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Heterocyclic Analogs of Prostaglandins: I. Synthesis of 3-Alkyl(Aralkyl)-2,5-dihydrofuran-2-ones as Synthons for 11-Deoxy-10-oxaprostanoids

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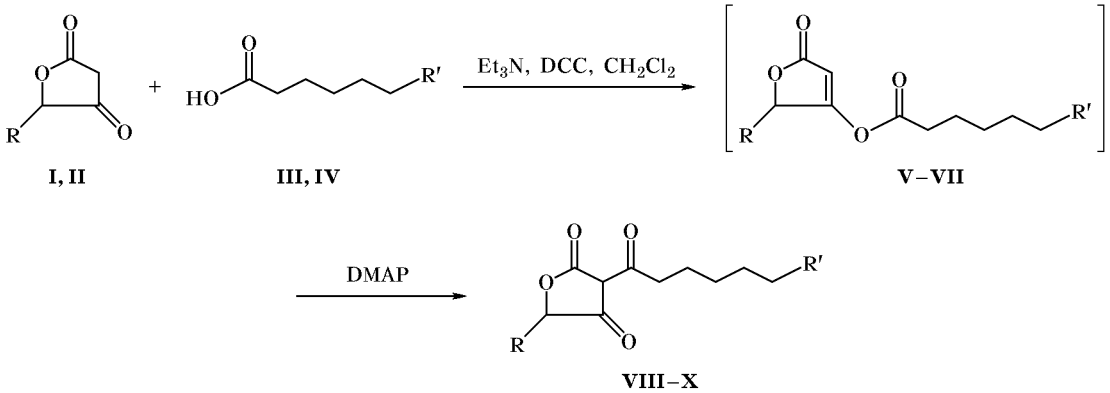
Abstract—3-Acyl(arylmethyleneacyl)tetronic acids were synthesized. Selective hydrogenation of the carbonyl group in the acyl fragment and reduction of the conjugated double bond afforded in high yield the corresponding 3-alkyl(aralkyl) derivatives possessing either natural or modified prostaglandin α-chain. Reduction of the conjugated double bond in vinylogous 3-alkyl(aralkyl)tetronic acid amides with sodium cyanotrihydridoborate gave a mixture of stereoisomeric β-amino lactones which underwent retro-Michael elimination of the amine residue, leading to 3-alkyl(aralkyl)-2,5-dihydrofuran-2-ones. The latter can be regarded as synthons for 11-deoxy-10-oxaprostanoids.

2,5-Dihydrofuran-2-one (2-buten-4-olide) system is a structural fragment of a series of natural compounds, such as acetogenins [1], muconolactones [2], leptosfaerin [3], and strigol [4], which exhibit antibiotic, cytotoxic, antitumor, antimalarial, immunosuppressive, pesticide, and other kinds of biological activity [5]. 2-Buten-4-olides turned out to be convenient intermediate products in the synthesis of natural compounds and their analogs having a γ-butyrolactone moiety [6], including biologically active prostaglandin heteroanalogs, 10-oxaprostanoids [7]. Therefore, development of efficient procedures for the preparation of 2,5-dihydrofuran-2-ones is important from the practical viewpoint.

The present communication describes a new synthesis of 3-alkyl(aralkyl)-2,5-dihydrofuran-2-ones as synthons for biologically active 10-oxaprostanoids. As starting compounds we used 3-acyl(arylmethylene-

Scheme 1.



I, II **III, IV** **V–VII** **VIII–X**

I, R = H; **II**, R = Me; **III**, R′ = Et; **IV**, R′ = COOMe; **V**, **VIII**, R = H, R′ = Et; **VI**, **IX**, R = H, R′ = COOMe; **VII**, **X**, R = Me, R′ = COOMe.

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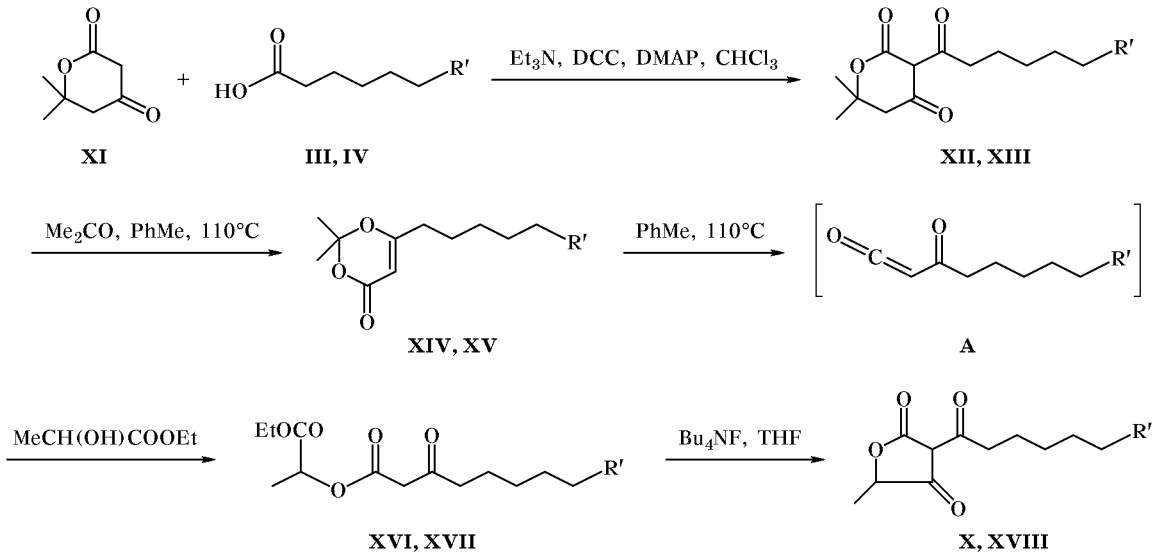
Scheme 2.



XI **III, IV** **XII, XIII** **XIV, XV** **A** **XVI, XVII** **X, XVIII**

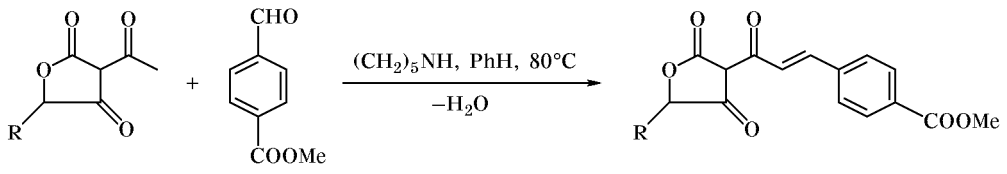
III, **XII**, **XIV**, **XVI**, **XVIII**, R = Me, R′ = Et; **IV**, **X**, **XIII**, **XV**, **XVII**, R = Me, R′ = COOMe.

acyl)tetronic acids. 3-Acyltetronic acids **VIII**–**X** were prepared by the procedure reported in [8]. O-Acylation of tetronic and 5-methyltetronic acid triethylammonium salts **I** and **II** [9] with caprylic acid (**III**) or pimelic acid monomethyl ester (**IV**) in the presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC), followed by isomerization of intermediate *O*-acyl derivatives **V**–**VII** under catalysis by 4-dimethylaminopyridine (DMAP), gave 3-acyltetrahydrofuran-2,4-diones **VIII**–**X** in 85–90% yield (Scheme 1).

Compound **X** and acyltetronic acid **XVIII** were also synthesized by an alternative method, according to which the heterocycic β-dicarbonyl fragment is built up in the final stage [10]. Acylation of Meldrum's acid (**XI**) with caprylic acid (**III**) or pimelic acid monomethyl ester (**IV**) in the presence of a catalytic amount of 4-dimethylaminopyridine and 1.2 equiv of DCC in methylene chloride gave acidic β-tricarbonyl compounds **XII** and **XIII**, respectively. The latter were treated with 0.5 equiv of acetone in boiling toluene to obtain their neutral synthetic equivalents **XIV** and **XV**. Thermolysis of **XIV** and **XV** leads to the same α-keto ketene intermediates **A** as those formed by thermolysis of **XII** and **XIII**. Unlike β-tricarbonyl precursors **XII** and **XIII**, compounds **XIV** and **XV** can readily be purified by chromatography on aluminum oxide. Heating of **XIV** and **XV** with an equimolar amount of ethyl lactate in boiling toluene afforded γ-substituted acetoacetic acid esters **XVI** and **XVII** in high yield. The latter underwent Dieckmann cyclization by the action of tetrabutylammonium fluoride [11] to give target 3-acyltetronic acids **X** and **XVIII** in 73 and 81% yield, respectively (Scheme 2).

With the goal of obtaining precursors of 1,5-interphenylene heteroprostanoids, 3-acetyltetronic acids **XIX** and **XX** were brought into condensation with methyl 4-formylbenzoate under conditions analogous to those described by us previously [12]. As a result, we obtained arylmethyleneacyl derivatives **XXI** and **XXII** in high yield (Scheme 3). It should be noted that, unlike condensation of 3-acetyltetronic acids

Scheme 3.



XIX, XX **XXI, XXII**

XIX, **XXI**, R = H; **XX**, **XXII**, R = Me.

Table 1. Yields, melting points, IR, ^{1}H NMR, and mass spectra, and elemental analyses of 3-acyltetronic acids **VIII**–**X**, **XVIII**, **XXI**, and **XXII**

Comp. no.	Yield, %	mp, °C (solvent)	Found, %		Formula	Calculated, %		Mass spectrum, *m/z* [M^+]
			C	H		C	H	
VIII	90	67–69 (ether–hexane)	63.74	7.95	$C_{12}H_{18}O_4$	63.70	8.02	226
IX	87	42–44 (ether–hexane)	56.23	6.38	$C_{12}H_{16}O_6$	56.24	6.30	256
X	85,[a] 73[b]		58.10	6.75	$C_{13}H_{18}O_6$	57.77	6.71	270
XVIII	81[b]	39–41 (ether)	65.10	8.44	$C_{13}H_{20}O_4$	64.98	8.39	240
XXI	75	171–172 (ethyl acetate)	62.54	4.19	$C_{15}H_{12}O_6$	62.50	4.20	288
XXII	72	163–166 (ether)	63.69	4.65	$C_{16}H_{14}O_6$	63.57	4.67	302

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)
VIII	1620, 1668, 1700 sh, 1755 sh, 1780	0.90 t (3H, CH_3, *J* = 6.5), 1.16–1.50 m (8H, $4CH_2$), 1.72 quint [2H, C**H**$_2$CH$_2$(CO), *J* = 7.5], 2.92 t and 2.94 t [2H, (CO)CH_2, *J* = 7.5], 4.58 s and 4.68 s (2H, CH_2, ring), 7.78–9.02 br.s (1H, OH, enol)
IX	1605 sh, 1615, 1665, 1695, 1740, 1780	1.34–1.56 m (2H, CH_2), 1.56–1.84 m (4H, $2CH_2$), 2.34 t (2H, CH_2CO_2Me, *J* = 7.2), 2.93 t and 2.96 t [2H, (CO)CH_2, *J* = 7.2], 3.69 s (3H, CO_2CH_3), 4.58 s and 4.70 s (2H, CH_2, ring), 9.89 br.s (1H, OH, enol)
X	1615, 1670, 1700, 1740, 1780	1.34–1.56 m (2H, CH_2), 1.53 d (3H, CHC**H**$_3$, *J* = 7.0), 1.56–1.84 m (4H, $2CH_2$), 2.34 t (2H, C**H**$_2$CO$_2$Me, *J* = 7.2), 2.93 t and 2.96 t [2H, (CO)CH_2, *J* = 7.2], 3.69 s (3H, CO2C**H**$_3$), 4.80 m (1H, C**H**CH_3), 9.89 br.s (1H, OH, enol)
XVIII	1595 sh, 1620, 1675, 1685 sh, 1760	0.90 t (3H, CH_3, *J* = 6.5), 1.18–1.46 m (8H, $4CH_2$), 1.53 d (3H, CHC**H**$_3$, *J* = 7.0), 1.71 quint [2H, C(O)CH_2C**H**$_2$, *J* = 7.5], 2.92 t [2H, C(O)CH_2, *J* = 7.5], 4.80 m (1H, C**H**CH_3), 9.38 br.s (1H, OH, enol)
XXI	1565, 1585, 1640, 1705, 1730, 1770	3.95 s (3H, CO_2CH_3), 4.63 s and 4.70 s (2H, CH_2, heteroring), 7.77 d (2H, H_{arom}, *J* = 8.0), 7.81 d and 7.86 d (1H, =CH, J_{trans} = 16.0), 8.04 d and 8.06 d (1H, CH=, J_{trans} = 16.0), 8.12 d (2H, H_{arom}, *J* = 8.0)
XXII	1580, 1600, 1650, 1698, 1745	1.58 d (3H, CHC**H**$_3$, *J* = 7.0), 3.96 s (3H, CO_2CH_3), 4.78 q and 4.86 q (1H, C**H**CH_3, *J* = 7.0), 7.77 d (2H, H_{arom}, *J* = 8.0), 7.84 d and 7.87 d (1H, =CH, J_{trans} = 16.0), 8.04 d and 8.06 d (1H, CH=, J_{trans} = 16.0), 8.12 d (2H, H_{arom}, *J* = 8.0), 9.50 br.s (1H, OH, enol)

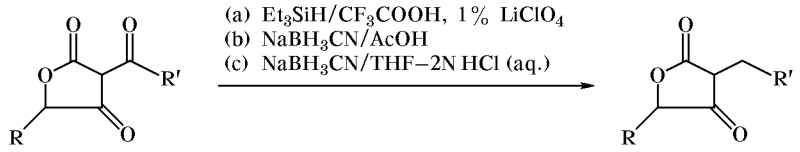
[a] By acylation of tetronic acid.

[b] By cyclization of γ-substituted acetoacetic acid ethyl ester.

XIX and **XX** with 4-formylbenzoic acid (which is characterized by a low yield because of a poor solubility of 4-formylbenzoic acid [12]), the use of the corresponding methyl ester considerably increases the yield of arylmethyleneacyl derivatives and facilitates their isolation and purification.

The transition to the corresponding β-dicarbonyl derivatives, 3-alkyl(aralkyl)tetronic acids implies chemoselective hydrogenation of the carbonyl group in the acyl substituent of cyclic β-tricarbonyl precursors. We tried to effect this transformation in three ways (a–c). Ionic hydrogenation of β-tricarbonyl

Scheme 4.



VIII–X, XVIII, XXI, XXII **XXIII–XXIX**

VIII, **XXIII**, R = H, R′ = C_7H_{15}; **IX**, **XXIV**, R = H, R′ = $(CH_2)_5COOMe$; **XXV**, R = H, R′ = $(CH_2)_5COOH$; **XXI**, R = H, R′ = (*E*)-CH=CHC_6H_4COOMe-*p*; **XXVIII**, R = H, R′ = $(CH_2)_2C_6H_4COOMe$-*p*; **X**, **XXVI**, R = Me, R′ = $(CH_2)_5COOMe$; **XVIII**, **XXVII**, R = Me, R′ = C_7H_{15}; **XXII**, R = Me, R′ = (*E*)-CH=$CHC_6H_4CO_2Me$-*p*; **XXIX**, R = Me, R′ = $(CH_2)_2C_6H_4COOMe$-*p*.

compounds **VIII**, **IX**, **XXI**, and **XXII** by the action of triethylsilane in trifluoroacetic acid [13] in the presence of a catalytic amount of $LiClO_4$ (a) gave β-dicarbonyl compounds **XXIII**, **XXIV**, **XXVIII**, and **XXIX** in high yield. Only the yield of **XXVII** was 63%, presumably due to loss of the product during washing of the reaction mixture with hexane to remove silanes (the product is appreciably soluble in hexane).

Selective hydrogenation of the acyl carbonyl group in tricarbonyl compounds **VIII**, **X**, **XVIII**, **XXI**, and **XXII** was also performed according to procedure (b) which was proposed for acyl derivatives of Meldrum's acid, 5-acylbarbituric acid, dehydroacetic acid, and 3-acyl-4-hydroxycoumarins. It includes reduction of the above substrates with sodium cyanotrihydridoborate [14]. We have found that this procedure is applicable to preparation of 3-alkyltetronic acids from β-tricarbonyl precursors. In the reaction with arylmethyleneacyl derivatives, as well as in ionic hydrogenation, the reduction involved the entire enone fragment of the arylmethyleneacyl substituent. The procedure turned out to be inconvenient from the experimental viewpoint because of difficulties in the isolation of products from the reaction mixtures containing high-boiling acetic acid which readily dissolves organic compounds. Following method (b), the yields of α-alkyl-β-dicarbonyl compounds **XXIII** and **XXVI**–**XXIX** were 65–80%.

Our experiments showed that the reduction of cyclic β-tricarbonyl compounds of the cyclopentane, cyclohexane, tetronic acid, and α-pyrone series with cyanotrihydridoborate (c) is more efficient when it is performed in the system THF–2 N aqueous HCl. In this case, the procedure for isolation of products from the reaction mixture is considerably simplified, so that the yield increases. Removal of THF under reduced pressure results in almost complete crystallization of the target β-dicarbonyl compounds from aqueous solution containing inorganic components; an additional amount of the product can be isolated by extraction from the aqueous phase with organic solvents. The isolation of oily products is also easy: here, preliminary removal of THF is not necessary. Thus we have proposed a general and efficient procedure for the synthesis of cyclic α-alkyl-β-dicarbonyl compounds [15]. The application of this procedure to β-tricarbonyl compounds **VIII**, **XVIII**, **XXI**, and **XXII** afforded products **XXIII** and **XXVII**–**XXIX** in 91–97% yield (Scheme 4).

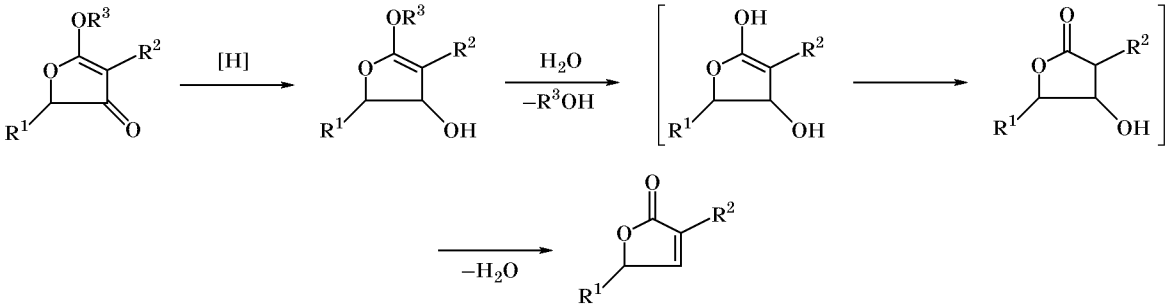
It should be noted that the ester group attached to the aromatic ring in compounds **XXI** and **XXII** is stable under conditions of procedure (c), while the ester group in compound **IX** is readily hydrolyzed to give acid **XXV** as the major product. We have found that replacement of tetrahydrofuran by methanol leads to considerable increase in the yield of target β-dicarbonyl compound **XXIV**. Nevertheless, the optimal procedure for the preparation of ester **XXIV** is (a) with the use of triethylsilane in trifluoroacetic acid, which rules out hydrolysis of the ester group during the reduction.

Wide synthetic potential of cyclic β-dicarbonyl compounds originates from versatile chemical reactions involving the ketomethylene fragment. The selectivity of these reactions can be governed by the use of β-dicarbonyl compounds *per se* or derivatives of their enol forms.

We then focused on the preparation of enol derivatives of alkyl-substituted tetronic acids and development of effective ways of their transformation into 2-buten-4-olides. A classical procedure for the synthesis of α,β-unsaturated cyclic ketones from cyclic β-diketones includes conversion of the latter into vinyl enol ethers and selective reduction of the conjugated carbonyl group therein with diisobutylaluminum hydride at low temperature (–78°C) [16]. Subsequent treatment of the reaction mixture results in decomposition of β-hydroxy ketones to enones via elimination of water.

Taking into account the known possibility for regioselective synthesis of enol ethers at the lactone

Scheme 5.



carbonyl group of 3-alkyltetronic acids by the action of Meerwein salts [17], we tried to apply this procedure to the preparation of butenolides. Theoretically, reduction of the ketone carbonyl group in enol ethers, followed by treatment of the reaction mixture with water, could lead to formation of β-hydroxylactones which could then be converted into 2-buten-4-olides through elimination of water (Scheme 5).

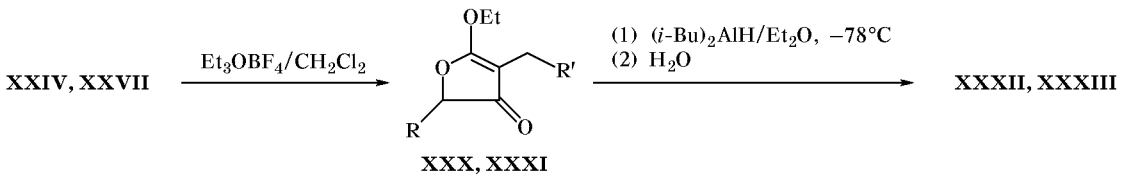
In order to verify the feasibility of the above approach, 3-(6-methoxycarbonylhexyl)tetronic acid (**XXIV**) and 5-methyl-3-octyltetronic acid (**XXVII**) were converted into enol ethers **XXX** and **XXXI**, respectively, by the action of triethyloxonium tetrafluoroborate. Enol ethers **XXX** and **XXXI** were reduced with diisobutylaluminum hydride in diethyl ether at –78°C, and subsequent treatment of the reaction mixtures with water gave desired butenolides **XXXII** and **XXXIII** (Scheme 6). However, the yield of **XXXIII** was as low as 28%, and the yield of **XXXII** was even smaller (12%) as a result of an appreciable contribution of reduction of the side-chain ester group. Our attempts to raise the yield of the target product through variation of the solvent, temperature, and way of addition of the reducing agent were unsuccessful.

Therefore, we examined another approach to butenolides through enamino derivatives of 3-alkyl-substituted tetronic acids (enaminolactones) and developed a convenient three-step procedure for the synthesis of 3-alkyl- and 3,5-dialkyl-substituted 2,5-dihydrofuran-2-ones. The procedure consists of reduction of the conjugated double bond in enamino derivatives of 3-alkyltetronic acids with subsequent retro-Michael elimination of the amine residue from the β-aminolactones thus formed [18]. By heating of 3-alkyltetronic acids **XXIII**, **XXIV**, and **XXVI**–**XXVIII** with pyrrolidine in boiling toluene we obtained the corresponding enamino lactones **XXXIV**–**XXXVIII** in 80–90% yield. The yield of sterically hindered enamino lactone **XXXIX** ranged from 50 to 60%. Prolonged boiling of the reaction mixture and addition of *p*-toluenesulfonic acid as catalyst did not result in appreciable increase of the yield of **XXXIX**.

The conjugated double bond in **XXXIV**–**XXXIX** was smoothly reduced by the action of sodium cyanotrihydridoborate on a solution of the substrate in 2 N methanolic hydrogen chloride at room temperature. After evaporation of methanol, treatment of the reaction mixture with aqueous alkali gave β-aminolactones **XL**–**XLV** as mixtures of diastereoisomers. Unlike enamino derivatives of tetronic acids, the double bond in enamino derivatives of carbocyclic β-dicarbonyl compounds is quite resistant to reduction under analogous conditions [19].

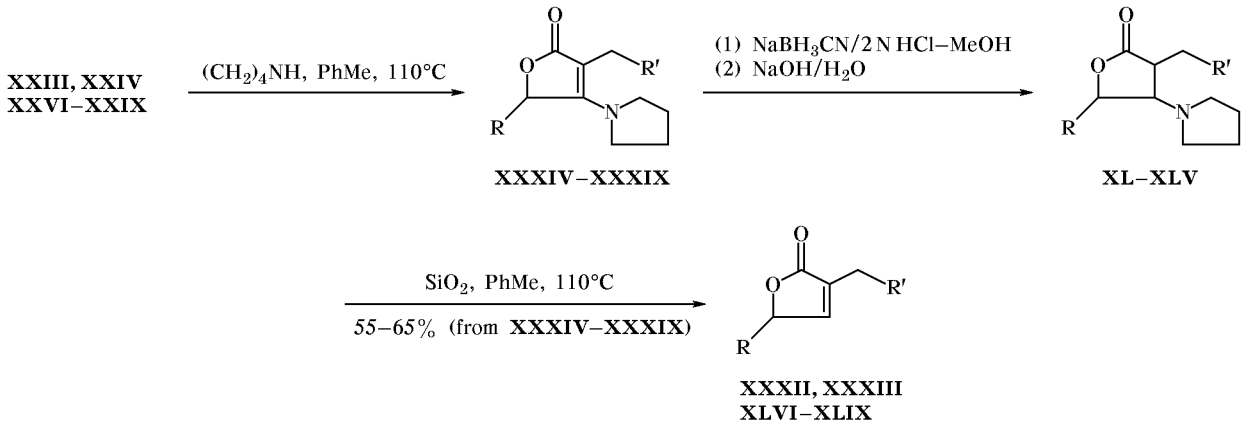
We have found that the resulting β-aminolactones undergo partial retro-Michael elimination of the pyrrolidine moiety to afford 2,5-dihydrofuran-2-ones during chromatographic purification on silica gel. In order to accelerate the transformation of aminolactones into butenolides, compounds **XL**–**XLV** were heated in boiling toluene in the presence of silica gel. Under these conditions, butenolides **XXXII**, **XXXIII**,

Scheme 6.



XXIV, **XXX**, **XXXII**, R = H, R′ = $(CH_2)_5COOMe$; **XXVII**, **XXXI**, **XXXIII**, R = Me, R′ = C_7H_{15}.

Scheme 7.



XXIII, **XXXIV**, **XL**, **XLVI**, R = H, R′ = C_7H_{15}; **XXIV**, **XXXII**, **XXXV**, **XLI**, R = H, R′ = $(CH_2)_5COOMe$; **XXVIII**, **XXXVIII**, **XLIV**, **XLVIII**, R = H, R′ = $(CH_2)_2C_6H_4COOMe$-4; **XXVI**, **XXXVI**, **XLII**, **XLVII**, R = Me, R′ = $(CH_2)_5COOMe$; **XXVII**, **XXXIII**, **XXXVII**, **XLIII**, R = Me, R′ = C_7H_{15}; **XXIX**, **XXXIX**, **XLV**, **XLIX**, R = Me, R′ = $(CH_2)_2C_6H_4COOMe$-4.

and **XLVI**–**XLIX** were formed in 55–65% yield (calculated on enamino lactones **XXXIV**–**XXXIX**) (Scheme 7). It is important that the yield of the target butenolides does not decrease when crude aminolactones **XL**–**XLV** are used (obtained after primary treatment of the reaction mixture). Unlike diisobutylaluminum hydride, sodium cyanotrihydridoborate as reducing agent ensures considerably higher yields of the target products and conservation of the ester moiety.

Thus, using 3-acyltetronic acids as starting compounds, we have developed a four-step procedure for the synthesis of 3-alkyl- and 3,5-dialkyl-substituted 2,5-dihydrofuran-2-ones. The products, butenolides **XXXII**, **XXXIII**, and **XLVI**–**XLIX** are convenient synthons for biologically active 11-deoxy-10-oxaprostanoids.

EXPERIMENTAL

The melting points were determined on a Boetius device. The ^1H NMR spectra were measured on a Bruker AC-200 spectrometer (200 MHz) from solutions in $CDCl_3$ containing TMS as internal reference. The IR spectra were recorded on a UR-20 instrument from samples prepared as thin films or KBr pellets. The mass spectra (70 eV) were run on a Varian MAT-311 mass spectrometer. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates. Silica gel 100/160 μm (Czechia) and aluminum oxide were used for column chromatography.

Acylation of tetronic acids I and II with carboxylic acids. Triethylamine, 1.38 ml (9.9 mmol), was added under stirring at 0°C to a suspension of 9 mmol of tetronic acid **I** or **II** in anhydrous CH_2Cl_2. To the resulting homogeneous solution we added in succession 0.36 g (2.97 mmol) of 4-dimethylaminopyridine, 1.56 ml (9.9 mmol) of caprylic acid (**III**) or 1.72 g (9.9 mmol) of pimelic acid monomethyl ester (**IV**), and (in portions) 2.22 g (10.8 mmol) of dicyclohexylcarbodiimide. The mixture was stirred for 10 min at 0°C, the cooling bath was removed, and the mixture was stirred for 15 h at room temperature. The precipitate of *N*,*N*′-dicyclohexylurea was filtered off and washed with ethyl acetate. The filtrate was combined with the washings and evaporated, 80 ml of diethyl ether and 25 ml of 1.5 N hydrochloric acid were added to the residue, and the mixture was shaken in a separatory funnel. The aqueous phase was removed, and the organic phase was washed with 20 ml of 1.5 N hydrochloric acid and 20 ml of water and dried over $MgSO_4$. The solvent was evaporated, and the residue was subjected to column chromatography on silica gel using hexane–ether as eluent (gradient elution). The product was recrystallized from appropriate solvent. The yields, melting points and spectral and analytical data of compounds **VIII**–**X** are given in Table 1.

6-Substituted 2,2-dimethyl-4*H*-1,3-dioxin-4-ones XIV and XV. Triethylamine, 3 ml (21.6 mmol), was added dropwise under stirring at 0°C to a solution of 2.59 g (18 mmol) of 2,2-dimethyl-1,3-dioxane-4,6-dione (**XI**) in dry chloroform. To the resulting mixture we added 0.73 g (6 mmol) of 4-dimethylaminopyridine and (dropwise) a solution of 2.84 ml (18 mmol) of caprylic acid (**III**) or 3.13 g (18 mmol) of pimelic acid monomethyl ester (**IV**) in 15 ml of chloroform.

Table 2. Yields, melting points, IR, ^{1}H NMR, and mass spectra, and elemental analyses of 3-alkyltetronic acids **XXIII**–**XXVII**, **XXVIII**,[a] and **XXIX**[a]

Comp. no.	Yield, % (method)	mp, °C (solvent)	Found, %		Formula	Calculated, %		Mass spectrum, *m*/*z* [M^+]
			C	H		C	H	
XXIII	91 (a), 65 (b),[b] 93 (c)	104–107 (ether)	67.91	9.56	$C_{12}H_{20}O_3$	67.89	9.50	212
XXIV	88 (a), 37 (b), 79 (c)[c]	76–78 (ether–hexane)	59.35	7.46	$C_{12}H_{18}O_5$	59.49	7.49	242
XXV[d]	60 (c)	125–128 (ether)	57.89	7.06	$C_{11}H_{16}O_5$	57.88	7.07	228
XXVI	80 (b)[e]		60.70	7.97	$C_{13}H_{20}O_5$	60.92	7.87	256
XXVII	63 (a), 77 (b),[e] 94 (c)	63.5–65[f] (hexane)	68.94	9.76	$C_{13}H_{22}O_3$	68.99	9.80	226

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)
XXIII	1410, 1455, 1465, 1605–1665, 1720, 2720	0.87 t (3H, CH_3, *J* = 6.5), 1.10–1.38 m (10H, $5CH_2$), 1.38–1.58 m (2H, CH_2), 2.21 t (2H, CH_2, *J* = 7.5), 4.70 s (2H, CH_2, ring)
XXIV	1410, 1440, 1645 br, 1735, 2715	1.34 m (4H, $2CH_2$), 1.50 quint (2H, CH_2, *J* = 7.2), 1.62 quint (2H, C**H**$_2$CH$_2$CO$_2$Me, *J* = 7.2), 2.20 t (2H, 3-CH_2, *J* = 7.2), 2.33 t (2H, C**H**$_2$CO$_2$Me, *J* = 7.2), 3.68 s (3H, CO_2CH_3), 4.66 s (2H, CH_2, ring)
XXV[d]	1420, 1475, 1580 sh, 1610–1660, 1715, 2715	1.34 m (4H, $2CH_2$), 1.54–1.81 m (4H, $2CH_2$), 2.43 t (2H, CH_2, *J* = 7.5), 2.47 t (2H, CH_2, *J* = 7.5), 4.83 s (2H, CH_2, ring)
XXVI	1410, 1440, 1635 br, 1680, 1720, 1740, 2715	1.34 m (4H, $2CH_2$), 1.50 d (3H, CHC**H**$_3$, *J* = 6.5), 1.50 m (2H, CH_2), 1.62 quint (2H, C**H**$_2$CH$_2$CO$_2$Me, *J* = 7.2), 2.20 t (2H, 3-CH_2, *J* = 7.2), 2.33 t (2H, C**H**$_2$CO$_2$Me, *J* = 7.2), 3.68 s (3H, CO_2CH_3), 4.85 q (1H, C**H**CH_3, *J* = 6.5)
XXVII	1410, 1480, 1635 br, 1725, 2400–2800	0.88 t (3H, CH_3, *J* = 6.5), 1.13–1.39 m (10H, $5CH_2$), 1.39–1.62 m (2H, CH_2), 1.51 d (3H, CHC**H**$_3$, *J* = 6.5), 2.20 t (2H, 3-CH_2, *J* = 7.5), 4.85 q (1H, C**H**CH_3, *J* = 6.5)

[a] The spectral parameters of compounds **XXVIII** [yield 97% (a), 76% (b),[b] 97% (c); mp 161–163°C (from ethyl acetate)] and **XXIX** [yield 89% (a), 71% (b),[b] 91% (c); mp 115–117°C (from ether–hexane)] are fully consistent with our previous data [12].

[b] Isolated by crystallization from dilute aqueous solutions of acetic acid.

[c] Yield of the reduction product upon replacement of THF by methanol.

[d] The ^{1}H NMR spectrum of **XXV** was recorded in pyridine-d_5.

[e] Isolated by column chromatography after evaporation of acetic acid under reduced pressure.

[f] Melting point of a sample prepared by method (c).

Dicyclohexylcarbodiimide, 4.45 g (21.6 mmol), was then added in portions, the cooling bath was removed, and the mixture was stirred for 15 h at room temperature. The precipitate of *N*,*N*′-dicyclohexylurea was filtered off and washed with chloroform. The filtrate was combined with the washings and evaporated, and 150 ml of diethyl ether and 50 ml of 1.5 N hydrochloric acid were added to the residue. The mixture was shaken in a separatory funnel, the aqueous phase was separated, and the organic phase was washed with 50 ml of 5% hydrochloric acid and 50 ml of water and dried over Na_2SO_4. The solvent was removed

Table 3. Yields, IR, ^{1}H NMR, and mass spectra, and elemental analyses of 3-alkyl(aralkyl)-substituted 2,5-dihydrofuran-2-ones **XXXII**, **XXXIII**, and **XLVI**–**XLIX**

Compound no.	Yield, %	Found, %		Formula	Calculated, %		Mass spectrum, m/z [M^+]
		C	H		C	H	
XXXII	12,[a] 58[b]	63.65	7.99	$C_{12}H_{18}O_4$	63.70	8.02	226
XXXIII	28,[a] 63[b]	74.34	10.51	$C_{13}H_{22}O_2$	74.24	10.54	210
XLVI	65	73.39	10.25	$C_{12}H_{20}O_2$	73.43	10.27	196
XLVII	55	65.14	8.37	$C_{13}H_{20}O_4$	64.98	8.39	240
XLVIII[c]	62	69.22	6.16	$C_{15}H_{16}O_4$	69.22	6.20	260
XLIX[d]	56	70.02	6.57	$C_{16}H_{18}O_4$	70.06	6.61	274

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm (J, Hz)
XXXII	1445, 1460, 1660, 1745, 1760	1.33 m (4H, $2CH_2$), 1.49-1.66 m (4H, $2CH_2$), 2.26 t.q (2H, 3-CH_2, ^3J = 7.5, ^4J = ^5J = 1.7), 2.28 t (2H, C**H**$_2CO_2$Me, J = 7.5), 3.64 s (3H, CO_2CH_3), 4.75 q (2H, OCH_2, ring, ^3J = ^5J = 1.7), 7.09 quint (1H, 4-H, ^3J = ^4J = 1.7)
XXXIII	1460, 1470, 1665, 1765	0.89 t (3H, CH_3, J = 6.0), 1.15–1.38 m (10H, $5CH_2$), 1.42 d (3H, CHC**H**$_3$, J = 7.0), 1.56 quint (2H, CH_2, J = 7.5), 2.28 br.t (2H, 3-CH_2, J = 7.5), 5.02 q.d (1H, C**H**CH_3, $^3J_1$ = 7.0, $^3J_2$ = 1.5), 7.01 q (1H, 4-H, ^3J = ^4J = 1.5)
XLVI	1470, 1665, 1765	0.89 t (3H, CH_3, J = 6.5), 1.10–1.48 m (10H, $5CH_2$), 1.58 quint (2H, CH_2, J = 7.0), 2.31 t.d (2H, 3-CH_2, ^3J = 7.5, ^4J = 1.5), 4.79 q (2H, OCH_2, ring, ^3J = ^5J = 1.5), 7.11 quint (1H, 4-H, ^3J = ^4J = 1.5)
XLVII	1465, 1660, 1740, 1760	1.33 m (4H, $2CH_2$), 1.38 d (3H, CHC**H**$_3$, J = 7.0), 1.48–1.68 m (4H, $2CH_2$), 2.24 t.t (2H, 3-CH_2, ^3J = 7.5, ^4J = ^5J = 1.5), 2.29 t (2H, C**H**$_2CO_2$Me, J = 7.5), 3.65 s (3H, CO_2CH_3), 4.98 q.t (1H, C**H**CH_3, $^3J_1$ = 7.0, $^3J_2$ = ^5J = 1.5), 6.98 q (1H, 4-H, ^3J = ^4J = 1.5)
XLVIII[c]	1435, 1465, 1620, 1665, 1720, 1763	1.94 quint (2H, C**H**$_2CH_2$Ar, J = 7.5), 2.36 t.d [2H, C**H**$_2(CH_2)_2$Ar, ^3J = 7.5, ^4J = 1.8], 2.74 t (2H, C**H**$_2$Ar, J = 7.5), 3.92 s (3H, CO_2CH_3), 4.78 q (2H, OCH_2, ring, ^3J = ^5J = 1.8), 7.14 quint (1H, 4-H, ^3J = ^4J = 1.8), 7.27 d (2H, H_{arom}, J = 8.0), 7.98 d (2H, H_{arom}, J = 8.0)
XLIX[d]	1443, 1465, 1620, 1665, 1730, 1765	1.40 d (3H, CHC**H**$_3$, J = 7.0), 1.92 quint (2H, C**H**$_2CH_2$Ar, J = 7.5), 2.33 br.t [2H, C**H**$_2(CH_2)_2$Ar, J = 7.5], 2.74 t (2H, C**H**$_2$Ar, J = 7.5), 3.91 s (3H, CO_2CH_3), 5.01 q.d (1H, C**H**CH_3, $^3J_1$ = 7.0, $^3J_2$ = 1.5), 7.03 q (1H, 4-H, ^3J = ^4J = 1.5), 7.26 d (2H, H_{arom}, J = 8.0), 7.97 d (2H, H_{arom}, J = 8.0)

[a] By reduction of tetronic acid enol ethers with diisobutylaluminum hydride.

[b] By reduction of enamino lactones with sodium cyanotrihydridoborate.

[c] mp 54.5–56°C (from ether).

[d] mp 36–37°C (from ether–hexane).

Table 4. Yields, IR, ^{1}H NMR, and mass spectra, and elemental analyses of 4-(1-pyrrolidinyl)-2,5-dihydrofuran-2-ones **XXXIV**–**XXXIX**

Comp. no.	Yield, %	Found, %			Formula	Calculated, %			Mass spectrum, m/z [M^+]
		C	H	N		C	H	N	
XXXIV	90	72.27	10.15	5.14	$C_{16}H_{27}NO_2$	72.41	10.25	5.28	265
XXXV	84	64.94	8.49	4.65	$C_{16}H_{25}NO_4$	65.06	8.53	4.74	295
XXXVI	89	66.12	8.81	4.54	$C_{17}H_{27}NO_4$	65.99	8.79	4.53	309
XXXVII	82	72.90	10.49	5.03	$C_{17}H_{29}NO_2$	73.07	10.46	5.01	279
XXXVIII	80	69.37	7.03	4.15	$C_{19}H_{23}NO_4$	69.28	7.04	4.25	329
XXXIX	50–60	69.97	7.34	4.01	$C_{20}H_{25}NO_4$	69.95	7.34	4.08	343

Comp. no.	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm (J, Hz)
XXXIV	1450, 1460, 1475 sh, 1615, 1640, 1730	0.88 t (3H, CH_3, J = 6.5), 1.15–1.53 m (12H, $6CH_2$), 2.00 m (4H, $2CH_2$, pyrrolidine), 2.31 t (2H, CH_2, J = 7.5), 3.46 m (4H, $2CH_2$, pyrrolidine), 4.54 s (2H, CH_2, butenolide)
XXXV	1450, 1465, 1640, 1745	1.21–1.52 m (6H, $3CH_2$), 1.62 m (2H, CH_2), 2.00 m (4H, $2CH_2$, pyrrolidine), 2.31 t (4H, C**H**$_2$$CO_2$Me, 3-$CH_2$, J = 7.2), 3.46 m (4H, $2CH_2$, pyrrolidine), 3.66 s (3H, CO_2CH_3), 4.56 s (2H, CH_2, butenolide)
XXXVI	1435, 1460, 1625, 1740	1.20–1.54 m (6H, $3CH_2$), 1.48 d (3H, CHC**H**$_3$, J = 6.5), 1.54–1.76 m (2H, CH_2), 1.82–2.14 m (4H, $2CH_2$, pyrrolidine), 2.32 t (4H, C**H**$_2$$CO_2$Me, 3-$CH_2$, J = 7.5), 3.50 m (4H, $2CH_2$, pyrrolidine), 3.67 s (3H, CO_2CH_3), 4.80 q (1H, C**H**CH_3, J = 6.5)
XXXVII	1435, 1460, 1630, 1740	0.89 t (3H, CH_3, J = 6.5), 1.22–1.41 m (12H, $6CH_2$), 1.49 d (3H, CHC**H**$_3$, J = 6.5), 1.85–2.13 m (4H, $2CH_2$, pyrrolidine), 2.33 t (2H, 3-CH_2, J = 7.5), 3.51 m (4H, $2CH_2$, pyrrolidine), 4.82 q (1H, C**H**CH_3, J = 6.5)
XXXVIII	1450, 1460, 1625, 1635, 1725 sh, 1735	1.82 quint (2H, C**H**$_2$$CH_2$Ar, J = 7.5), 1.93 m (4H, $2CH_2$, pyrrolidine), 2.37 t [2H, C**H**$_2$$(CH_2)_2$Ar, J = 7.5], 2.72 t (2H, C**H**$_2$Ar, J = 7.5), 3.33 m (4H, $2CH_2$, pyrrolidine), 3.90 s (3H, CO_2CH_3), 4.52 s (2H, OCH_2, ring), 7.26 d (2H, H_{arom}, J = 8.0), 7.94 d (2H, H_{arom}, J = 8.0)
XXXIX	1440, 1460, 1620, 1730	1.46 d (3H, CHC**H**$_3$, J = 6.5), 1.69–2.04 m (6H, C**H**$_2$$CH_2$Ar, $2CH_2$, pyrrolidine), 2.38 t [2H, C**H**$_2$$(CH_2)_2$Ar, J = 7.5], 2.72 t (2H, C**H**$_2$Ar, J = 7.5), 3.38 m (4H, $2CH_2$, pyrrolidine), 3.90 s (3H, CO_2CH_3), 4.78 q (1H, C**H**CH_3, J = 6.5), 7.26 d (2H, H_{arom}, J = 8.0), 7.95 d (2H, H_{arom}, J = 8.0)

under reduced pressure, the oily residue (acylated Meldrum's acid **XII** or **XIII**) was dissolved in 25 ml of toluene, and 0.66 ml (9 mmol) of acetone was added. The mixture was heated for 1.5 h under reflux and was concentrated under reduced pressure. The residue was purified by column chromatography on aluminum oxide using hexane–ether as eluent (gradient elution). The products were pale yellow oily substances.

6-Heptyl-2,2-dimethyl-4*H*-1,3-dioxin-4-one (XIV). Yield 71%. ^{1}H NMR spectrum, δ, ppm: 0.89 t (3H, CH_3, J = 6.5 Hz), 1.22–1.40 m (8H, $4CH_2$),

1.45–1.62 m (2H, CH_2), 1.69 s (6H, 2-CH_3), 2.22 t (2H, $CH_2C{=}C$, J = 7.5 Hz), 5.23 s (1H, 5-H). IR spectrum, ν, cm^{-1}: 1635, 1735.

2,2-Dimethyl-6-(5-methoxycarbonylpentyl)-4*H*-1,3-dioxin-4-one (XV). Yield 67%. ^{1}H NMR spectrum, δ, ppm: 1.33–1.45 m (2H, CH_2), 1.48–1.72 m (4H, $2CH_2$), 1.69 s (6H, 2-CH_3), 2.23 t (2H, CH_2, J = 7.5 Hz), 2.33 t (2H, CH_2CO_2Me, J = 7.5 Hz), 3.68 s (3H, CO_2CH_3), 5.24 s (1H, 5-H). IR spectrum, ν, cm^{-1}: 1640, 1735, 1745.

Thermolysis of 6-substituted 2,2-dimethyl-4*H*-1,3-dioxin-4-ones XIV and XV with ethyl lactate in toluene. A mixture of 12.8 mmol of compound **XIV** or **XV** and 1.46 ml (12.8 mmol) of ethyl lactate in 50 ml of toluene was heated for 1.5 h under reflux. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel using hexane–ether as eluent (gradient elution). The products were pale yellow oily substances.

1-Ethoxycarbonylethyl 3-oxodecanoate (XVI). Yield 92%. ^{1}H NMR spectrum, δ, ppm (enol-to-ketone ratio 1 : 6.5): 0.90 t (3H + 3/6.5H, CH_3, J = 6.5 Hz), 1.16–1.42 m (11H + 11/6.5H, $4CH_2$ + $CO_2CH_2C\mathbf{H}_3$), 1.51 d (3H + 3/6.5H, $CHC\mathbf{H}_3$, J = 7.0 Hz), 1.61 m (2H + 2/6.5H, CH_2), 2.22 t [2/6.5H, $=C(OH)C\mathbf{H}_2$, J = 7.5 Hz], 2.60 t [2H, $C(O)CH_2$, J = 7.5 Hz], 3.52 s [2H, $C(O)CH_2C(O)O$], 4.23 q (2H + 2/6.5H, $CO_2C\mathbf{H}_2CH_3$, J = 7.0 Hz), 5.11 s [1/6.5H, $C(OH){=}C\mathbf{H}C(O)O$], 5.14 q (1H + 1/6.5H, $C\mathbf{H}CH_3$, J = 7.0 Hz), 11.82 s (1/6.5H, OH, enol). IR spectrum, ν, cm^{-1}: 1640, 1670, 1730, 1760.

1-Ethoxycarbonylethyl 8-methoxycarbonyl-3-oxooctanoate (XVII). Yield 90%. ^{1}H NMR spectrum, δ, ppm (enol-to-ketone ratio 1 : 6): 1.30 t (3H + 3/6H, $CO_2CH_2C\mathbf{H}_3$, J = 7.0 Hz), 1.33–1.45 m (2H + 2/6H, CH_2), 1.53 d (3H + 3/6H, $CHC\mathbf{H}_3$, J = 7.0 Hz), 1.56–1.76 m (4H + 4/6H, $2CH_2$), 2.32 t [2H + 4/6H, $C\mathbf{H}_2CO_2Me$ (enol + ketone), $=C(OH)C\mathbf{H}_2$, J = 7.2 Hz], 2.62 t [2H, $C(O)CH_2$, J = 7.0 Hz], 3.52 s [2H, $C(O)CH_2C(O)O$], 3.67 s (3H + 3/6H, CO_2CH_3), 4.22 q (2H + 2/6H, $CO_2C\mathbf{H}_2CH_3$, J = 7.0 Hz), 5.10 s [1/6H, $C(OH){=}C\mathbf{H}C(O)O$], 5.14 q (1H + 1/6H, $C\mathbf{H}CH_3$, J = 7.0 Hz), 11.82 s (1/6H, OH, enol). IR spectrum, ν, cm^{-1}: 1640, 1670, 1730 sh, 1755.

Dieckmann cyclization of thermolysis products XVI and XVII by the action of tetrabutylammonium fluoride in THF. To 11.5 mmol of compound **XVI** or **XVII** we added under argon 25 ml of a 1 M solution of tetrabutylammonium fluoride (25 mmol) in THF, and the mixture was stirred at room temperature. When the reaction was complete (TLC), the solvent was removed under reduced pressure, and 40 ml of 10% hydrochloric acid was added to the residue. The aqueous phase was extracted with ether (5 × 25 ml). The combined extracts were dried over Na_2SO_4 and evaporated, and the residue was purified by column chromatography on silica gel using hexane–ether as eluent (gradient elution).

The yields, melting points, and spectral data of compounds **X** and **XVIII** thus obtained are given in Table 1.

Condensation of 3-acetyltetronic acids XIX and XX with methyl 4-formylbenzoate. 3-Acetyltetronic acids **XIX** and **XX** were prepared by the procedure described in [20]. A 20-mmol portion of compound **XIX** or **XX** was dissolved in 40 ml of dry benzene, and 2.96 ml (30 mmol) of piperidine and 2.95 g (18 mmol) of methyl 4-formylbenzoate were added. The mixture was heated for 5 h under reflux in a flask equipped with a Dean–Stark trap, and was left to stand overnight at room temperature. The solvent was distilled off under reduced pressure, and the residue was treated with 1 N hydrochloric acid to pH 2. The crystals of condensation product were filtered off, washed with some amount of 1 N hydrochloric acid and with water, dried in air, and recrystallized. The yields, melting points, and spectral data of compounds **XXI** and **XXII** thus obtained are given in Table 1.

3-Alkyl-substituted tetronic acids XXIII–XXIX (Table 2). *a. Reduction of 3-acyltetronic acids with triethylsilane in trifluoroacetic acid.* To a solution of 1 mmol of β-tricarbonyl compound in 5 ml of trifluoroacetic acid containing 1% of lithium perchlorate we added in portions 0.48 ml (3 mmol, in the reduction of 3-acyltetronic acids) or 0.64 ml (4 mmol, in the reduction of arylmethyleneacyltetronic acids) of triethylsilane, and the mixture was left overnight at room temperature. The solvent was distilled off under reduced pressure, and the residue was cooled and washed with several portions of cold hexane. After solidification, the cryctalline product was transferred to a filter, washed with water, dried in air, and recrystallized. Oily products were purified by column chromatography on silica gel using hexane–ether as eluent (gradient elution).

b. Reduction of 3-acyltetronic acids with sodium cyanotrihydridoborate in acetic acid. To a solution of 10 mmol of β-tricarbonyl compound in 15 ml of glacial acetic acid we added in portions under stirring at 0°C 1.26 g (20 mmol) of sodium cyanotrihydridoborate. When the entire amount of the reducing agent was added, the cooling bath was removed, and the mixture was stirred for 5 h at room temperature. If the product was a crystalline substance, the mixture

was poured onto ice (in a beaker), the overall volume was adjusted to 60 ml, and the mixture was acidified with 2 ml of concentrated hydrochloric acid. The mixture was cooled for several hours, and the product was filtered off, washed with water, dried in air, and purified by recrystallization. If the product was an oily substance, acetic acid was removed under reduced pressure, 50 ml of 1 N hydrochloric acid was added to the residue, and the mixture was extracted with chloroform. The extracts were dried over Na_2SO_4, filtered, and evaporated, and the residue was purified by column chromatography on silica gel using hexane–ether as eluent (gradient elution).

c. Reduction of 3-acyltetronic acids with sodium cyanotrihydridoborate in the system THF–2 N hydrochloric acid. To a solution of 1 mmol of β-tricarbonyl compound in 6 ml of THF we added under stirring 5 ml of 2 N hydrochloric acid. In some cases, the initial compound partially precipitated from the solution. To the resulting mixture (solution or suspension) we added under stirring in portions 0.16 g (2.5 mmol, in the reduction of 3-acyltetronic acids) or 0.22 g (3.5 mmol, in the reduction of 3-arylmethyleneacyltetronic acids) of sodium cyanotrihydridoborate. The mixture was stirred until the reaction was complete (TLC). By the end of the process, the mixture divided into two layers containing no solid species. The organic phase was separated, and the aqueous phase was estracted with ether or chloroform. The extracts were combined with the organic phase, dried over Na_2SO_4, and evaporated. Oily products were purified by column chromatography on silica gel. Poorly soluble crystalline products were isolated from the aqueous phase after evaporation of THF under reduced pressure. An additional amount was isolated from the aqueous phase by extraction with chloroform. Portions of the products isolated by filtration and extraction were combined and finally purified by recrystallization from appropriate solvent.

O-Alkylation of 3-alkyltetronic acids XXIV and XXVII with triethyloxonium tetrafluoroborate. To a solution of 2.5 mmol of 3-alkyltetronic acid **XXIV** or **XXVII** in 30 ml of methylene chloride we added under stirring 1.42 g (7.5 mmol) of triethyloxonium tetrafluoroborate. When the reaction was complete (TLC), the mixture was passed through a layer of silica gel using chloroform as eluent. The eluate was evaporated under reduced pressure, and the residue was subjected to chromatography in a short column charged with aluminum oxide using ether–hexane as eluent. The corresponding enol ethers were isolated as mobile oily substances.

5-Ethoxy-4-(6-methoxycarbonylhexyl)-2,3-dihydrofuran-3-one (XXX). Yield 81%. ^{1}H NMR spectrum, δ, ppm: 1.20–1.38 m (4H, $2CH_2$), 1.38–1.52 m (2H, CH_2), 1.44 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.0 Hz), 1.61 quint (2H, $C\mathbf{H}_2CH_2CO_2CH_3$, J = 7.0 Hz), 2.07 t (2H, CH_2, J = 7.0 Hz), 2.30 t (2H, $C\mathbf{H}_2CO_2CH_3$, J = 7.5 Hz), 3.66 s (3H, CO_2CH_3), 4.44 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.0 Hz), 4.53 s [2H, $OCH_2C(O)$, ring]. IR spectrum, ν, cm^{-1}: 1620, 1710, 1745. Mass spectrum, *m*/*z*: 270 [M^+].

5-Ethoxy-2-methyl-4-octyl-2,3-dihydrofuran-3-one (XXXI). Yield 89%. ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, CH_3, J = 6.5 Hz), 1.18–1.33 m (10H, $5CH_2$), 1.36–1.52 m (2H, CH_2), 1.42 t (3H, $OCH_2C\mathbf{H}_3$, J = 7.0 Hz), 1.48 d (3H, $CHC\mathbf{H}_3$, J = 7.0 Hz), 2.06 t (2H, CH_2, J = 7.5 Hz), 4.42 q (2H, $OC\mathbf{H}_2CH_3$, J = 7.0 Hz), 4.60 q (1H, $C\mathbf{H}CH_3$, J = 7.0 Hz). IR spectrum, ν, cm^{-1}: 1615, 1705. Mass spectrum, *m*/*z*: 254 [M^+].

Reduction of 4-alkyl-5-ethoxy-2,3-dihydrofuran-3-ones XXX and XXXI with diisobutylaluminum hydride. To a mixture of 1 mmol of enol ether **XXX** or **XXXI** and diethyl ether we added at –78°C under argon 1.5 ml of a 1 M solution of diisobutylaluminum hydride in hexane (1.5 mmol). The mixture was stirred at –78°C until the initial compound disappeared completely (TLC), 1.5 ml of water was added at that temperature, and the mixture was allowed to warm up to room temperature. To the resulting suspension we added 50 ml of ether, and the mixture was dried over $MgSO_4$. The drying agent was filtered off, the filtrate was evaporated, and the residue was purified by column chromatography on silica gel (hexane–ether, gradient elution). The yields and spectral parameters of compounds **XXXII** and **XXXIII** are given in Table 3.

4-(1-Pyrrolidinyl)-2,5-dihydrofuran-2-ones XXXIV–XXXIX. Pyrrolidine, 1 ml (12 mmol), was added dropwise under stirring to a suspension of 10 mmol of appropriate 3-alkyltetronic acid in 30 ml of toluene. The resulting mixture containing pyrrolidinium salt of β-dicarbonyl compound was heated for 5–8 h under reflux in a flask equipped with a Dean–Stark trap (to remove liberated water). The mixture was filtered, the solvent was distilled under reduced pressure, and the residue was purified by column chromatography on silica gel using chloroform as eluent. Enamino lactones **XXXIV–XXXIX** were isolated as viscous oily substances. Their yields and spectral parameters are given in Table 4.

2,5-Dihydrofuran-2-ones XXXII, XXXIII, and XLVI–XLIX. To a solution of 1 mmol of enamino

lactone **XXXIV**–**XXXIX** in 5 ml of methanol we added under stirring 0.5 mg of Methyl Orange and then several drops of a 6 N solution of HCl in methanol until the mixture turned bright red. Sodium cyanotrihydridoborate, 0.15 g (2.4 mmol), was added in portions, and a 6 N methanolic solution of HCl was added dropwise at such a rate that the bright red color of the mixture was maintained. The progress of the reaction was monitored by the rate of HCl absorption and by TLC. The solvent was removed under reduced pressure, 5 ml of water and 15 ml of diethyl ether were added to the residue, and a 1 N aqueous solution of sodium hydroxide was then added dropwise until the aqueous phase turned yellow. The organic phase was separated, and the aqueous phase was extracted with ether (2×10 ml). The extracts were combined with the aqueous phase and evaporated to dryness to obtain aminolactones **XL**–**XLV** as mixtures of diastereoisomers. Crude products **XL**–**XLV** were heated for 6–12 h in 10 ml of boiling toluene in the presence of 2 g of silica gel (until the initial compounds were completely converted into the corresponding butenolides, according to TLC). The mixture was filtered from silica gel, and the precipitate was washed with toluene (2×10 ml). The filtrate was combined with the washings and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel using hexane–ether as eluent (gradient elution). The yields and spectral parameters of compounds **XXXII**, **XXXIII**, and **XLVI**–**XLIX** are given in Table 3.

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