ISSN 1070-4280, Russian Journal of Organic Chemistry, 2008, Vol. 44, No. 5, pp. 657–670. © Pleiades Publishing, Ltd., 2008.
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Heterocyclic Analogs of Prostaglandines: IV.* Synthesis of 3,7-Interphenylene 3,10(11)-Dioxa-13-azaprostanoids and 9-Oxa-7-azaprostanoids Based on Tetronic Acid and Aromatic Aldehydes

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Received May 30, 2007

Abstract—An approach was developed to the synthesis of stable in metabolism 3,7-interphenylene 3,10-dioxa-13-aza- and 3,11-dioxa-13-azaprostanoids, and also 9-oxa-7-azaprostanoids with interphenylene and terminal phenyl fragments in the ω-chain based on 3-(alkoxybenzylidene)- and 3-(3-phenylallylidene)tetrahydrofuran-2,4-diones obtained by Knoevenagel condensation of tetronic acid with alkoxy-substituted aromatic aldehydes and cinnamic aldehyde.

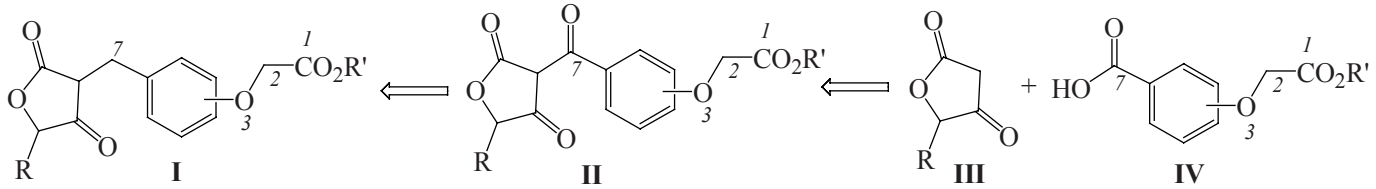
DOI: 10.1134/S1070428008050047

One of the principal shortcomings of natural prostaglandines and related eicosanoids for application as drugs is their metabolic instability and an excessively wide range of biological action. A significant place in the metabolic decomposition of eicosanoids takes the β-oxidation of the α-chain involving successive stages of eliminating two molecules of acetic acid yielding biologically inert dinor and tetranor derivatives [2]. Introducing an oxygen atom into the position *3* of the prostanic acid skeleton [3] or 3,7-interphenylene fragment, and also a replacement of the carboxy group by other finctional moieties [2] block the β- oxidation of the α-chain thus significantly increasing the metabolic stability of such prostanoids and related compounds without decrease in their activity in most cases.

We report here on the approach to the synthesis of stable in metabolism 3,7-interphenylene 3,10-dioxa-13-aza- and 3,11-dioxa-13-azaprostanoids, and also 9-oxa-7-azaprostanoids with interphenylene and terminal phenyl fragments in the ω-prostanoid chain based in tetronic acid. Prostanoids with a phenyl fragment in the ω-chain are widely used in veterinary practice [2], and also in ophthalmology (Latanoprost) in glaucoma treatment [3].

The most obvious approach to the synthesis of β-dicarbonyl precursors **I** of 3,7-interphenylene heteroprostanoids consists in preparation of the corresponding 3-benzoyltetrahydrofuran-2,4-diones **II** based on tetronic acids **III** and aromatic acids **IV** containing as a substituent the C^1–C^3 fragment of the α-prostanoid chain with subsequent selective hydrogenolysis of the carbonyl group in their acyl side chain. In thus obtained β-di-carbonyl precursors **I** the carbon atom of the carboxy group of aromatic acid becomes C^7 atom of the prostanic skeleton (in keeping with prostaglandine nomenclature), and the enolized cyclic β-dicarbonyl system is used further to form the ω-prostanoid chain (Scheme 1).

Scheme 1.



*For communication III, see [1].

The published data on the synthesis and properties of 3-benzoyltetronic acids are scanty [4]. Like the other cyclic β-tricarbonyl compounds the 3-benzoyltetronic acids can be obtained by the O–C-isomerization of the corresponding enol acylates [(5-oxo-2,5-dihydrofuran-3-yl)alkoxybenzoates]. However the classic isomerization catalysts [chlorides of aluminum, zinc, and tin, imidazole, 4-(dimethylamino)pyridine] are unsuitable for the synthesis of 2-aroylcycloalkane-1,3-diones [5] and their heterocyclic analogs. For the synthesis of 2-aroyl-cycloalkane-1,3-diones [5] and a series of their heterocyclic analogs [6] isomerization methods of the corresponding enol acylates were developed under the action of sources of cyanide ions (potassium cyanide, acetone cyanohydrin) leading to the formation of target triacylmethanes in high yields.

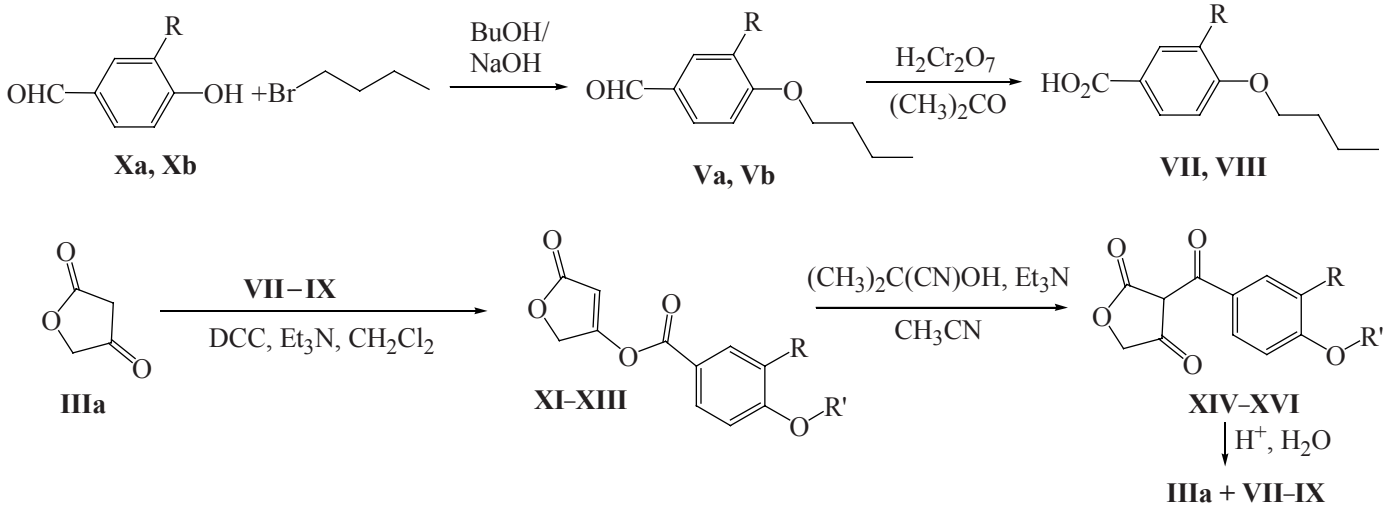
The reaction of tetronic acid **IIIa** with acids **VII** and **VIII** prepared by alkylating aldehydes **Xa** and **Xb** followed by Jones oxidation of the corresponding aldehydes **Va** and **Vb**, and also with *p*-methoxybenzoic acid (**IX**) by procedure [7] but without 4-(dimethylamino)pyridine led to the formation of the corresponding O-acyl derivatives **XI–XIII** in high yields. Enol acylates **XI–XIII** treated with acetone cyanohydrin in acetonitrile rearranged into 3-benzoyltetronic acids **XIV–XVI** as showed the characteristic coloration of spots at TLC analysis of the reaction mixtures when developed with iron(III) chloride. However these compounds suffer deacylation already at the workup of the reaction mixture and at further purification. Therefore we failed to obtain compounds **XIV** and **XV** in individual state. Only 3-(4-methoxybenzoyl)tetronic acid (**XVI**) was obtained in a pure state in a moderate yield. The structure of the latter was confirmed by ^{1}H NMR and IR spectra (Scheme 2).

At an attempt to reduce the carbonyl group of the benzoyl moiety in compound **XVI** by triethylsilane in trifluoroacetic acid as we had previously described for the other 3-acyltetronic acids [7] instead of the target β-dicarbonyl compound only deacylation products of the initial compound were found in the reaction mixture. Thus the instability of 3-benzoyltetronic acids impedes both their isolation in preparative quantity and further reduction under acid conditions.

In this connection we suggested for the synthesis of heterocyclic interphenyleneoxaprostanoids to use alternative to 3-benzoyltetronic acids 3-arylidenetetrahydrofuran-2,4-diones **XVIII** obtained by Knoevenagel condensation of tetronic acids with aromatic aldehydes [8–10]. Compounds **XVIII** under reduction are synthetically equivalent to the 3-benzoyltetronic acids since they should result in the same reaction products, 3-(alkoxybenzyl)tetronic acids **I**. In contrast to 3-arylidenetetrahydrofuran-2,4-diones **XVIII** their carbocyclic and some heterocyclic analogs are highly reactive and form only as intermediates in various multicomponent reactions involving β-dicarbonyl compounds and aromatic aldehydes [11].

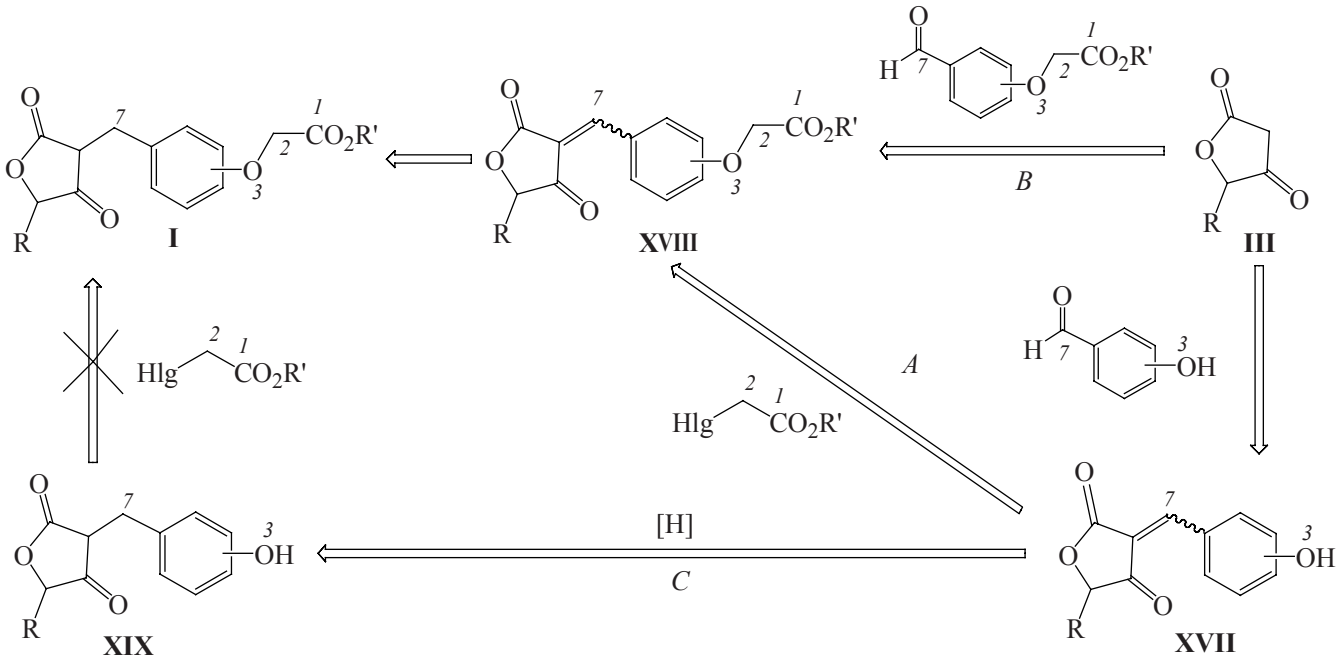
Compounds **XVIII** may be prepared in two ways: by condensation of hydroxyl-containing aromatic aldehydes with tetronic acids **III** with subsequent O-alkylation of hydroxybenzylidene derivatives **XVII** by a synthons

Scheme 2.



R = H (**Va,VII, Xa**), OCH_3 (**Vb,VIII, Xb**); R = H, R' = C_4H_9 (**XI, XIV**), CH_3 (**XIII, XVI**); R = OCH_3, R' = C_4H_9 (**XII, XV**).

Scheme 3.



of C^1–C^2-α-prostanoid chain (*A*), or by condensation of tetronic acids with aldehydes supplied with already formed structure of the interphenylene α-chain (*B*). The (*C*) version of the synthesis of key compounds **I** involving primary reduction of the cross-conjugated multiple bond in the hydroxybenzylidenetetronic acids **XVII** seems less probable for the O-alkylation of the reduction products **XIX** can occur both at the phenol hydroxy group and at the enolized cyclic β-dicarbonyl system (Scheme 3).

To test the probability of the way *A* tetronic acid **IIIa** was put into condensation with 4-hydroxybenzaldehyde (**Xa**) and vanillin (**Xb**) in the presence of concn. HCl [8] (Scheme 4). However we failed to obtain in this case the target hydroxybenzylidenetetrahydrofuran-2,4-diones **XX** and **XXI** for under the given conditions a tarring of the reaction mixture occurred. The replacement of HCl by *p*-toluenesulfonic acid also did not help to avoid tarring.

In [9] the Knoevenagel condensation of tetronic acid with a series of heteroaromatic aldehydes was performed in anhydrous ethanol. In this procedure the reaction was catalyzed by acid protons of the enolyzed cyclic β-dicarbonyl compound. The application of this method to 4-hydroxybenzaldehyde and vanillin showed that although the condensation of acid **IIIa** occurred with both aldehydes (as seen from the gradual change of the reaction mixture color from colorless to bright yellow), the reaction was fast enough only with vanillin proceeding with precipitation of reaction product **XXI** formed in 89% yield. We found that the hydroxybenzylidenetetronic acids **XX** and **XXI** formed in 40–47% yield at melting the tetronic acid with excess hydroxyaldehydes without catalyst. Presumably autocatalysis occurred also in this reaction.

We tried to alkylate compounds **XX** and **XXI** with butyl bromide in the presence of a base but failed to obtain the target 3-arylidenetetronic acids **XXIII** and **XXIV**. Under the given conditions the heterocycle of the initial substances suffered degradation.

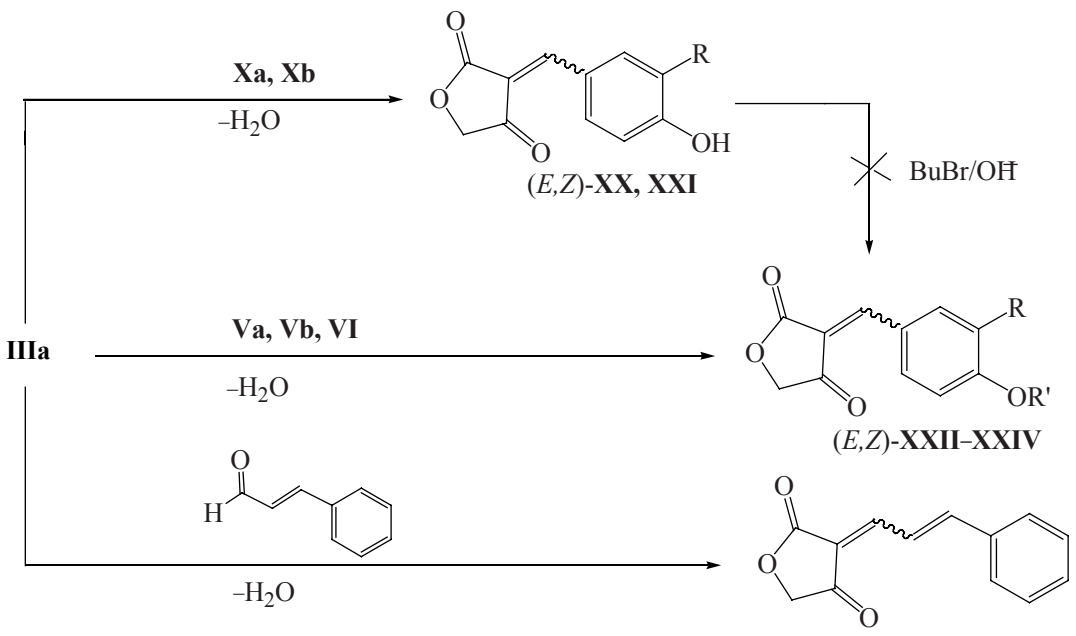
Unlike hydroxyaldehydes anisaldehyde (**VI**), 4-butoxybenzaldehyde (**Va**), and 4-butoxy-3-methoxybenzaldehyde (**Vb**) cleanly reacted with tetronic acid under the action of concn. HCl giving the corresponding alkoxybenzylidenetetronic acids **XXII–XXIV** in high yields.

The condensation of tetronic acid **IIIa** with cinnamic aldehyde easily proceeded both in the presence of concn. HCl and under autocatalysis conditions in methanol solution. In the latter case the yield of 3-(3-phenylallylidene)tetrahydrofuran-2,4-dione (**XXV**) was 56%.

From the above mentioned studies it was concluded that the building of the structure of the key β-dicarbonyl precursors **I** of interphenyleneoxaprostanoids should be more feasible to perform by condensation of tetronic acid with alkoxy derivatives of aromatic aldehydes.

Therefore we prepared by O-alkylation of phenolates of 4-hydroxybenzaldehyde, 3-hydroxybenzaldehyde, vanillin, and isovanillin with chloroacetic acid by method [12] formylphenoxyacetic acids **XXVI–XXIX**.

Scheme 4.

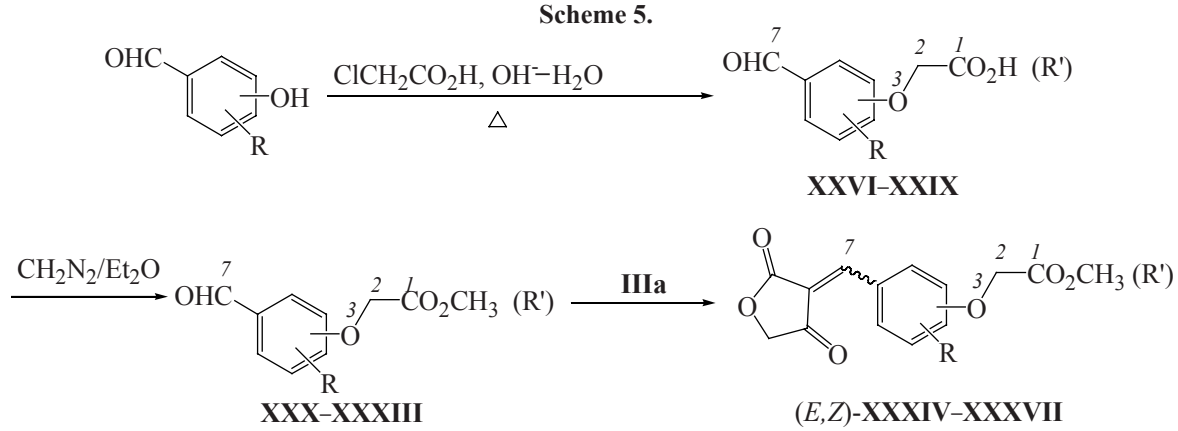


R = H (**XX**), OCH_3 (**XXI**); R = H, R' = CH_3 (**XXII**), C_4H_9 (**XXIII**); R = OCH_3, R' = C_4H_9 (**XXIV**).

The treatment of the latter with diazomethane led to the formation of methyl esters **XXX–XXXIII** (Scheme 5). Compounds **XXVI–XXXIII** are synthons for preparation 3-oxa-3,7-inter-*para*- or -*meta*-phenylene α-chains both of various type and substitution character of the aromatic ring. The residue of the acetic acid serves as a fragment C^1–C^2 of the α-chain, and the formyl group would be a binding unit between the α-chain and the cyclic part of the future prostanoid and C^7 atom of its carbon skeleton.

Among the esters of formylphenoxyacetic acids **XXX–XXXIII** only compound **XXXII** reacted with tetronic acid under autocatalytic conditions, and the condensation product **XXXVI** formed in 48% yield. It proved that the presence of an ester group in the oily methyl ester **XXXI** did not prevent the use of concn. HCl as a condensation agent, and the corresponding arylidene derivative **XXXV** was obtained in 65% yield. According to the ^{1}H NMR spectrum of compound **XXXV** it contained over 92% of ester. Inasmuch as under the action of concn. HCl the condensation proceeded readily only with liquid and difficultly crystallizable aldehydes in reactions of tetronic acid with solid esters of formylphenoxyacetic acids **XXX**

Scheme 5.



R = H, R' = *p*-OCH_2CO_2H (**XXVI**), *m*-OCH_2CO_2H (**XXVII**), *p*-$OCH_2CO_2CH_3$ (**XXX, XXXIV**), *m*-$OCH_2CO_2CH_3$ (**XXXI**, **XXXV**); R = *m*-OCH_3, R' = *p*-OCH_2CO_2H (**XXVIII**), *p*-$OCH_2CO_2CH_3$ (**XXXII, XXXVI**); R = *p*-OCH_3, R' = *m*-OCH_2CO_2H (**XXIX**), *m*-$OCH_2CO_2CH_3$ (**XXXIII, XXXVII**). (Position of R and R' in aromatic ring is indicated with respect to C^7-substituent).

and **XXXIII** we used as catalyst aluminum chloride (2 equiv) in THF [10]. The instability of the ester group in the course of reaction mixture workup for neutralization of the catalyst reduced the yield of condensation products **XXXIV** and **XXXVII** to 27–29%.

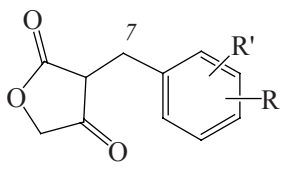
A double set of some signals in the ^{1}H and ^{13}C NMR spectra of 3-arylidenetetronic acids **XX–XXIV**, **XXXIV–XXXVII** indicates that these compounds are mixtures of *E*- and *Z*-isomers. In the ^{1}H NMR spectra the greatest difference in the chemical shifts (Δ 0.11–0.12 ppm) is observed for the singlets of methylene group protons of the heterocycle of both isomers in the region 4.60–4.76 ppm. The measuring of the ratio of integral intensity of these signals indicated that the ratio of geometrical isomers of compounds **XX–XXIV**, **XXXIV–XXXVII** in the mixture equaled ~1:2. In the case of 3-(3-phenylallylidene)tetronic acid (**XXV**) the ratio of (*E,E*)- and (*Z,E*)-isomers in the mixture was ~ 1:1. The ratio in the mixture of isomers of the cited compounds virtually did not depend on the method of their preparation.

The final stage of building up the 3,7-interphenylene α-prostanoid chain involves the reduction of the activated exocyclic cross-conjugated (*E,Z*)-double bond of the mixture of isomeric 3-aryloxybenzylidenetetronic acids **XXII–XXIV, XXXIV–XXXVII**. To this end we applied the methods developed for selective hydrogenolysis of a carbonyl group of the acyl side chain of cyclic β-tricarbonyl compounds: the treatment with triethylsilane in trifluoroacetic acid (method *a*) and with the sodium cyanoborohydride in a system THF–2 N aqueous HCl (method *b*) [7].

As expected, the cross-conjugated double bond of compounds **XXII–XXIV, XXXIV–XXXVII** selectively and equally efficiently was reduced by both methods; therewith the reaction by method *a* did not require catalysis by Lewis acids.

(*E,Z*)-**XXII**–**XXIV, XXXIV**–**XXXVII**

Et_3SiH, CF_3CO_2H (*a*),
$NaBH_3CN$/ THF
2 N aqueous HCl (*b*)



XXXVIII–**XLIV**

R = H, R' = *p*-OCH_3 (**XXII, XXXVIII**), *p*-OC_4H_9 (**XXIII, XXXIX**), *p*-$OCH_2CO_2CH_3$ (**XXXIV, XLI**), *m*-$OCH_2CO_2CH_3$ (**XXXV**, **XLII**); R = *m*-OCH_3, R' = *p*-OC_4H_9 (**XXIV, XL**), *p*-$OCH_2CO_2CH_3$ (**XXXVI, XLIII**); R = *p*-OCH_3, R' = *m*-$OCH_2CO_2CH_3$ (**XXXVII, XLIV**).

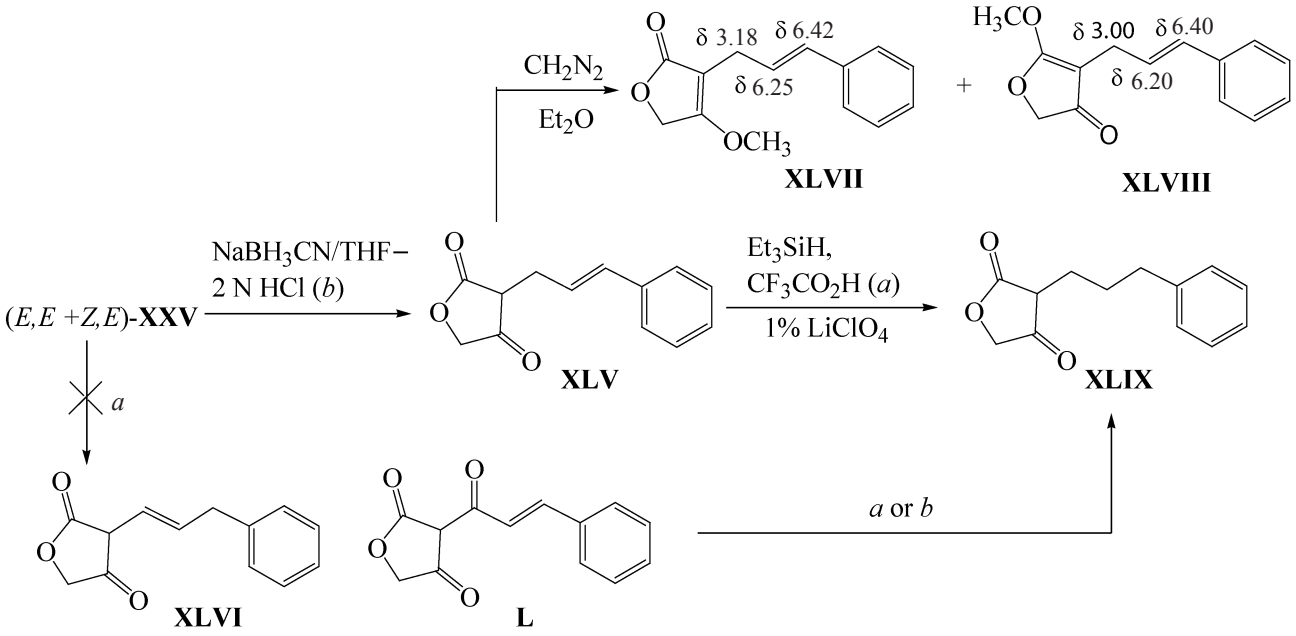
The reduction of compounds **XXXIV** and **XXXVII** by method *b* is complicated by the hydrolysis of ester group; however the process under controlled conditions followed by a fast workup of the reaction mixture provided the corresponding esters in good yield. For instance, ester **XLII** was thus obtained in 59% yield.

Unlike 3-arylidenetetronic acids **XXII–XXIV, XXXIV–XXXVII** 3-(3-phenylallylidene)tetronic acid **XXV** containing two conjugated multiple bonds in the side chain under the treatment with triethylsilane in trifluoroacetic acid was converted in to intractable mixture of substances. Yet the reaction of compound **XXV** with the sodium cyanoborohydride in a mixture of THF with 2 N aqueous HCl yielded a product of reduction of one double bond of the side chain. Hypothetically the partial reduction of the 1,3-diene system of 3-(3-phenylallylidene)tetronic acid **XXV** may result in 3-cinnamyltetronic acid (**XLV**) or in its regioisomer 3-(3-phenylpropen-1-yl)tetronic acid **XLVI**. However the ^{1}H NMR and IR spectra do not unambiguously indicate the position of the double bond.

To establish the location of the double bond the reduction product was treated with diazomethane, and we obtained a mixture (~2:1) of regioisomeric enol methyl ethers **XLVII** and **XLVIII**. In the ^{1}H NMR spectrum of the mixture the greatest difference in the chemical shifts is observed for the doublets of the protons of the methylene group in the side chain of both isomers (Δδ 0.18 ppm), whereas Δδ of the doublet of triplets belonging to vinyl proton contiguous to the methylene group amounts to 0.05 ppm, and Δδ of the doublets of the second vinyl proton is 0.02 ppm. Hence the methylene group of the chain in the mentioned enol ethers is adjacent to the chemically modified heterocyclic β-dicarbonyl system. This fact unambiguously testifies to structure **XLV** of their precursor and not to structure **XLVI** where the methylene group is maximally remote from the heterocycle.

The reaction of 3-cinnamyltetronic acid (**XLV**) with triethylsilane in trifluoroacetic acid led to the formation of 3-(3-phenylpropyl)tetronic acid (**XLIX**) in 79% yield. Hence the reduction of the double bond of the cinnamyl fragment of compound **XLV** is related to the increase in the acidity of the reaction medium. Apparently these experiments suggest that by varying the pH of the medium it would be possible to control the degree of selectivity of reduction with cyanoborohydride system of the diene moiety in the 3-(3-phenylallylidene)tetronic acid (**XXV**). However the increase in HCl concentration from 2N to 12N in the reaction mixture during compound **XXV**

Scheme 6.



reduction with sodium cyanoborohydride did not result in formation even of traces of 3-(3-phenylpropyl)tetronic acid (**XLIX**), and the only product was compound **XLV** (Scheme 6).

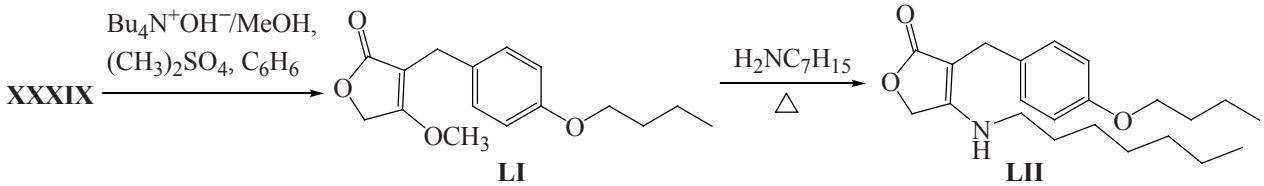
The results obtained are totally different from the results of reduction of 3-cinnamoyltetronic acid (**L**). The reduction of compound **L** both by method *a* and method *b* using 2N HCl involved the hydrogenolysis of the carbonyl group and the reduction of the double bond of the acyl chain conjugated with the carbonyl resulting in a high yield of 3-(3-phenylpropyl)tetronic acid (**XLIX**) as the only reaction product.

3-Arylalkyl-substituted tetrahydrofuran-2,4-diones **XXXVIII–XLV** and **XLIX** possess the β-dicarbonyl system of the initial tetronic acid indispensable for building in the nitrogen-containing ω-prostanoid chains. The methods of introducing these chains into the β-dicarbonyl precursors of heteroprostanoids were described in detail in the previous communication [1]. Here we consider some important examples.

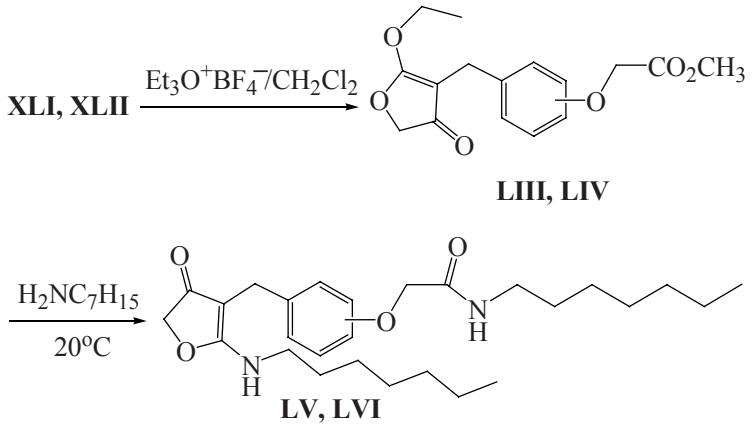
The alkylation of 3-(4-butoxybenzyl)tetronic acid tetrabutylammonium salt (**XXXIX**) with dimethyl sulfate led to the formation of 4-methoxy derivative **LI**. The boiling of the latter with heptylamine gave 3,7-interphenylene 3,10-dioxa-13-azaprostanoid (**LII**) without a characteristic for natural prostaglandines terminal carboxy group in the α-chain (Scheme 7).

The stringent conditions of the reaction between 4-methoxy derivatives of tetrahydrofuran-2,4-diones and amines hamper the preparation of 10-oxa-13-azaprostanoids with an ester group in the α-chain, for in this event the amine competitively reacts with the latter. In contrast to 4-methoxy-2,5-dihydrofuran-2-ones the 5-ethoxy-2,3-dihydrofuran-3-ones obtained by treating the corresponding 3-substituted tetronic acids with triethyloxonium tetrafluoroborate cleanly react with amines at room temperature providing in high yield 11-oxa-13-aza-prostanoids with an ester group in the α-chain [1]. A phenoxy group in the interphenylene α-chain of the obtained prostanoid precursors activates

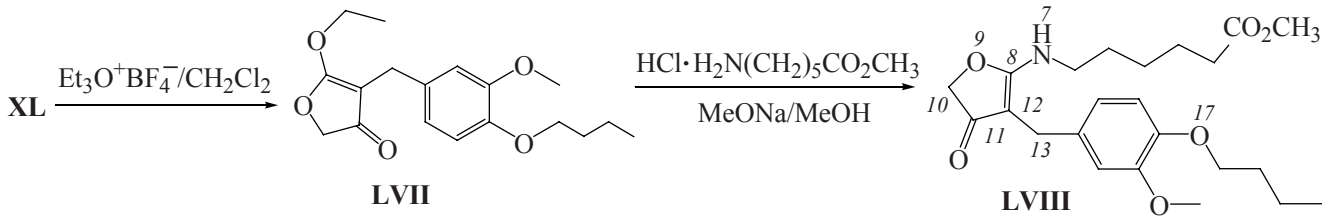
Scheme 7.



Scheme 8.



Scheme 9.



the ester group that reacts with amine even at room temperature. For instance, reaction of compounds **LIII** and **LIV** with heptylamine led to the formation of products **LV** and **LVI** originating from the amine attack on two reaction centers in 58 and 47% yield respectively (Scheme 8).

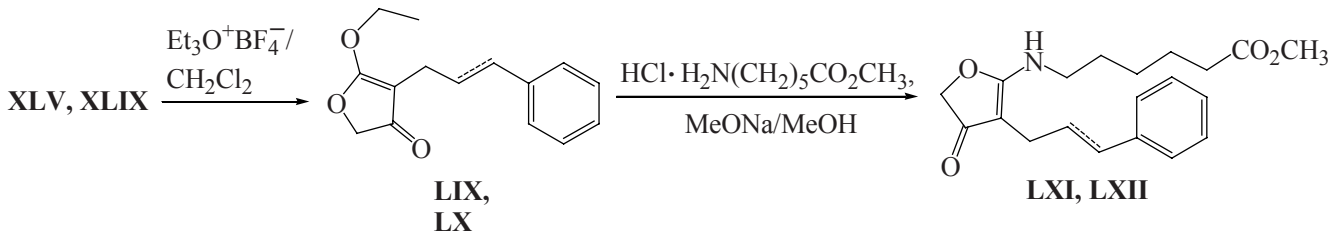
The use as a source of amino group amino acids esters in the reaction with 4-substituted 5-ethoxy-2,3-dihydrofuran-3-ones results in 9-oxa-7-azaprostanoids. For instance, the reaction of enol derivative **LVII** with methyl ε-aminocaproate gave 9,17-dioxa-7-aza-13,17-inter-*p*-phenylene prostanoid (**LVIII**) (Scheme 9).

In its turn the reaction of 5-ethoxy-2,3-dihydrofuran-3-ones **LIX** and **LX** with methyl ε-aminocaproate resulted in 9-oxa-7-azaprostanoids **LXI** and **LXII** with a benzene ring in the ω-chain of various degree of saturation (Scheme 10).

EXPERIMENTAL

Melting points of compounds obtained were measured on a Boëtius heating block. IR spectra were recorded on a spectrophotometer UR-20 from samples in films or pellets with KBr. ^{1}H (500 MHz) and ^{13}C (125.7 MHz) NMR spectra were registered on a spectrometer Bruker Avance-500, internal reference TMS. Mass spectra were taken on MKh-1320 instrument at ionizing electrons energy 70 eV.

Scheme 10.



LIII, *p*-$OCH_2CO_2CH_3$, LIV, *m*-$OCH_2CO_2CH_3$, **LV**, *p*-$OCH_2CONHC_7H_{15}$, **LVI**, *m*-$OCH_2CONHC_7H_{15}$.

4-Butoxybenzaldehyde (**Va**) and 4-butoxy-3-methoxybenzaldehyde (**Vb**) were prepared by boiling phenolates of 4-hydroxybenzaldehyde (**Xa**) and vanillin (**Xb**) with butyl bromide in 1-butanol in 80 and 81% yield respectively. 4-Butoxybenzoic acid (**VII**) and 4-butoxy-3-methoxybenzoic acid (**VIII**) were obtained by oxidation of compounds **Va** and **Vb** with Jones reagent in 54–58% yield.

The synthesis of 5-oxo-2,5-dihydrofuran-3-ylalkoxy-benzoates **XI–XIII** were performed by a published procedure [7] except for the use of 4-(dimethylamino)pyridine.

5-Oxo-2,5-dihydrofuran-3-yl-4-butoxybenzoate (XI). Yield 67%, mp 89–91°C (from ethyl acetate). IR spectrum, cm^{-1}: 1260 (max), 1610, 1630, 1750 sh, 1760, 1780. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.00 t [3H, $O(CH_2)_3C\underline{H}_3$, ^3J 7.5 Hz], 1.51 sextet [2H, $O(CH_2)_2C\underline{H}_2CH_3$, ^3J 7.5 Hz], 1.81 quintet (2H, $OCH_2C\underline{H}_2CH_2CH_3$, ^3J 7.0 Hz), 4.06 t [2H, $OC\underline{H}_2(CH_2)_2CH_3$, ^3J 6.5 Hz], 5.06 narrow d (2H, CH_2 of cycle, ^4J 1.0 Hz), 6.11 narrow t ($1H_{vinyl}$, ^4J 1.0 Hz), 6.98 d ($2H_{arom}$, ^3J 8.5 Hz), 8.05 d ($2H_{arom}$, ^3J 8.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.8 (CH_3), 19.2 (CH_2), 31.0 (CH_2), 68.2 (CH_2), 68.8 (CH_2), 100.6 (CH), 114.8 (2CH), 118.7 (C), 132.9 (2CH), 161.3 (C), 164.7 (C), 169.5 (C), 172.6 (C). Found, %: C 65.07; H 5.79. $[M]^+$ 276. $C_{15}H_{16}O_5$. Calculated, %: C 65.21; H 5.84.

5-Oxo-2,5-dihydrofuran-3-yl-4-butoxy-3-methoxybenzoate (XII). Yield 70%, mp 110–112°C (from ether). IR spectrum, cm^{-1}: 1275 (max), 1605, 1630, 1745, 1765, 1775 sh. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.00 t [3H, $O(CH_2)_3C\underline{H}_3$, ^3J 7.5 Hz], 1.52 sextet [2H, $O(CH_2)_2C\underline{H}_2CH_3$, ^3J 7.5 Hz], 1.88 quintet (2H, $OCH_2C\underline{H}_2CH_2CH_3$, ^3J 7.0 Hz), 3.94 s (3H, OCH_3), 4.12 t [2H, $OC\underline{H}_2(CH_2)_2CH_3$, J 6.5 Hz], 5.06 narrow d (2H, CH_2 of cycle, ^4J 1.5 Hz), 6.11 narrow t ($1H_{vinyl}$, ^4J 1.5 Hz), 6.94 d ($1H^5_{arom}$, ^3J 8.5 Hz), 7.54 narrow d ($1H^2_{arom}$, ^4J 2.5 Hz), 7.75 d.d ($1H^6_{arom}$, ^3J 8.5, ^4J 2.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.8 (CH_3), 19.1 (CH_2), 30.9 (CH_2), 56.2 (CH_3), 68.8 (CH_2), 68.9 (CH_2), 100.7 (CH), 111.5 (CH), 112.8 (CH), 118.7 (C), 125.3 (CH), 149.4 (C), 154.6 (C), 161.4 (C), 169.5 (C), 172.5 (C). Found, %: C 62.59; H 5.87. $[M]^+$ 306. $C_{16}H_{18}O_6$. Calculated, %: C 62.74; H 5.92.

5-Oxo-2,5-dihydrofuran-3-yl-4-methoxybenzoate (XIII). Yield 75%, mp 117–119°C (from ether). IR spectrum, cm^{-1}: 1255 (max), 1610, 1630, 1750, 1770. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.91 s (3H, OCH_3), 5.06 nar-row d (2H, CH_2, ^4J 1.5 Hz), 6.12 narrow t ($1H_{vinyl}$, ^4J 1.5 Hz), 7.00 d ($2H_{arom}$, ^3J 9.0 Hz), 8.07 d ($2H_{arom}$, ^3J 9.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 55.7 (CH_3), 68.7 (CH_2), 100.6 (CH), 114.4 (2CH), 119.0 (C), 132.9 (2CH), 161.3 (C), 165.1 (C), 169.5 (C), 172.5 (C). Found, %: C 61.43; H 4.23. $[M]^+$ 234. $C_{12}H_{10}O_5$. Calculated, %: C 61.54; H 4.30.

Izomerization of 5-oxo-2,5-dihydrofuran-3-yl-alkoxybenzoates XI–XIII under the action of acetone cyanohydrin. To a solution of 12 mmol of enol acylate **XI–XIII** in 10 ml of CH_3CN was added 24 mmol of Et_3N and 0.4 ml of acetone cyanohydrin. The reaction mixture was stirred at room temperature for 24 h. The acetonitrile was removed in a vacuum, the residue was treated with 25 ml of 1.5 N HCl, the reaction product was extracted from the water phase into chloroform (3×30 ml). The combined extracts were washed with water and dried over Na_2SO_4. After filtration and evaporation of the solvent in a vacuum the residue was recrystallized from ethyl acetate.

3-(4-Methoxybenzoyl)tetrahydrofuran-2,4-dione (XVI). Yield 45%, mp 126–128°C (from ethyl acetate). IR spectrum, cm^{-1}: 1515, 1545, 1590, 1615, 1685, 1750. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.92 s (3H, OCH_3), 4.67 br.s (2H, CH_2), 7.01 d ($2H_{arom}$, ^3J 9.0 Hz), 8.49 d ($2H_{arom}$, ^3J 9.0 Hz).

Formylphenoxyacetic acids **XXVI–XXIX** were prepared by procedure [12] in 49–59% yield. Methyl esters of formylphenoxyacetic acids **XXX–XXXIII** were obtained in 98–99% yield treating compounds **XXVI–XXIX** with diazomethane solution in ether.

Condensation of tetronic acid IIIa with substituted aromatic aldehydes by Knoevenagel reaction. *a*. To a dispersion of 0.2 g (2 mmol) of tetronic acid in 6 mmol of an appropriate aldehyde was added at stirring 0.18 ml (2.2 mmol) of concn. HCl. After 2 h the solid reaction product was dispersed in ethyl ether. After cooling the dispersion to 0°C the precipitate was filtered off, washed with ether, then with distilled water, dried in air, and recrystallized.

b. A solution of 0.5 g (5 mmol) of tetronic acid and 15 mmol of aromatic aldehyde in 5 ml of anhydrous methanol was stirred for 24–48 h at room temperature. The solid reaction product was filtered off, washed with ethyl ether, dried in air, and recrystallized.

c. A mixture of 0.3 g (3 mmol) of tetronic acid and 9 mmol of hydroxyl-containing aromatic aldehyde was heated at stirring till the reaction mixture melted. After the formation of water drops on the walls of reactor ended the reaction mixture was cooled to room temperature. The solid residue was washed with ethyl ether and recrystallized.

d. To a mixture of 0.54 g (5.4 mmol) of tetronic acid and 5.7 mmol of aromatic aldehyde in 35 ml of THF was added in one portion 1.42 g (10.6 mmol) of anhydrous aluminum chloride. The reaction mixture was stirred for 46 h at room temperature. The solid product was filtered off, dried in air, and recrystallized. The treatment of the organic phase with Na_2CO_3 along procedure [10] did not provide additional portion of the condensation product.

(*E,Z*)-3-(4-Hydroxybenzylidene)tetrahydrofuran-2,4-dione (XX). Yield 40% (*c*). IR spectrum, cm^{-1}: 1175 (max), 1560, 1585 sh, 1625, 1705, 1750. ^{1}H NMR spectrum ($CDCl_3$+CD_3OD), δ, ppm: 3.95 br.s (1H, OH_{phenol}), 4.62 s (1.4H, CH_2) and 4.73 s (0.6H, CH_2), 6.96 d (2H$_{arom}$, ^3J 9.0 Hz), 7.90 s (0.7H, H_{vinyl}) and 7.94 s (0.3H, H_{vinyl}), 8.50 d (2H$_{arom}$, ^3J 9.0 Hz). Found, %: C 64.58; H 3.87. $[M]^+$ 204. $C_{11}H_8O_4$. Calculated, %: C 64.71; H 3.95.

(*E,Z*)-3-(4-Hydroxy-3-methoxybenzylidene)-tetrahydrofuran-2,4-dione (XXI). Yield 89 (*a*), 47% (*b*). IR spectrum, cm^{-1}: 1175, 1570 (max), 1620, 1700, 1750. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.04 s (1.05H, OCH_3) and 4.07 s (1.95H, OCH_3), 4.61 s (1.3H, CH_2) and 4.73 s (0.7H, CH_2), 7.04 d and 7.05 d (1H, H$^5_{arom}$, ^3J 8.5 Hz), 7.64 d.d (0.35H$^6_{arom}$, ^3J 8.5, ^4J 2.0 Hz) and 7.69 d.d (0.65H$^6_{arom}$, ^3J 8.5, ^4J 2.0 Hz), 7.92 s (0.65H, H_{vinyl}) and 7.93 s (0.35H, H_{vinyl}), 8.86 d (0.65H, H$^2_{arom}$, ^4J 2.0 Hz) and 8.94 d (0.35H, H$^2_{arom}$, ^4J 2.0 Hz). Found, %: C 61.46; H 4.21. $[M]^+$ 234. $C_{12}H_{10}O_5$. Calculated, %: C 61.54; H 4.30.

(*E,Z*)-3-(4-Methoxybenzylidene)tetrahydrofuran-2,4-dione (XXII). Yield 66% (*a*). IR spectrum, cm^{-1}: 1170, 1570 sh, 1585 (max), 1625, 1705, 1755. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.94 s (1.05H, OCH_3) and 3.95 s (1.95H, OCH_3), 4.61 Cs(1.3H, CH_2) and 4.72 s (0.7H, CH_2), 7.04 d (2H$_{arom}$, ^3J 9.0 Hz), 7.93 s (0.65H, H_{vinyl}) and 7.95 s (0.35H, H_{vinyl}), 8.55 d and 8.56 d (2H$_{arom}$, ^3J 9.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 55.8 (2CH_3), 71.6 (CH_2), 72.6 (CH_2), 113.6 (C), 113.8 (C), 114.8 (2CH), 114.9 (2CH), 125.2 (C), 126.5 (C), 138.2 (2CH), 139.2 (2CH), 153.4 (CH), 155.6 (CH), 165.8 (C), 166.1 (C), 168.0 (C), 170.9 (C), 194.4 (C), 196.5 (C). Found, %: C 65.93; H 4.50. $[M]^+$ 218. $C_{12}H_{10}O_4$. Calculated, %: C 66.05; H 4.62.

(*E,Z*)-3-(4-Butoxybenzylidene)tetrahydrofuran-2,4-dione (XXIII). Yield 71% (*a*). IR spectrum, cm^{-1}: 1175, 1560 (max), 1585 (max), 1615, 1715, 1765. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.00 t [3H, O(CH$_2$)$_3$C<u>H</u>$_3$, ^3J 7.5 Hz], 1.52 sextet [2H, O(CH$_2$)$_2$C<u>H</u>$_2$CH$_3$, ^3J 7.5 Hz], 1.82 quintet (2H, OCH$_2$C<u>H</u>$_2$CH$_2$CH$_3$, ^3J 7.0 Hz), 4.10 t, 4.11 t [2H, OC<u>H</u>$_2$(CH$_2$)$_2$CH$_3$, ^3J 6.5 Hz], 4.60 s (1.3H, CH_2 of cycle) and 4.71 s (0.7H, CH_2 of cycle), 7.01 d (2H$_{arom}$, ^3J 9.0 Hz), 7.92 s (0.65H, H_{vinyl}) and 7.94 s (0.35H, H_{vinyl}), 8.53 d and 8.54 d (2H$_{arom}$, ^3J 9.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.8 (2CH_3), 19.1 (2CH_2), 31.0 (2CH_2), 68.5 (2CH_2), 71.6 (CH_2), 72.6 (CH_2), 113.3 (C), 113.5 (C), 115.2 (2CH), 115.4 (2CH), 125.0 (C), 126.3 (C), 138.3 (2CH), 139.3 (2CH), 153.5 (CH), 155.6 (CH), 165.5 (C), 165.9 (C), 168.2 (C), 171.1 (C), 194.4 (C), 196.5 (C). Found, %: C 69.12; H 6.16. $[M]^+$ 260. $C_{15}H_{16}O_4$. Calculated, %: C 69.22; H 6.20.

(*E,Z*)-3-(4-Butoxy-3-methoxybenzylidene)tetrahydrofuran-2,4-dione (XXIV). Yield 79% (*a*). IR spectrum, cm^{-1}: 1165, 1575 br, 1615, 1705, 1765. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.00 t [3H, O(CH$_2$)$_3$C<u>H</u>$_3$, ^3J 7.5 Hz], 1.52 sextet [2H, O(CH$_2$)$_2$C<u>H</u>$_2$CH$_3$, ^3J 7.5 Hz], 1.89 quintet (2H, OCH$_2$C<u>H</u>$_2$CH$_2$CH$_3$, ^3J 7.0 Hz), 3.98 s (1.05H, OCH_3) and 4.01 s (1.95H, OCH_3), 4.16 t and 4.17 t [2H, OC<u>H</u>$_2$(CH$_2$)$_2$CH$_3$, ^3J 6.5 Hz], 4.60 s (1.3H, CH_2 of cycle) and 4.72 s (0.7H, CH_2 of cycle), 6.96 d (0.35H, H$^5_{arom}$, ^3J 8.0 Hz) and 6.97 d (0.65H, H$^5_{arom}$, ^3J 8.5 Hz), 7.74 br.d (0.35H, H$^6_{arom}$, ^3J 8.0 Hz) and 7.76 br.d (1H, H$^6_{arom}$, ^3J 8.5 Hz), 7.90 s (0.65H, H_{vinyl}) and 7.91 s (0.35H, H_{vinyl}), 8.74 br.s (0.65H, H$^2_{arom}$) and 8.79 br.s (0.35H, H$^2_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.8 (2CH_3), 19.1 (2CH_2), 30.8 (2CH_2), 56.1 (2CH_3), 69.1 (2CH_2), 71.6 (CH_2), 72.7 (CH_2), 111.7 (2CH), 113.1 (C), 113.4 (C), 115.8 (CH), 116.7 (CH), 125.4 (C), 126.7 (C), 133.1 (CH), 134.2 (CH), 149.2 (C), 149.4 (C), 154.0 (CH), 155.7 (C), 156.1 (C), 156.3 (CH), 168.5 (C), 171.2 (C), 194.6 (C), 196.5 (C). Found, %: C 66.03; H 6.19. $[M]^+$ 290. $C_{16}H_{18}O_5$. Calculated, %: C 66.19; H 6.25.

(*E,Z*)-3-[(*E*)-3-Phenylallylidene]tetrahydrofuran-2,4-dione (XXV). Yield 81 (*a*), 56% (*b*). IR spectrum, cm^{-1}: 1180, 1590 (max), 1610 (max), 1645 sh, 1715, 1770. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.59 s (1.1H, CH_2) and 4.64 s (0.9H, CH_2), 7.42–7.55 m (3H$_{arom}$ + H_{vinyl}), 7.69 d (2H, H$^2_{arom}$+H$^6_{arom}$, ^3J 7.0 Hz), 7.74 d (0.55H, H_{vinyl}, ^3J 12.0 Hz) and 7.80 d (0.45H, H_{vinyl}, ^3J 12.0 Hz), 8.27 d.d and 8.32 d.d [1H_{vinyl}, $^3J_1$ 15.0 (8.27), 15.5 (8.32), $^3J_2$ 12.0 Hz]. ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 72.1 (CH_2), 72.3 (CH_2), 115.4 (C), 115.7 (C), 122.8 (CH), 123.2 (CH), 129.3 (4CH), 129.5 (4CH), 132.3 (2CH), 134.7 (C), 134.9 (C), 151.7 (CH), 153.2 (CH), 155.7 (CH), 156.0 (CH), 167.9 (C), 169.3 (C), 195.6 (C), 195.8 (C). Found, %: C 72.80; H 4.61. $[M]^+$ 214. $C_{13}H_{10}O_3$. Calculated, %: C 72.89; H 4.71.

(*E,Z*)-Methyl 2-{4-[(2,4-dioxodihydrofuran-3(2*H*)-ylidene)methyl]phenoxy}acetate (XXXIV). Yield 29% (*d*). IR spectrum, cm^{-1}: 1170, 1570, 1590 (max), 1620, 1700, 1745, 1755. ^{1}H NMR spectrum ($CDCl_3$+CD_3OD), δ, ppm: 3.85 s (3H, CO_2CH_3), 4.65 s (1.4H, CH_2 of cycle) and 4.76 s (0.6H, CH_2 of cycle), 4.83 br.s (2H, OCH_2CO_2Me), 7.06 d (2H$_{arom}$, ^3J 8.5 Hz), 7.94 s (0.7H, H$_{vinyl}$) and 7.97 s (0.3H, H$_{vinyl}$), 8.57 d (2H$_{arom}$, ^3J 8.5 Hz). ^{13}C NMR spectrum ($CDCl_3$+CD_3OD), δ, ppm: 52.7 ($2CH_3$), 65.3 ($2CH_2$), 72.1 (CH_2), 73.1 (CH_2), 114.5 (C), 114.7 (C), 115.5 (2CH), 115.6 (2CH), 126.2 (C), 127.5 (C), 138.4 (2CH), 139.3 (2CH), 153.7 (CH), 155.7 (CH), 163.9 (C), 164.3 (C), 169.0 (3C), 171.7 (C), 194.8 (C), 197.0 (C). Found, %: C 60.69; H 4.29. $[M]^+$ 276. $C_{14}H_{12}O_6$. Calculated, %: C 60.87; H 4.38.

(*E,Z*)-Methyl 2-{3-[(2,4-dioxodihydrofuran-3(2*H*)-ylidene)methyl]phenoxy}acetate (XXXV). Yield 65% (*a*). IR spectrum, cm^{-1}: 1170 (max), 1590, 1615, 1715, 1775. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.84 s and 3.85 s (3H, CO_2CH_3), 4.64 s (1.4H, CH_2 of cycle) and 4.75 s (0.6H, CH_2 of cycle), 4.76 s (0.6H, OCH_2CO_2Me) and 4.78 s (1.4H, OCH_2CO_2Me), 7.26–7.31 m (1H, H$^4_{arom}$), 7.45 t and 7.47 t (1H, H$^5_{arom}$, ^3J 8.0 Hz), 7.76 br.d (1H, H$^6_{arom}$, ^3J 7.5 Hz), 7.96 s and 7.97 s (1H, H$_{vinyl}$), 8.42 narrow t (0.7H, H$^2_{arom}$, ^4J 2.0 Hz) and 8.46 narrow t (0.3H, H$^2_{arom}$, ^4J 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 52.4 ($2CH_3$), 65.1 (CH_2), 65.2 (CH_2), 71.8 (CH_2), 72.8 (CH_2), 116.9 (CH), 117.2 (C), 117.3 (C), 118.0 (CH), 123.6 (CH), 124.0 (CH), 129.6 (CH), 130.2 (CH), 130.3 (CH), 130.6 (CH), 133.0 (C), 134.0 (C), 153.7 (CH), 156.0 (CH), 158.1 (2C), 168.9 (3C), 169.7 (C), 194.4 (C), 196.0 (C). Found, %: C 60.79; H 4.33. $[M]^+$ 276. $C_{14}H_{12}O_6$. Calculated, %: C 60.87; H 4.38.

(*E,Z*)-Methyl 2-{4-[(2,4-dioxodihydrofuran-3(2*H*)-ylidene)methyl]-2-methoxyphenoxy}acetate (XXXVI). Yield 48% (*b*). IR spectrum, cm^{-1}: 1165, 1570, 1585, 1610, 1710, 1760, 1770. ^{1}H NMR spectrum ($CDCl_3$ + CD_3OD), δ, ppm: 3.84 s (3H, CO_2CH_3), 4.01 s (1.05H, OCH_3) and 4.04 s (1.95H, OCH_3), 4.64 s (1.3H, CH_2 of cycle) and 4.76 s (0.7H, CH_2 of cycle), 4.86 s and 4.87 s (2H, OCH_2CO_2Me), 6.88 d and 6.89 d (1H, H$^6_{arom}$, ^3J 8.5 Hz), 7.75 d.d and 7.77 d.d (1H, H$^5_{arom}$, ^3J 8.5, ^4J 2.0 Hz), 7.92 s (0.65H, H$_{vinyl}$) and 7.94 s (0.35H, H$_{vinyl}$), 8.76 d (0.65H, H$^3_{arom}$, ^4J 2.0 Hz) and 8.80 d (0.35H, H$^3_{arom}$, ^4J 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$ + CD_3OD), δ, ppm: 52.7 ($2CH_3$), 56.3 ($2CH_3$), 65.7 ($2CH_2$), 71.9 (CH_2), 72.9 (CH_2), 112.5 (2CH), 114.3 (C), 114.5 (C), 116.5 (CH), 117.4 (CH), 126.2 (C), 127.9 (C), 132.4 (CH), 133.4 (CH), 149.4 (2C), 154.0 (CH), 154.1 (2C), 156.2 (CH), 168.5 (3C), 171.3 (C), 194.8 (C), 196.8 (C). Found, %: C 58.66; H 4.53. $[M]^+$ 306. $C_{15}H_{14}O_7$. Calculated, %: C 58.82; H 4.61.

(*E,Z*)-Methyl 2-{5-[(2,4-dioxodihydrofuran-3(2*H*)-ylidene)methyl]-2-methoxyphenoxy}acetate (XXXVII). Yield 27% (*d*). IR spectrum, cm^{-1}: 1300 (max), 1565, 1605, 1700, 1730, 1745. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.85 s and 3.86 s (3H, CO_2CH_3), 4.02 s and 4.03 s (3H, OCH_3), 4.60 s (1.4H, CH_2 of cycle) and 4.72 s (0.6H, CH_2 of cycle), 4.84 s (0.6H, OCH_2CO_2Me) and 4.87 s (1.4H, OCH_2CO_2Me), 7.01 d and 7.02 d (1H, H$^3_{arom}$, ^3J 8.5 Hz), 7.74 br.d (1H, H$^4_{arom}$, ^3J 8.5 Hz), 7.88 s and 7.89 s (1H, H$_{vinyl}$), 8.73 d (0.7H, H$^6_{arom}$, ^4J 1.5 Hz) and 8.76 d (0.3H, H$^6_{arom}$, ^4J 2.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 52.5 ($2CH_3$), 56.4 ($2CH_3$), 65.5 ($2CH_2$), 71.6 (CH_2), 72.7 (CH_2), 111.5 (2CH), 113.7 (C), 114.0 (C), 116.6 (CH), 117.7 (CH), 125.4 (C), 126.7 (C), 133.9 (CH), 134.9 (CH), 147.1 (C), 147.3 (C), 153.5 (CH), 155.8 (CH), 155.9 (C), 156.2 (C), 168.2 (C), 168.6 (C), 168.7 (C), 170.9 (C), 194.7 (C), 196.4 (C). Found, %: C 58.62; H 4.55. $[M]^+$ 306. $C_{15}H_{14}O_7$. Calculated, %: C 58.82; H 4.61.

3-Cinnamoyltetrahydrofuran-2,4-dione (L) was prepared by procedure [1]. Yield 69%, mp 141–143°C (from ethyl acetate) (138–140°C [13]).

Reduction of 3-arylidenetetronic acids XXII–XXV, XXXIV–XXXVII and cinnamoyl-tetrahydrofuran-2,4-dione (L) was performed with triethylsilane in trifluoroacetic acid (method *a*) and with sodium cyanoborohydride in a system ТГТ–2 N aqueous HCl (method *b*) along procedures of reduction of 3-acyltetronic acids [7].

3-(4-Methoxybenzyl)tetrahydrofuran-2,4-dione (XXXVIII). Yield 95 (*a*), 75% (*b*), mp 173–175°C. IR spectrum, cm^{-1}: 1605 br (max), 1650 br. sh, 1715, 2380–2820 br. ^{1}H NMR spectrum (CD_3OD), δ, ppm: 3.41 s (2H, C$\underline{H}_2$PhOCH$_3$), 3.73 s (3H, OCH_3), 4.63 s (2H, CH_2 of cycle), 6.79 d (2H$_{arom}$, ^3J 8.5 Hz), 7.14 d (2H$_{arom}$, ^3J 8.5 Hz). ^{13}C NMR spectrum (CD_3OD), δ, ppm: 26.9 (CH_2), 55.7 (CH_3), 68.4 (CH_2), 101.4 (C), 114.8 (2CH), 130.2 (2CH), 132.7 (C), 159.6 (C), 175.6 (C), 178.5 (C). Found, %: C 65.39; H 5.45. $[M]^+$ 220. $C_{12}H_{12}O_4$. Calculated, %: C 65.45; H 5.49.

3-(4-Butoxybenzyl)tetrahydrofuran-2,4-dione (XXXIX). Yield 89 (*a*), 87% (*b*), mp 166–168°C. IR spectrum, cm^{-1}: 1600 br (max), 1655 sh, 1710, 2700 (2380–2840) br. ^{1}H NMR spectrum ($CDCl_3$ + CD_3OD), δ, ppm: 0.96 t [3H, O(CH$_2$)$_3$C$\underline{H}_3$, ^3J 7.5 Hz], 1.47 sextet [2H, O(CH$_2$)$_2$C$\underline{H}_2$CH$_3$, ^3J 7.5 Hz], 1.74 quintet (2H, OCH$_2$C$\underline{H}_2$CH$_2$CH$_3$, ^3J 7.0 Hz), 3.45 s (2H, CH$_2$PhOBu),

3.92 t [2H, OC$\underline{H}_2(CH_2)_2CH_3$, ^3J 6.5 Hz], 4.54 s (2H, CH_2 of cycle), 6.80 d (2H_{arom}, ^3J 8.5 Hz), 7.19 d (2H_{arom}, ^3J 8.5 Hz). ^{13}C NMR spectrum ($CDCl_3$ + CD_3OD), δ, ppm: 13.9 (CH_3), 19.3 (CH_2), 26.3 (CH_2), 31.4 (CH_2), 67.0 (CH_2), 67.8 (CH_2), 100.9 (C), 114.5 (2CH), 129.4 (2CH), 131.2 (C), 157.6 (C), 173.1 (C), 176.6 (C). Found, %: C 68.53; H 6.85. $[M]^+$ 262. $C_{15}H_{18}O_4$. Calculated, %: C 68.68; H 6.92.

3-(4-Butoxy-3-methoxybenzyl)tetrahydrofuran-2,4-dione (XL). Yield 84 (*a*), 93% (*b*), mp 107–109°C. IR spectrum, cm^{-1}: 1600 sh, 1610 (max), 1640–1680 br, 1720, 2700 (2380–2820) br. ^{1}H NMR spectrum (CD_3OD), δ, ppm: 0.96 t [3H, O$(CH_2)_3C\underline{H}_3$, ^3J 7.5 Hz], 1.48 sextet [2H, O$(CH_2)_2C\underline{H}_2CH_3$, ^3J 7.5 Hz], 1.72 quintet (2H, $OCH_2C\underline{H}_2CH_2CH_3$, ^3J 7.0 Hz), 3.41 s (2H, CH_2Ar), 3.79 s (3H, OCH_3), 3.93 t [2H, OC$\underline{H}_2(CH_2)_2CH_3$, ^3J 6.5 Hz], 4.63 s (2H, CH_2 of cycle), 6.74 d.d (1H, H^6_{arom}, ^3J 8.0, ^4J 2.0 Hz), 6.79 d (1H, H^5_{arom}, ^3J 8.0 Hz), 6.88 d (1H, H^2_{arom}, ^4J 2.0 Hz). ^{13}C NMR spectrum (CD_3OD), δ, ppm: 14.2 (CH_3), 20.3 (CH_2), 27.4 (CH_2), 32.5 (CH_2), 56.5 (CH_3), 68.3 (CH_2), 70.2 (CH_2), 101.3 (C), 113.9 (CH), 114.9 (CH), 121.6 (CH), 133.7 (C), 148.3 (C), 150.8 (C), 175.6 (C), 178.5 (C). Found, %: C 65.55; H 6.84. $[M]^+$ 292. $C_{16}H_{20}O_5$. Calculated, %: C 65.74; H 6.90.

Methyl 2-{4-[(2,4-dioxotetrahydrofuran-3-yl)-methyl]phenoxy}acetate (XLI). Yield 89% (*a*), mp 166–168°C (from MeOH). IR spectrum, cm^{-1}: 1220 (max), 1620 sh, 1650 sh, 1665, 1720, 1750, 2710 (2380–2810) br. ^{1}H NMR spectrum (CD_3OD), δ, ppm: 3.41 s (2H, CH_2Ar), 3.75 s (3H, CO_2CH_3), 4.63 s (2H, CH_2 of cycle), 4.65 s (2H, OCH_2CO_2Me), 6.80 d (2H_{arom}, ^3J 8.5 Hz), 7.15 d (2H_{arom}, ^3J 8.5 Hz). ^{13}C NMR spectrum (CD_3OD), δ, ppm: 27.0 (CH_2), 52.6 (CH_3), 66.2 (CH_2), 68.4 (CH_2), 101.2 (C), 115.6 (2CH), 130.4 (2CH), 133.8 (C), 157.9 (C), 171.6 (C), 175.7 (C), 178.4 (C). Found, %: C 60.26; H 5.04. $[M]^+$ 278. $C_{14}H_{14}O_6$. Calculated, %: C 60.43; H 5.07.

Methyl 2-{3-[(2,4-dioxotetrahydrofuran-3-yl)methyl]phenoxy}acetate (XLII). Yield 72 (*a*), 59% (*b*), mp 105–110°C (decomp.). IR spectrum, cm^{-1}: 1240 br, 1600 sh, 1620, 1655 sh, 1675 br, 1750, 2380–2820 br. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.45 s (2H, CH_2Ar), 3.77 s (3H, CO_2CH_3), 4.54 br.s (2H, CH_2 of cycle), 4.57 C (2H, OCH_2CO_2Me), 6.67 d (1H_{arom}, ^3J 7.5 Hz), 6.80 br.s (1H, H^2_{arom}), 6.87 d (1H_{arom} , ^3J 7.5 Hz), 7.14 t (1H, H^5_{arom}, ^3J 7.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 27.0 (CH_2), 52.4 (CH_3), 65.1 (CH_2), 67.7 (CH_2), 100.3 (C), 112.0 (CH), 115.0 (CH), 122.0 (CH), 129.6 (CH), 140.6 (C), 157.7 (C), 170.1 (C), 174.5 (C), 174.6 (C). Found, %: C 60.29; H 4.99. $[M]^+$ 278. $C_{14}H_{14}O_6$. Calculated, %: C 60.43; H 5.07.

Methyl 2-{4-[(2,4-dioxotetrahydrofuran-3-yl)methyl]-2-methoxyphenoxy}acetate (XLIII). Yield 91% (*a*), mp 76–79°C. IR spectrum, cm^{-1}: 1230, 1605, 1640 sh, 1650 sh, 1675 br, 1755, 2380–2830 br. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.46 s (2H, CH_2Ar), 3.72 s (3H, OCH_3), 3.76 s (3H, CO_2CH_3), 4.47 br.s (2H, CH_2 of cycle), 4.57 s (2H, OCH_2CO_2Me), 6.62 br.d (1H_{arom}, ^3J 7.0 Hz), 6.71 br (1H_{arom}), 6.82 br (1H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 26.7 (CH_2), 52.4 (CH_3), 55.8 (CH_3), 66.4 (CH_2), 67.9 (CH_2), 99.4 (C), 112.6 (CH), 114.3 (CH), 120.4 (CH), 134.3 (C), 145.1 (C), 149.1 (C), 170.3 (C), 176.3 (C), 177.9 (C). Found, %: C 58.22; H 5.16. $[M]^+$ 308. $C_{15}H_{16}O_7$. Calculated, %: C 58.44; H 5.23.

Methyl 2-{5-[(2,4-dioxotetrahydrofuran-3-yl)-methyl]-2-methoxyphenoxy}acetate (XLIV). Yield 97% (*a*), mp 128–131°C. IR spectrum, cm^{-1}: 1240, 1595, 1670 br, 1740, 1765 sh, 2420–2820 br. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.41 s (2H, CH_2Ar), 3.78 s (3H, CO_2CH_3), 3.80 s (3H, OCH_3), 4.58 s (2H, CH_2 of cycle), 4.64 s (2H, OCH_2CO_2Me), 6.76 m (2H_{arom}), 6.85 d.d (1H, H^4_{arom}, ^3J 8.5, ^4J 1.5 Hz), 8.11 br (1H, OH enol). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 26.4 (CH_2), 52.6 (CH_3), 55.9 (CH_3), 66.2 (CH_2), 67.8 (CH_2), 100.8 (C), 112.2 (CH), 114.8 (CH), 122.4 (CH), 131.3 (C), 146.7 (C), 148.0 (C), 170.6 (C), 174.5 (C), 178.3 (C). Found, %: C 58.31; H 5.19. $[M]^+$ 308. $C_{15}H_{16}O_7$. Calculated, %: C 58.44; H 5.23.

3-Cinnamyltetrahydrofuran-2,4-dione (XLV). Yield 83% (*b*), mp 153–156°C. IR spectrum, cm^{-1}: 1280, 1455 (max), 1605–1665 br, 1725, 2720 (2380–2840) br. ^{1}H NMR spectrum (CD_3OD), δ, ppm: 3.06 d (2H, $C\underline{H}_2CH$=CHPh, ^3J 6.5 Hz), 4.65 s (2H, CH_2 of cycle), 6.24 d.t (1H, $CH_2C\underline{H}$=CHPh, ^3J 15.5, 6.5 Hz), 6.41 br.d (1H, CH_2CH=C$\underline{H}$Ph, $^3J_{trans}$ 15.5 Hz), 7.16 br.t (1H, H^4_{arom}, ^3J 7.5 Hz), 7.25 br.t (2H, H^3_{arom} + H^5_{arom}, ^3J 7.5 Hz), 7.32 br.d (2H, H^2_{arom}+ H^6_{arom}, ^3J 7.5 Hz). ^{13}C NMR spectrum (CD_3OD), δ, ppm: 25.3 (CH_2), 68.4 (CH_2), 99.4 (C), 127.0 (CH), 127.1 (2CH), 128.1 (CH), 129.5 (2CH), 131.8 (CH), 138.9 (C), 175.9 (C), 178.4 (C). Found, %: C 72.14; H 5.51. $[M]^+$ 216. $C_{13}H_{12}O_3$. Calculated, %: C 72.21; H 5.59.

3-(3-Phenylpropyl)tetrahydrofuran-2,4-dione (XLIX). Yield 91 (from **L**), 79 (from **XLV**) (*a*), 88% (from **L**) (*b*), mp 132–133°C (from ethyl acetate). IR spectrum, cm^{-1}: 1240, 1280, 1605–1665 br (max), 1725, 2725 (2380–2850) br. ^{1}H NMR spectrum (CD_3OD), δ,

ppm: 1.78 quintet (2H, $CH_2C\underline{H}_2CH_2Ph$, ^3J 7.5 Hz), 2.20 t [2H, $C\underline{H}_2(CH_2)_2Ph$, ^3J 7.5 Hz], 2.60 t (2H, CH_2Ph, ^3J 7.5 Hz), 4.56 s (2H, CH_2 of cycle), 7.12 t (1H, H^4_{arom}, ^3J 7.5 Hz), 7.17 d (2H, $H^2_{arom} + H^6_{arom}$, ^3J 7.0 Hz), 7.23 t (2H, $H^3_{arom} + H^5_{arom}$, ^3J 7.5 Hz). ^{13}C NMR spectrum (CD_3OD), δ, ppm: 21.8 (CH_2), 30.7 (CH_2), 36.6 (CH_2), 68.1 (CH_2), 101.1 (C), 126.7 (CH), 129.2 (2CH), 129.3 (2CH), 143.4 (C), 175.3 (C), 178.7 (C). Found, %: C 71.45; H 6.44. $[M]^+$ 218. $C_{13}H_{14}O_3$. Calculated, %: C 71.54; H 6.47.

3-(4-Butoxybenzyl)-4-methoxy-2,5-dihydrofuran-2-one (LI) was obtained from 3-arylalkyltetronic acid **XXXIX** by procedure from [1]. Yield 65%. IR spectrum, cm^{-1}: 1605 sh, 1620, 1675 (max), 1750. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.96 t [3H, $O(CH_2)_3C\underline{H}_3$, ^3J 7.5 Hz], 1.47 sextet [2H, $O(CH_2)_2C\underline{H}_2CH_3$, ^3J 7.5 Hz], 1.74 quintet (2H, $OCH_2C\underline{H}_2CH_2CH_3$, ^3J 7.0 Hz), 3.53 s (2H, CH_2Ar), 3.92 t [2H, $OC\underline{H}_2(CH_2)_2CH_3$, ^3J 6.5 Hz], 3.93 s (3H, OCH_3), 4.68 s (2H, CH_2 of cycle), 6.80 d ($2H_{arom}$, ^3J 8.5 Hz), 7.16 d ($2H_{arom}$, ^3J 8.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.6 (CH_3), 19.0 (CH_2), 26.7 (CH_2), 31.1 (CH_2), 57.4 (CH_3), 65.1 (CH_2), 67.4 (CH_2), 102.9 (C), 114.2 (2CH), 129.0 (2CH), 130.7 (C), 157.5 (C), 172.5 (C), 174.5 (C). Found, %: C 69.49; H 7.38. $[M]^+$ 276. $C_{16}H_{20}O_4$. Calculated, %: C 69.54; H 7.30.

3-(4-Butoxybenzyl)-4-(heptylamino)-2,5-dihydrofuran-2-one (LII) was obtained from methyl enol ether **LI** and heptylamine by procedure from [1]. Yield 70%. IR spectrum, cm^{-1}: 1635 br (max), 1730, 3310 br. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.88 t [3H, $NH(CH_2)_6C\underline{H}_3$, ^3J 7.0 Hz], 0.97 t [3H, $O(CH_2)_3C\underline{H}_3$, ^3J 7.5 Hz], 1.12 m [2H, $NH(CH_2)_5C\underline{H}_2CH_3$], 1.18–1.24 m [4H, $NH(CH_2)_3(C\underline{H}_2)_2CH_2CH_3$], 1.27 quintet [2H, $NH(CH_2)_2C\underline{H}_2(CH_2)_3CH_3$, ^3J 7.0 Hz], 1.37 quintet (2H, $NHCH_2C\underline{H}_2$, ^3J 7.0 Hz), 1.48 sextet [2H, $O(CH_2)_2C\underline{H}_2CH_3$, ^3J 7.5 Hz], 1.75 quintet [2H, $OCH_2C\underline{H}_2CH_2CH_3$, ^3J 7.0 Hz], 2.94 q ($NHC\underline{H}_2$, ^3J 6.5 Hz), 3.48 C (2H, CH_2PhOBu), 3.93 t [2H, $OC\underline{H}_2(CH_2)_2CH_3$, ^3J 6.5 Hz], 4.19 br (1H, NH), 4.63 s (2H, CH_2 of cycle), 6.82 d ($2H_{arom}$, ^3J 8.5 Hz), 7.14 d ($2H_{arom}$, ^3J 8.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.9 (CH_3), 14.0 (CH_3), 19.2 (CH_2), 22.5 (CH_2), 26.4 (CH_2), 27.6 (CH_2), 28.8 (CH_2), 30.3 (CH_2), 31.4 (CH_2), 31.6 (CH_2), 44.0 (CH_2), 65.4 (CH_2), 67.7 (CH_2), 92.3 (C), 114.6 (2CH), 129.2 (2CH), 130.6 (C), 157.8 (C), 163.6 (C), 176.3 (C). Found, %: C 73.39; H 9.27. $[M]^+$ 359. $C_{22}H_{33}NO_3$. Calculated, %: C 73.50; H 9.25.

Synthesis of 4-substituted 5-ethoxy-2,3-dihydrofuran-3-ones LIII, LIV, LVII, LIX, LX was described in [1].

Methyl 2-{4-[(4-oxo-2-ethoxy-4,5-dihydrofuran-3-yl)methyl]phenoxy}acetate (LIII). Yield 98%. IR spectrum, cm^{-1}: 1600 (max), 1690, 1735 sh, 1750. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.40 t (3H, $OCH_2C\underline{H}_3$, ^3J 7.0 Hz), 3.35 s (2H, CH_2Ar), 3.80 s (3H, CO_2CH_3), 4.42 q (2H, $OC\underline{H}_2CH_3$, ^3J 7.0 Hz), 4.57 s (2H, CH_2 of cycle), 4.60 s (2H, OCH_2CO_2Me), 6.80 d ($2H_{arom}$, ^3J 8.5 Hz), 7.18 d ($2H_{arom}$, ^3J 8.5 Hz). ^{13}C ($CDCl_3$), δ, ppm: 14.8 (CH_3), 24.7 (CH_2), 52.2 (CH_3), 65.4 (CH_2), 65.9 (CH_2), 74.9 (CH_2), 94.0 (C), 114.5 (2CH), 129.4 (2CH), 133.7 (C), 156.1 (C), 169.6 (C), 181.6 (C), 195.6 (C). Found, %: C 62.84; H 5.99. $[M]^+$ 306. $C_{16}H_{18}O_6$. Calculated, %: C 62.74; H 5.92.

Methyl 2-{3-[(4-oxo-2-ethoxy-4,5-dihydrofuran-3-yl)methyl]phenoxy}acetate (LIV). Yield 83%. IR spectrum, cm^{-1}: 1600 (max), 1690, 1735 sh, 1750. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.40 t (3H, $OCH_2C\underline{H}_3$, ^3J 7.0 Hz), 3.39 s (2H, CH_2Ar), 3.80 s (3H, CO_2CH_3), 4.42 q (2H, $OC\underline{H}_2CH_3$, ^3J 7.0 Hz), 4.57 s (2H, CH_2 of cycle), 4.61 s (2H, OCH_2CO_2Me), 6.70 d.d ($1H_{arom}$, ^3J 8.0, ^4J 2.5 Hz), 6.83 br (1H, H^2_{arom}), 6.90 d ($1H_{arom}$, ^3J 8.0 Hz), 7.17 t (1H, H^5_{arom}, ^3J 8.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.8 (CH_3), 25.6 (CH_2), 52.2 (CH_3), 65.4 (CH_2), 66.0 (CH_2), 75.0 (CH_2), 93.5 (C), 112.0 (CH), 114.9 (CH), 121.9 (CH), 129.4 (CH), 142.1 (C), 157.9 (C), 169.5 (C), 181.6 (C), 195.5 (C). Found, %: C 62.80; H 6.00. $[M]^+$ 306. $C_{16}H_{18}O_6$. Calculated, %: C 62.74; H 5.92.

4-(4-Butoxy-3-methoxybenzyl)-5-ethoxy-2,3-dihydrofuran-3-one (LVII). Yield 99%. IR spectrum, cm^{-1}: 1595 sh, 1620 (max), 1700. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.96 t [3H, $O(CH_2)_3C\underline{H}_3$, ^3J 7.5 Hz], 1.41 t (3H, $OCH_2C\underline{H}_3$, ^3J 7.0 Hz), 1.47 sextet [2H, $O(CH_2)_2C\underline{H}_2CH_3$, ^3J 7.5 Hz], 1.80 quintet (2H, $OCH_2C\underline{H}_2CH_2CH_3$, ^3J 7.0 Hz), 3.35 s (2H, CH_2Ar), 3.84 s (3H, OCH_3), 3.97 t [2H, $OC\underline{H}_2(CH_2)_2CH_3$, ^3J 7.0 Hz], 4.43 q (2H, $OC\underline{H}_2CH_3$, ^3J 7.0 Hz), 4.57 s (2H, CH_2 of cycle), 6.76 narrow m ($2H_{arom}$), 6.85 s ($1H_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.9 (CH_3), 14.8 (CH_3), 19.2 (CH_2), 25.2 (CH_2), 31.3 (CH_2), 56.0 (CH_3), 65.9 (CH_2), 68.8 (CH_2), 74.9 (CH_2), 94.2 (C), 112.3 (CH), 112.8 (CH), 120.1 (CH), 133.0 (C), 146.8 (C), 149.2 (C), 181.6 (C), 195.7 (C). Found, %: C 67.51; H 7.63. $[M]^+$ 320. $C_{18}H_{24}O_5$. Calculated, %: C 67.48; H 7.55.

4-Cinnamyl-5-ethoxy-2,3-dihydrofuran-3-one (LIX). Yield 97%. IR spectrum, cm^{-1}: 1605 (max), 1690. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.42 t (3H, $OCH_2C\underline{H}_3$, ^3J 7.0 Hz), 3.00 d.d (2H, $C\underline{H}_2CH{=}CHPh$, ^3J 6.5, ^4J 1.0 Hz), 4.45 q (2H, $OC\underline{H}_2CH_3$, ^3J 7.0 Hz),

4.59 s (2H, CH_2 of cycle), 6.21 d.t (1H, $CH_2C\underline{H}$=CHPh, ^3J 16.0, 6.5 Hz), 6.40 br.d (1H, CH_2CH=C$\underline{H}$Ph, $^3J_{trans}$ 16.0 Hz), 7.18 br.t (1H, H^4_{arom}, ^3J 7.5 Hz), 7.27 t (2H, H^3 + H^5_{arom}, ^3J 7.5 Hz), 7.33 br.d (2H, H^2+H^6_{arom}, ^3J 7.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.8 (CH_3), 23.0 (CH_2), 65.9 (CH_2), 74.9 (CH_2), 92.1 (C), 126.1 (2CH), 126.9 (2CH), 128.4 (2CH), 130.2 (CH), 137.5 (C), 181.6 (C), 195.7 (C). Found, %: C 73.84; H 6.65. $[M]^+$ 244. $C_{15}H_{16}O_3$. Calculated, %: C 73.75; H 6.60.

4-(3-Phenylpropyl)-5-ethoxy-2,3-dihydrofuran-3-one (LX). Yield 95%. IR spectrum, cm^{-1}: 1610 br (max), 1705. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.42 t (3H, $OCH_2C\underline{H}_3$, ^3J 7.0 Hz), 1.78 quintet (2H, $CH_2C\underline{H}_2CH_2Ph$, ^3J 7.5 Hz), 2.15 t [2H, $C\underline{H}_2(CH_2)_2Ph$, ^3J 7.5 Hz], 2.61 t (2H, $C\underline{H}_2Ph$, ^3J 7.5 Hz), 4.42 q (2H, $OC\underline{H}_2CH_3$, ^3J 7.0 Hz), 4.52 s (2H, CH_2 of cycle), 7.15–7.19 m ($3H_{arom}$), 7.24–7.27 m ($2H_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.8 (CH_3), 19.3 (CH_2), 29.7 (CH_2), 35.6 (CH_2), 65.7 (CH_2), 74.7 (CH_2), 93.7 (C), 125.6 (CH), 128.2 (2CH), 128.4 (2CH), 142.4 (C), 181.6 (C), 196.3 (C). Found, %: C 73.27; H 7.47. $[M]^+$ 246. $C_{15}H_{18}O_3$. Calculated, %: C 73.15; H 7.37.

The reaction of 4-substituted 5-ethoxy-2,3-dihydrofuran-3-ones XLI and XLII with heptylamine was carried out by the procedure of the synthesis of 11-oxa-13-azaprostanoids [1].

***N*-Heptyl-2-{4-[(2-(heptylamino)-4-oxo-4,5-dihydrofuran-3-yl)methyl]phenoxy}acetamide (LV).** Yield 58%, mp 140–142°C (from ethyl acetate). IR spectrum, cm^{-1}: 1515 sh, 1535 sh, 1550 sh, 1580 br (max), 1605 sh, 1655, 3065, 3290. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.87 t (3H, CH_3, ^3J 7.5 Hz), 0.88 t (3H, CH_3, ^3J 7.5 Hz), 1.14–1.35 m (16H, $8CH_2$), 1.44 quintet [2H, $C(O)NHCH_2C\underline{H}_2$, ^3J 7.5 Hz], 1.54 quintet (2H, $NHCH_2C\underline{H}_2$, ^3J 7.0 Hz), 3.24 q (2H, $NHC\underline{H}_2$, ^3J 6.5 Hz), 3.32 q [2H, $C(O)NHC\underline{H}_2$, ^3J 7.0 Hz], 3.43 s (2H, CH_2Ar), 4.33 s [2H, $OC\underline{H}_2C(O)NH$], 4.51 s (2H, CH_2 of cycle), 5.42 br (1H, NH), 6.64 br [1H, C(O)NH], 6.79 d ($2H_{arom}$, ^3J 8.5 Hz), 7.15 d ($2H_{arom}$, ^3J 8.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.0 ($2CH_3$), 22.5 (CH_2), 22.6 (CH_2), 25.1 (CH_2), 26.4 (CH_2), 26.8 (CH_2), 28.8 (CH_2), 28.9 (CH_2), 29.6 (CH_2), 30.0 (CH_2), 31.7 ($2CH_2$), 39.1 (CH_2), 41.4 (CH_2), 67.5 (CH_2), 74.3 (CH_2), 90.8 (C), 114.8 (2CH), 129.4 (2CH), 133.2 (C), 155.8 (C), 168.1 (C), 177.9 (C), 192.6 (C). Found, %: C 70.67; H 9.25. $[M]^+$ 458. $C_{27}H_{42}N_2O_4$. Calculated, %: C 70.71; H 9.23.

***N*-Heptyl-2-{3-[(2-(heptylamino)-4-oxo-4,5-dihydrofuran-3-yl)methyl]phenoxy}acetamide (LVI).** Yield 47%, mp 99–101°C (from ether). IR spectrum, cm^{-1}: 1535 sh, 1570 br (max), 1590 sh, 1615 sh, 1660, 3080 br, 3320. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.87 t (3H, CH_3, ^3J 7.0 Hz), 0.88 t (3H, CH_3, ^3J 7.0 Hz), 1.15 m (2H, CH_2), 1.19–1.33 m (14H, $7CH_2$), 1.44 quintet [2H, $C(O)NHCH_2C\underline{H}_2$, ^3J 7.0 Hz], 1.54 quintet (2H, $NHCH_2C\underline{H}_2$, ^3J 6.5 Hz), 3.25 q (2H, $NHC\underline{H}_2$, ^3J 7.0 Hz), 3.32 q [2H, $C(O)NHC\underline{H}_2$, ^3J 7.0 Hz], 3.47 s (2H, CH_2Ar), 4.41 s [2H, $OC\underline{H}_2C(O)NH$], 4.55 s (2H, CH_2 of cycle), 5.16 br (1H, NH), 6.64 br [1H, C(O)NH], 6.72 br.d ($1H_{arom}$, ^3J 8.0 Hz), 6.81 br.s (1H, H^2_{arom}), 6.89 d ($1H_{arom}$, ^3J 8.0 Hz), 7.22 t (1H, H^5_{arom}, ^3J 8.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.1 ($2CH_3$), 22.5 (CH_2), 22.6 (CH_2), 26.0 (CH_2), 26.3 (CH_2), 26.8 (CH_2), 28.7 (CH_2), 28.9 (CH_2), 29.6 (CH_2), 30.0 (CH_2), 31.6 (CH_2), 31.7 (CH_2), 39.1 (CH_2), 41.4 (CH_2), 67.2 (CH_2), 74.4 (CH_2), 90.5 (C), 112.0 (CH), 115.0 (CH), 121.8 (CH), 129.9 (CH), 141.7 (C), 157.6 (C), 168.0 (C), 177.8 (C), 192.6 (C). Found, %: C 70.56; H 9.29. $[M]^+$ 458. $C_{27}H_{42}N_2O_4$. Calculated, %: C 70.71; H 9.23.

9-Oxa-7-azaprostanoids **LVIII**, **LXI**, and **LXII** were obtained by procedure from [1].

Methyl 6-[3-(4-butoxy-3-methoxybenzyl)-4-oxo-4,5-dihydrofuran-2-ylamino]hexanoate (LVIII). Yield 40%, mp 63–65°C (from ether). IR spectrum, cm^{-1}: 1530 br, 1575 br, 1615 sh, 1680, 1735. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.97 t (3H, CH_3, ^3J 7.5 Hz), 1.19 quintet [2H, $NH(CH_2)_2C\underline{H}_2(CH_2)_2CO_2Me$, ^3J 7.5 Hz], 1.43 quintet (2H, $C\underline{H}_2CH_2CO_2Me$, ^3J 7.5 Hz), 1.48 sextet [2H, $O(CH_2)_2C\underline{H}_2CH_3$, ^3J 7.5 Hz], 1.56 quintet (2H, $NHCH_2C\underline{H}_2$, ^3J 7.5 Hz), 1.80 quintet (2H, $OCH_2C\underline{H}_2CH_2CH_3$, ^3J 7.0 Hz), 2.27 t (2H, CH_2CO_2Me, ^3J 7.5 Hz), 3.22 q (2H, $NHC\underline{H}_2$, ^3J 6.5 Hz), 3.44 s (2H, CH_2Ar), 3.66 s (3H, CO_2CH_3), 3.82 s (3H, OCH_3), 3.97 t [2H, $OC\underline{H}_2(CH_2)_2CH_3$, ^3J 6.5 Hz], 4.52 br.s (2H, CH_2 of cycle), 5.27 br (1H, NH), 6.72–6.78 m ($3H_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 13.9 (CH_3), 19.2 (CH_2), 24.2 (CH_2), 25.7 (CH_2), 25.8 (CH_2), 29.6 (CH_2), 31.2 (CH_2), 33.6 (CH_2), 40.9 (CH_2), 51.6 (CH_3), 56.0 (CH_3), 68.8 (CH_2), 74.2 (CH_2), 91.2 (C), 112.1 (CH), 112.9 (CH), 120.0 (CH), 131.8 (C), 147.2 (C), 149.7 (C), 173.9 (C), 177.8 (C), 192.5 (C). Found, %: C 65.78; H 7.92. $[M]^+$ 419. $C_{23}H_{33}NO_6$. Calculated, %: C 65.85; H 7.93.

(*E*)-Methyl 6-(4-oxo-3-cinnamyl-4,5-dihydrofuran-2-ylamino)hexanoate (LXI). Yield 49%. IR spectrum, cm^{-1}: 1500, 1535 sh, 1555 sh, 1580 br (max), 1650, 1680, 1735, 3030 br, 3220 br. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.27 quintet [2H, $NH(CH_2)_2C\underline{H}_2(CH_2)_2$—$CO_2Me$, ^3J 7.5 Hz], 1.55 m [4H, $NHCH_2C\underline{H}_2CH_2C\underline{H}_2CH_2$–$CO_2Me$], 2.20 t (2H, CH_2CO_2Me, ^3J 7.5 Hz), 3.07 d (2H,

C$\underline{H}_2$CH=CHPh, ^3J 6.5 Hz), 3.32 q (2H, NHC$\underline{H}_2$, ^3J 6.5 Hz), 3.65 s (3H, CO_2CH_3), 4.53 s (2H, CH_2 of cycle), 6.01 br (1H, NH), 6.15 d.t (1H, $CH_2C\underline{H}$=CHPh, $^3J_{1trans}$ 15.5, $^3J_2$ 6.5 Hz), 6.43 d (1H, CH_2CH=C$\underline{H}$Ph, $^3J_{trans}$ 15.5 Hz), 7.19 br.t (1H, H^4_{arom}, ^3J 7.0 Hz), 7.26–7.31 m ($4H_{arom}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 23.4 (CH_2), 24.0 (CH_2), 25.8 (CH_2), 29.5 (CH_2), 33.5 (CH_2), 41.0 (CH_2), 51.4 (CH_3), 74.2 (CH_2), 89.1 (C), 125.9 (2CH), 127.1 (CH), 127.5 (CH), 128.4 (2CH), 130.4 (CH), 136.9 (C), 173.8 (C), 178.0 (C), 192.1 (C). Found, %: C 69.90; H 7.43. $[M]^+$ 343. $C_{20}H_{25}NO_4$. Calculated, %: C 69.95; H 7.34.

Methyl 6-[4-oxo-3-(3-phenylpropyl)-4,5-dihydrofuran-2-ylamino]hexanoate (LXII). Yield 39%. IR spectrum, cm^{-1}: 1500, 1535 sh, 1555 sh, 1575 br (max), 1675, 1735, 3030, 3220 br. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.33 quintet [2H, NH$(CH_2)_2C\underline{H}_2(CH_2)_2CO_2Me$, ^3J 7.5 Hz], 1.57 quintet (2H, $NHCH_2C\underline{H}_2$, ^3J 7.0 Hz), 1.63 quintet (2H, $C\underline{H}_2CH_2CO_2Me$, ^3J 7.5 Hz), 1.73 quintet (2H, $CH_2C\underline{H}_2CH_2Ph$, ^3J 7.5 Hz), 2.15 t [2H, $C\underline{H}_2(CH_2)_2Ph$, ^3J 7.5 Hz], 2.31 t (2H, CH_2CO_2Me, ^3J 7.5 Hz), 2.59 t (2H, CH_2Ph, ^3J 7.5 Hz), 3.31 q (2H, NHC$\underline{H}_2$, ^3J 6.5 Hz), 3.65 s (3H, CO_2CH_3), 4.51 br.s (2H, CH_2 of cycle), 6.41 br (1H, NH), 7.15 narrow m ($3H_{arom}$), 7.24 t (2H, $H^3_{arom} + H^5_{arom}$, ^3J 7.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 19.7 (CH_2), 24.2 (CH_2), 26.0 (CH_2), 29.6 (CH_2), 30.0 (CH_2), 33.7 (CH_2), 35.4 (CH_2), 41.1 (CH_2), 51.6 (CH_3), 74.3 (CH_2), 92.2 (C), 125.7 (CH), 128.2 (2CH), 128.4 (2CH), 142.3 (C), 174.1 (C), 178.1 (C), 192.4 (C). Found, %: C 69.53; H 7.98. $[M]^+$ 345. $C_{20}H_{27}NO_4$. Calculated, %: C 69.54; H 7.88.

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