxo-11α-isopropoxy--15-hydroxy-15-methyl--13-trans,17-cis-prostadienoic acid
583	277	9-oxo-11α-isopropoxy-15--hydroxy-15-methyl-13--trans-prostenoic acid
584	279	9-oxo-4-n-butoxy-15--hydroxy-15-methyl-13--trans-prostenoic acid
585	285	9-oxo-11α-methoxy-15--hydroxy-15-methyl-2--methyl-13-trans-prostenoic acid
586	319	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-13-trans-prostenoic acid
587	321	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-17,18-cis--methano-13-trans-prostenoic acid
588	323	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-20-ethyl-13--trans-prostenoic acid

TABLE 14-Continued

Example	Starting 9-oxo--11-oxy-15-hydroxy prostenoic acid of Example	Product 9-oxo-11-oxy--15-hydroxy-15-methyl--13-trans-prostenoic acid
589	327	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-13-trans,17-cis--prostadienoic acid
590	328	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-6,7,19,20-tetranor-13-trans-prostenoic acid
591	330	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-5,6,7,18,19,20--hexanor-13-trans-prostenoic acid
592	332	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-7a,7b-bishomo--20-ethyl-13-trans-prostenoic acid
593	334	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-7a,7b-bishomo--13-trans-prostenoic -acid
594	336	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-2-ethyl-20--cyclopentyl-13-trans--prostenoic acid
595	337	9-oxo-11α-(2-hydroxyethoxy(-15-hydroxy-15--methyl-2-ethyl-13--trans,17-cis-prostadienoic acid
596	338	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-3,3-dimethyl--13-trans-prostenoic acid
597	341	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-3-oxa-13-trans--prostenoic acid
598	345	9-oxo-11α-(2-hydroxy--ethoxy)-15-hydroxy-15--methyl-3-oxa-13-trans,-17-cis-prostadienoic acid
599	348	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-2-fluoro-13--trans-prostenoic acid
600	350	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-7,20-bisnor-13--trans-prostenoic acid
601	352	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-7α-homo-20--methyl-13-trans-prostenoic acid
602	355	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15--methyl-2-phenyl-13--trans-prostenoic acid
603	356	9-oxo-11α-(2-hydroxypropoxy)-15-hydroxy-15--methyl-13-trans--prostenoic acid
604	359	9-oxo-11α-(2-hydroxypropoxy)-15-hydroxy-15--methyl-13-trans,17-cis--prostadienoic acid
605	360	9-oxo-11α-(4-hydroxybutoxy)-15-hydroxy-15--methyl-13-trans-prostenoic acid

EXAMPLE 606

Preparation of 9-oxo-11α-methoxy-15-hydroxy-prostanoic acid

A 2 g. sample of 9-oxo-11α-methoxy-15-hydroxy-13-

trans-prostenoic acid (Example 227) is hydrogenated using 700 mg. of 10% palladium on carbon in 50 ml. of absolute alcohol The catalyst is removed by filtration and the mother liquor is taken to dryness to give 2 g. of subject compound as an oil.

EXAMPLE 607

Not included: 608 follows directly after 606.

EXAMPLE 608–835

Catalytic hydrogenation of the 13-trans-prostenoic acids and esters listed in Table 15 below by the procedure described in Example 606 furnishes the product prostanoic acids and esters of the table.

TABLE 15

Example	Starting 13--trans-prostenoic acid or ester of Example	Product 11-oxy-15-oxy-prostanoic acid or ester
608	228	9-oxo-11α-methoxy-15--hydroxy-20-ethyl-prostanoic acid
609	229	9-oxo-11α-methoxy-15--hydroxy-16-ethyl-prostanoic acid
610	230	9-oxo-11α-methoxy-15--methoxy-prostanoic acid
611	232	9-oxo-11α-methoxy-15--hydroxy-16,16-dimethyl-prostanoic acid
612	233	9-oxo-11α-methoxy-15--hydroxy-17,17-dimethyl-prostanoic acid
613	234	9-oxo-11α-methoxy-15--hydroxy-17,18-cis--methano-prostanoic acid
614	235	9-oxo-11α-methoxy-15--hydroxy-16,17,18,19,20--pentano)-15-(1-adamantyl)-prostanoic acid
615	237	9-oxo-11α-methoxy-15--hydroxy-16,20-ethano--prostanoic acid
616	238	9-oxo-11α-methoxy-15--hydroxy-16,19-trans--ethano-prostanoic acid
617	239	9-oxo-11α-methoxy-15--hydroxy-6,7,19,20-tetranor-prostanoic acid
618	242	9-oxo-11α-methoxy-15--hydroxy-5,6,7,18,19,20--hexanor-prostanoic acid
619	243	9-oxo-11α-methoxy-15--hydroxy-7a,7b-bishomo--20-ethyl-prostanoic acid
620	244	9-oxo-11α-methoxy-15--hydroxy-7a,7b-bishomo--16,16-dimethyl-prostanoic acid
621	245	9-oxo-11α-methoxy-15--hydroxy-7a,7b-bishomo--16,20-(1,3-propano)--prostanoic acid
622	246	9-oxo-11α-methoxy-15--hydroxy-2-ethyl-20-nor--prostanoic acid
623	248	9-oxo-11α-methoxy-15--hydroxy-3,3-dimethyl--16(1-adamantyl-17,18,-19,20-tetranor-prostanoic acid
624	250	9-oxo-11α-methoxy-15--hydroxy-3-oxa-prostanoic acid
625	251	9-oxo-11α,15-dimethoxy--3-oxa-prostanoic acid
626	252	9-oxo-11α-methoxy-15--hydroxy-3-oxa-16,16--dimethyl-prostanoic acid
627	254	9-oxo-11α-methoxy-15--hydroxy-17,20-ethano--prostanoic acid
628	255	9-oxo-11α-methoxy-15--hydroxy-2-fluoro-18,20--ethano-prostanoic acid
629	257	9-oxo-11α-methoxy-15--hydroxy-7,20-dinor--prostanoic acid
630	259	9-oxo-11α-methoxy-15--hydroxy-7a-homo-20--methyl-prostanoic acid
631	260	9-oxo-11α-methoxy-15--hydroxy-7a-homo-17,18--cis-methano-prostanoic acid
632	262	9-oxo-11α-methoxy-15--hydroxy-2-phenyl-17,17--dimethyl-prostanoic acid
633	264	9-oxo-11α-ethoxy-15-hydroxy-16,16-dimethyl--prostanoic acid
634	268	9-oxo-11α-propoxy-15-hydroxy-16,16-dimethyl--prostanoic acid
635	270	9-oxo-11α-propoxy-15-hydroxy-prostanoic acid
636	271	9-oxo-11α-propoxy-15-hydroxy-16,17,18,19,20--pentanor-15-(2-adamantyl)-prostanoic acid
637	274	9-oxo-11α-isopropoxy--15-methoxy-prostanoic acid
638	275	9-oxo-11α-isopropoxy--15-hydroxy-16,16-dimethyl-prostanoic acid
639	277	9-oxo-11α-isopropoxy--prostanoic acid
640	278	9-oxo-4-n-butoxy-15-hydroxy-16,16-dimethyl--prostanoic acid
641	279	9-oxo-4-n-butoxy-15-hydroxy-prostanoic acid
642	282	9-oxo-4-n-butoxy-15-hydroxy-16,20-ethano-prostanoic acid
643	284	9-oxo-11α-methoxy-15-hydroxy-2,16,16-trimethyl-prostanoic acid
644	285	9-oxo-11α-methoxy-15-hydroxy-2-methyl-prostanoic acid
645	286	ethyl 9-oxo-11α-ethoxy--15-hydroxy-prostanoate
646	288	methyl 9-oxo-11α-methoxy-15-hydroxy-16,16--dimethyl-prostanoate
647	295	ethyl 9-oxo-11α-butoxy--15-hydroxy-2-ethyl--16,16-dimethyl-prostanoate
648	296	ethyl 9-oxo-11α-methoxy-15-hydroxy-3,3-dimethyl-prostanoate
649	297	ethyl 9-oxo-11α-methoxy-15-hydroxy-3,3,16,-16-tetramethyl-prostanoate
650	298	ethyl 9-oxo-11α-ethoxy--15-hydroxy-3-oxa-20--ethyl-prostanoate
651	300	ethyl 9-oxo-11α-sec--butoxy-15-hydroxy-7--nor-20-methyl-prostanoate
652	302	ethyl 9-oxo-11α-methoxy--15-hydroxy-7a-homo-17,-20-(1,3-propano)prostanoate
653	304	butyl 9-oxo-11α-methoxy-15-hydroxy-20,20--(1,4-butano)-prostanoate
654	305	butyl 9-oxo-11α-methoxy-15-hydroxy-16,16-dimethyl-prostanoate
655	306	butyl 9-oxo-11α-methoxy-15-hydroxy-prostanoate

TABLE 15-Continued

Example	Starting 13-trans-prostenoic acid or ester of Example	Product 11-oxy-15-oxy-prostanoic acid or ester
656	307	isopropyl 9-oxo-11α-methoxy-15-hydroxy-16,16-dimethyl-prostanoate
657	308	isopropyl 9-oxo-11α-methoxy-15-hydroxy-prostanoate
658	310	isopropyl 9-oxo-11α-methoxy-15-hydroxy-17,18-cis-methano-prostanoate
659	311	decyl 9-oxo-11α-methoxy-15-hydroxy-prostanoate
660	312	decyl 9-oxo-11α-methoxy-15-hydroxy-16,16-dimethyl-prostanoate
661	314	decyl 9-oxo-11α-methoxy-15-hydroxy-17,20-(1,3-propano)-prostanoate
662	316	ethyl 9-oxo-11α-t-butoxy-15-hydroxy-prostanoate
663	317	ethyl 9-oxo-11α-t-butoxy-15-hydroxy-16,16-dimethyl-prostanoate
664	319	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-prostanoic acid
665	320	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-prostanoic acid
666	321	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-17,18-cis-methano-prostanoic acid
667	322	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,17,18,19,20-pentanor-15-(1-adamantyl)-prostanoic acid
668	323	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-20-ethyl-prostanoic acid
669	325	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,20-ethano-prostanoic acid
670	326	9-oxo-11α-(2-hydroxyethoxy)-15-methoxy-prostanoic acid
671	328	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-6,7,19,20-tetranor-prostanoic acid
672	330	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-5,6,7,18,19,20-hexanor-prostanoic acid
673	332	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo-20-ethyl-prostanoic acid
674	333	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo-16,16-dimethyl-prostanoic acid
675	334	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo-prostanoic acid
676	335	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo-16,20-(1,3-propano)-prostanoic acid
677	336	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-2-ethyl-20-cyclopentyl-prostanoic acid
678	338	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3,3,-dimethyl-prostanoic acid
679	341	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-prostanoic acid
680	342	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-16,16-dimethyl-prostanoic acid
681	343	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-16,19-trans-ethano-prostanoic acid
682	344	9-oxo-11α-(2-hydroxyethoxy)-15-methoxy-3-oxa-prostanoic acid
683	347	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-2-fluoro-16,16-dimethyl-prostanoic acid
684	350	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7,20-bisnor-prostanoic acid
685	352	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a-homo-20-methyl-prostanoic acid
686	353	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a-homo-16,16-dimethyl-prostanoic acid
687	355	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-2-phenyl-prostanoic acid
688	356	9-oxo-11α-(2-hydroxypropoxy)-15-hydroxy-prostanoic acid
689	357	9-oxo-11α-(2-hydroxypropoxy)-15-hydroxy-16,16-dimethyl-prostanoic acid
690	360	9-oxo-11α-(4-hydroxybutoxy)-15-hydroxy-prostanoic acid
691	361	9-oxo-11α-(4-hydroxybutoxy)-15-hydroxy-16,16-dimethyl-prostanoic acid
692	362	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-prostanoate
693	366	methyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-20-nor-prostanoate
694	367	methyl 9-oxo-11α-(2-hydroxyethoxy)-15-methoxy-prostanoate
695	370	ethyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo-17,18-cis-methano-prostanoate
696	377	ethyl 9-oxo-11α-(2-hydroxypropoxy)-15-hydroxy-3-oxa-16,16-dimethyl-prostanoate
697	379	butyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-prostanoate
698	380	butyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-prostanoate
699	381	butyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-17,18-cis-methano-prostanoate
700	387	isopropyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-prostanoate
701	389	decyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-prostanoate
702	390	decyl 9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-prostanoate
703	391	decyl 9-oxo-11α-(2-hydroxyethoxy)-15-methoxy-prostanoate
704	392	decyl 9-oxo-11α-(2-hydroxyethoxy)15-hydroxy-20-nor-17,18-trans-(1,3-propano)-prostanoate
705	395	9α-hydroxy-11α-methoxy-

TABLE 15-Continued

Example	Starting 13-trans-prostenoic acid or ester of Example	Product 11-oxy-15-oxy-prostanoic acid or ester
		-15-hydroxy-20-ethyl--prostanoic acid
706	396	9α-hydroxy-11α -methoxy--15-hydroxy-16-ethyl--prostanoic acid
707	397	9α-hydroxy-11α-methoxy--15-methoxy-prostanoic acid
708	399	9α-hydroxy-11α-methoxy--15-hydroxy-16,16-dimethyl-prostanoic acid
709	401	9α-hydroxy-11α-methoxy--15-hydroxy-17,18-cis--methano-prostanoic acid
710	402	9α-hydroxy-11α-methoxy--15-hydroxy-16,17,18,19,20-pentanor-15-(1--adamantly)-prostanoic acid
711	404	9α-hydroxy-11α-methoxy--15-hydroxy-16,20--ethano-prostanoic acid
712	405	9α-hydroxy-11α-methoxy--15-hydroxy-16,19--trans-ethano-prostanoic acid
713	406	9α-hydroxy-11α-methoxy--15-hydroxy-6,7,19,20--tetranor-prostanoic acid
714	410	9α-hydroxy-11α-methoxy--15-hydroxy-7a,7b-bis-homo-20-ethyl-prostanoic acid
715	411	9α-hydroxy-11α-methoxy--15-hydroxy-7a,7b-bis-homo-16,16-dimethyl--prostanoic acid
716	413	9α-hydroxy-11α-methoxy--15-hydroxy-2-ethyl--20-nor-prostanoic acid
717	416	9α-hydroxy-11α-methoxy--15-hydroxy-3,3,20--trimethyl-prostanoic acid
718	417	9α-hydroxy-11α-methoxy--15-hydroxy-3-oxa--prostanoic acid
719	419	9α-hydroxy-11α-methoxy--15-hydroxy-3-oxa--16,16-dimethyl-prostanoic acid
720	422	9α-hydroxy-11α-methoxy--15-hydroxy-2-fluoro--18,20-ethano-prostanoic acid
721	424	9α-hydroxy-11α-methoxy--15-hydroxy-7,20-dinor--prostanoic acid
722	426	9α-hydroxy-11α-methoxy--15-hydroxy-7a-homo--20-methyl-prostanoic acid
723	429	9α-hydroxy-11α-methoxy--15-hydroxy-2-phenyl--17,17-dimethyl-prostanoic acid
724	431	9α-hydroxy-11α-ethoxy--15-hydroxy-16,16-dimethyl-prostanoic acid
725	432	9α-hydroxy-11α-ethoxy--15-hydroxy-16-methyl--18,20-ethano-prostanoic acid
726	435	9α-hydroxy-11α-propoxy--15-hydroxy-16,16-dimethyl-prostanoic acid
727	437	9α-hydroxy-11α-propoxy--15-hydroxy-prostanoic acid
728	441	9α-hydroxy-11α-propoxy--15-methoxy-prostanoic acid
729	442	9α-hydroxy-11α-propoxy--15-hydroxy-16,16-dimethyl-prostanoic acid
730	443	9α-hydroxy-11α-isopropoxy-15-hydroxy-20-nor--16,19-methano-prostanoic acid
731	444	9α-hydroxy-11α-isopropoxy-15-hydroxy-prostanoic acid
732	445	9α-hydroxy-4-n-butoxy--15-hydroxy-16,16-dimethyl-prostanoic acid
733	446	9α-hydroxy-4-n-butoxy--15-hydroxy-prostanoic acid
734	451	9α-hydroxy-11α-methoxy--15-hydroxy-2,16,16--trimethyl-prostanoic acid
735	452	9α-hydroxy-11α-methoxy--15-hydroxy-2-methyl--prostanoic acid
736	453	ethyl 9α-hydroxy-11α--ethoxy-15-hydroxy--prostanoate
737	454	ethyl 9α-hydroxy-11α--ethoxy-15-hydroxy-20--methyl-17,20-ethano--prostanoate
738	455	methyl 9α-hydroxy-11α--methoxy-15-hydroxy-16,16-dimethyl-prostanoate
739	461	ethyl 9α-hydroxy-11α-butoxy-15-methoxy-2-ethyl--prostanoate
740	462	ethyl 9α-hydroxy-11α-butoxy-15-hydroxy-2-ethyl--16,16-dimethyl-prostanoate
741	463	ethyl 9α-hydroxy-11α--methoxy-15-hydroxy-3,3--dimethyl-prostanoate
742	464	ethyl 9α-hydroxy-11α--methoxy-15-hydroxy-3,3,16,16-tetramethyl-prostanoate
743	465	ethyl 9α-hydroxy-11α--ethoxy-15-hydroxy-3--oxa-20-ethyl -prostanoate
744	467	ethyl 9α-hydroxy-11α--sec-butoxy-15-hydroxy--7-nor-20-methyl-prostanoate
745	469	ethyl 9α-hydroxy-11α--methoxy-15-hydroxy-7a--homo-7,20-(1,3-propano)-prostanoate
746	472	butyl 9α-hydroxy-11α--methoxy-15-hydroxy-16,16-dimethyl-prostanoate
747	473	butyl 9α-hydroxy-11α--methoxy-15-hydroxy--prostanoate
748	474	isopropyl 9α-hydroxy--11α-methoxy-15-hydroxy--16,16-dimethyl-prostanoate
749	475	isopropyl 9α-hydroxy--11α-methoxy-15-hydroxy--prostanoate
750	477	isopropyl 9α-hydroxy--11α-methoxy-15-hydroxy--17,18-cis-methano--prostanoate
751	478	decyl 9α-hydroxy-11α--methoxy-15-hydroxy--prostanoate
752	479	decyl 9α-hydroxy-11α--methoxy-15-hydroxy--16,16-dimethyl--prostanoate
753	480	decyl 9α-hydroxy-11α--methoxy-15-hydroxy-20--ethyl-prostanoate
754	481	decyl 9α-hydroxy-11α--methoxy-15-hydroxy--17,20-(1,3-propano)--prostanoate

TABLE 15-Continued

Example	Starting 13-trans-prostenoic acid or ester of Example	Product 11-oxy-15-oxy-prostanoic acid or ester
755	483	ethyl 9α-hydroxy-11α-t-butoxy-15-hydroxy-prostanoate
756	484	ethyl 9α-hydroxy-11α-t-butoxy-15-hydroxy-16,16-dimethyl-prostanoate
757	487	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-prostanoic acid
758	487	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-prostanoic acid
759	488	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-17,18-cis-methano-prostanoic acid
760	489	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16,17,18,19,20-pentanor-15-(1-adamantyl)-prostanoic acid
761	490	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-20-ethyl-prostanoic acid
762	491	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16-ethyl-prostanoic acid
763	492	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16,20-ethano-prostanoic acid
764	493	9α-hydroxy-11α-(2-hydroxyethoxy)-15-methoxy-prostanoic acid
765	495	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-6,7,19,20-tetranor-prostanoic acid
766	497	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-5,6,7,18,19,20-hexanor-prostanoic acid
767	499	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo-20-ethyl-prostanoic acid
768	500	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo-16,16-dimethyl-prostanoic acid
769	502	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo-16,20-(1,3-propano)-prostanoic acid
770	505	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3,3-dimethyl-prostanoic acid
771	508	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-prostanoic acid
772	509	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-16,16-dimethyl-prostanoic acid
773	510	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-3-oxa-16,19-trans-ethano-prostanoic acid
774	551	9α-hydroxy-11α-(2-hydroxyethoxy)-15-methoxy-3-oxa-prostanoic acid
775	514	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-2-fluoro-16,16-dimethyl-prostanoic acid
776	515	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-2-fluoro-prostanoic acid
777	517	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7,20-bisnor-prostanoic acid
778	519	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7a-homo-20-methyl-prostanoic acid
779	520	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7a-homo-16,16-dimethyl-prostanoic acid
780	522	9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-2-phenyl-prostanoic acid
781	523	9α-hydroxy-11α-(2-hydroxypropoxy)-15-hydroxy-prostanoic acid
782	524	9α-hydroxy-11α-(2-hydroxypropoxy)-15-hydroxy-16,16-dimethyl-prostanoic acid
783	527	9α-hydroxy-11α-(4-hydroxbutoxy)-15-hydroxy-prostanoic acid
784	528	9α-hydroxy-11α-(4-hydroxybutoxy)-15-hydroxy-16,16-dimethyl-prostanoic acid
785	529	ethyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-prostanoate
786	531	ethyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-19,20-dinor-16,17-(1,3-propano)-prostanoate
787	533	methyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-20-nor-prostanoate
788	534	methyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-methoxy-prostanoate
789	537	ethyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-7a,7b-bishomo-17,18-cis-methano-prostanoate
790	544	ethyl 9α-hydroxy-11α-(3-hydroxypropoxy)-15-hydroxy-3-oxa-16,16-dimethyl-prostanoate
791	545	ethyl 9α-hydroxy-11α-(3-hydroxypropoxy)-15-hydroxy-3-oxa-16,20-methano-prostanoate
792	546	butyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-prostenoate
793	547	butyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-prostanoate
794	548	butyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-17,18-cis-methano-prostanoate
795	549	butyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-17,19-(1,3-propano)-prostanoate
796	554	isopropyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-prostanoate
797	556	decyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-prostanoate
798	557	decyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-16,16-dimethyl-prostanoate
799	558	decyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-methoxy-prostanoate

TABLE 15-Continued

Example	Starting 13-trans-prostenoic acid or ester of Example	Product 11-oxy-15-oxy-prostanoic acid or ester
800	559	decyl 9α-hydroxy-11α-(2-hydroxyethoxy)-15-hydroxy-20-nor-17,18-trans-(1,3-propano)-prostanoate
801	562	9-oxo-11α-methoxy-15-hydroxy-15-methyl-20-ethyl-prostanoic acid
802	564	9-oxo-11α-methoxy-15-hydroxy-15-methyl-6,7,-19,20-tetranor-prostanoic acid
803	565	9-oxo-11α-ethoxy-15-hydroxy-15-methyl-5,6,7,18,19,20-hexanor-prostanoic acid
804	566	9-oxo-11α-methoxy-15-hydroxy-15-methyl-7a,7b-bishomo-20-ethyl-prostanoic acid
805	567	9-oxo-11α-methoxy-15-hydroxy-15-methyl-2-ethyl-20-nor-prostanoic acid
806	568	9-oxo-11α-methoxy-15-hydroxy-15-methyl-3,3-20-trimethyl-prostanoic acid
807	569	9-oxo-11α-methoxy-15-hydroxy-15-methyl-3-oxa-prostanoic acid
808	571	9-oxo-11α-methoxy-15-hydroxy-15-methyl-2-fluoro-18,20-ethano-prostanoic acid
809	572	9-oxo-11α-methoxy-15-hydroxy-15-methyl-7,20-diner-prostanoic acid
810	573	9-oxo-11α-methoxy-15-hydroxy-15-methyl-7-nor-17,20-(1,4-butano)-prostanoic acid
811	574	9-oxo-11α-methoxy-15-hydroxy-15-methyl-7a-homo-20-methyl-prostanoic acid
812	575	9-oxo-11α-methoxy-15-hydroxy-15-methyl-7a-homo-17,18-cis-methano-prostanoic acid
813	576	9-oxo-11α-methoxy-15-hydroxy-15-methyl-7a-homo-20-cyclopentyl-prostanoic acid
814	577	9-oxo-11α-methoxy-15-hydroxy-15-methyl-2-phenyl-18,20-(1,3-propano)-prostanoic acid
815	580	9-oxo-11α-propoxy-15-hydroxy-15-methyl-20-nor-prostanoic acid
816	581	9-oxo-11α-propoxy-15-hydroxy-15-methyl-prostanoic acid
817	583	9-oxo-11α-isopropoxy-15-hydroxy-15-methyl-prostanoic acid
818	584	9-oxo-4-n-butoxy-15-hydroxy-15-methyl-prostanoic acid
819	585	9-oxo-11α-methoxy-15-hydroxy-15-methyl-2-methyl-prostanoic acid
820	586	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-prostanoic acid
821	587	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-17,18-cis-methano-prostanoic acid
822	588	9-oxo-11α-(2-hydroxyethoxy-15-hydroxy-15-methyl-20-ethyl-prostanoic acid
823	590	9-oxo-11α-(2-hydroxyethoxy-15-hydroxy-15-methyl-6,7,19,20-tetranor-prostanoic acid
824	591	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-5,6,7,18,19,20-hexanor-prostanoic acid
825	592	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-7a,7b-bishomo-20-ethyl-prostanoic acid
826	593	9-oxo-11α-(β-hydroxyethoxy)-15-hydroxy-15-methyl-7a,7b-bishomo-prostanoic acid
827	594	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-2-ethyl-20-cyclopentyl-prostanoic acid
828	596	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-3,3-dimethyl-prostanoic acid
829	597	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-3-oxa-prostanoic acid
830	599	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-2-fluoro-prostanoic acid
831	600	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-7,20-bisnor-prostanoic acid
832	601	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-7a-homo-20-methyl-prostanoic acid
833	602	9-oxo-11α-(2-hydroxyethoxy)-15-hydroxy-15-methyl-2-phenyl-prostanoic acid
834	603	9-oxo-11α-(2-hydroxypropoxy)-15-hydroxy-15-methyl-prostanoic acid
835	605	9-oxo-11α-(4-hydroxybutoxy)-15-hydroxy-15-methyl-prostanoic acid

EXAMPLE 836

Preparation of 9α/β,15-dihydroxy-11α-methoxy-13-trans-prostenoic acid

A solution containing 200 mg. of 9-oxo-11α-methoxy-15-hydroxy-13-trans-prostenoic acid (Example 227) and 20 mg. of sodium borohydride in 1 ml. of absolute alcohol is stirred at ambient temperature for 18 hours. The solution is diluted with 30 ml. of water, acidified with 2N hydrochloric acid and extracted with ether several times. The combined extracts are washed with saturated sodium chloride, dried with anhydrous magnesium sulfate and take to dryness to give an oily product, which is a mixture of 9α- and 9β-hydroxy derivatives, separable by chromatography.

EXAMPLE 837

Preparation of
4,4-dimethyl-3-triphenylmethoxy-1-octyne

Treatment of 23.1 g. (0.150 mole) of 4,4-dimethyl-1-octyn-3-ol (Example 149) with 56.5 g. of triphenylmethyl bromide in 150 ml. of pyridine and purification on Florisil, all as described in Example 127 gives the title compound, m.p. 75°–77°C.

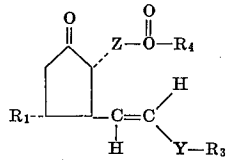
EXAMPLE 838

Preparation of
4,4-dimethyl-1-iodo-3-triphenylmethoxy-trans-1-octene

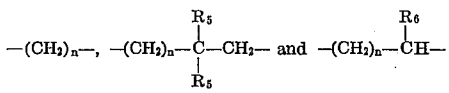
To 256 ml. of a 0.43 N solution of disiamylborane in diglyme cooled to 0°C. under an inert atmosphere is added 39.6 g. (0.10 mole) of 4,4-dimethyl-3-triphenylmethoxy-1-octyne (Example 837). The cooling bath is removed and the mixture is stirred at ambient temperatures for 3 hours. The mixture is cooled to 0°C. and 26.3 g. (0.35 mole) of finely divided trimethylamine oxide is added over a 10 minute period, the cooling bath is removed, and the mixture is allowed to exotherm but not above 40°C. after the mixture has cooled to room temperature, it is poured into 800 ml. of 15% sodium hydroxide solution and a solution of 38.1 g. of iodine in 100 ml. of tetrahydrofuran is added immediately. The mixture is stirred at room temperature for 0.5 hour and is partitioned between water and ether. The organic phase is decolorized with 5% sodium thiosulfate solution and is washed with water and saturated brine, dried ($NaSO_4$) and evaporated. The residue is purified by passing through a column of Florisil and eluting with 5–15% (v/v) benzene in hexane to yield the title compound.

We claim:

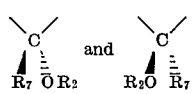
1. An optically active compound of the formula:



or a racemic compound of that formula and the mirror image thereof, wherein R_1 is lower alkoxy; Z is a divalent radical selected from the group consisting of those of the formulae:



wherein n is an integer from 3 to 8, inclusive, R_5 is an alkyl group having up to 3 carbon atoms, and R_6 is an alkyl group having up to 3 carbon atoms, a fluorine atom or a phenyl group; Y is a divalent radical selected from the group consisting of those of the formulae:



wherein R_2 is hydrogen or triphenylmethyl and R_7 is hydrogen or a lower alkyl group having up to 3 carbon atoms with the proviso that when R_7 is a lower alkyl group then R_2 must be hydrogen; R_3 is a straight chain alkyl group having from 2 to 10 carbon atoms or a straight chain alkyl group having from 2 to 10 carbon atoms and substituted with one or two lower alkyl groups; and R_4 is hydroxy, an alkoxy group having from 1 to 12 carbon atoms, or tetrahydropyranyloxy; and the pharmacologically acceptable cationic salt thereof when R_4 is hydroxy.

2. The compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen, R_7 is hydrogen, R_3 is n-pentyl, and R_4 is hydroxy; l-9-oxo-11α-methoxy-15-hydroxy-13-trans-prostenoic acid.

3. The compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen and R_7 is hydrogen, R_3 is n-pentyl, and R_4 is hydroxy; l-9-oxo-11α-methoxy-15-epi-hydroxy-13-trans-prostenoic acid.

4. The racemic compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen and R_7 is hydrogen, R_3 is n-pentyl, and R_4 is hydroxy; dl-9-oxo-11α-methoxy-15-hydroxy-13-trans-prostenoic acid.

5. The racemic compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

The R_2 is hydrogen and R_7 is hydrogen, may **3** is n-pentyl, and R_1 process is hydroxy; dl-9-oxo-11α-methoxy-Flowsheet -epi-hydroxy-13-trans-prostenoic acid. R''

6. The compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen and R_7 is methyl, R_3 is n-pentyl, and R_4 is hydroxy; l-9-oxo-11α-methoxy-15-hydroxy-15-methyl-13-trans-prostenoic acid.

7. The compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen and R_7 is methyl, R_3 is n-pentyl, and R_4 is hydroxy; l-9-oxo-11-α-methoxy-15-epi-hydroxy-15-methyl-13-trans-prostenoic acid.

8. The racemic compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen and R_7 is methyl, R_3 is n-pentyl, and R_4 is hydroxy; dl-9-oxo-11α-methoxy-15-hydroxy-15-methyl-13-trans-prostenoic acid.

9. The racemic compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen and R_7 is methyl, R_3 is n-pentyl, and R_4 is hydroxy; dl-9-oxo-11α-methoxy-15-epi-hydroxy-15-methyl-13-trans-prostenoic acid.

10. The compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen and R_7 is hydrogen, R_3 is 1,1-dimethyl-n-pentyl, and R_4 is hydroxy; l-9-oxo-11α-methoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoic acid.

11. The compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen and R_7 is hydrogen, R_3 is 1,1-dimethyl-n-pentyl, and R_4 is hydroxy; l-9-oxo-11α-methoxy-15-eip-hydroxy-16,16-dimethyl-13-trans-prostenoic acid.

12. The racemic compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen and R_7 is hydrogen, R_3 is 1,1-dimethyl-n-pentyl, and R_4 is hydroxy; dl-9-oxo-11α-methoxy-15-hydroxy-16,16-dimethyl-13-trans-prostenoic acid.

13. The racemic compound according to claim **1** wherein R_1 is methoxy, Z is hexamethylene, Y is

wherein R_2 is hydrogen and R_7 is hydrogen, R_3 is 1,1-dimethyl-n-pentyl, and R_4 is hydroxy; dl-9-oxo-11α-methoxy-15-epi-hydroxy-16,16-dimethyl-13-trans-prostenoic acid.

* * * * *

UNITED STATES PATENT OFFICE

CERTIFICATE OF CORRECTION

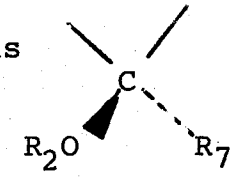
PATENT NO. : 3,876,690
DATED : April 8, 1975
INVENTOR(S) : Middleton Brawner Floyd, Jr., Martin Joseph Weiss

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

The title should read 11-alkoxy instead of 1-alkoxy.

Claim 5 should read as follows instead of as in patent:

5. The racemic compound according to Claim 1 wherein R_1 is methoxy, Z is hexamethylene, Y is



wherein R_2 is hydrogen and R_7 is hydrogen, R_3 is n-pentyl, and R_4 is hydroxy; dl-9-oxo-11α-methoxy-15-epi-hydroxy-13--trans-prostenoic acid.

Signed and Sealed this

seventh Day of October 1975

[SEAL]

Attest:

RUTH C. MASON
Attesting Officer

C. MARSHALL DANN
Commissioner of Patents and Trademarks