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Original scientific paper

Microbiological transformation of a synthetic benzofurane type lactone

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The aim of this work was the investigation of the biotransformation ability of a synthetic benzofurane type γ-lactone. This work was based on the microbiological reactions of *Aspergillus niger, Saccharomyces cerevisiae, Bacillus mycoides, Agrobacterium tumefaciens, Pseudomonas glicinea* and *Pseudomonas fluorescens* to obtain new active derivatives. Four biotransformation products were determined. The lactone was used for two purposes, as an additive for the nutrient substrate and as a source of organic carbon.

Keywords: synthesis, γ-lactone, biotransformation, δ-lactone.

The physiological activity of lactones of natural origin has been known ever since santonin was used as an important antihelminatic and ascaricidol agent. Owing to their high level of physiological activity, natural and synthetic lactones have been the subject of biochemical investigations as potential therapeutic agents since 1970.[1-3]

From the chemical point of view, the potential cytotoxic activity of many sesquiterpene lactones of plant origin is based on their ability to selectively inhibit certain enzyme systems. The numerous results published so far prove that the presence of the O=C–C=CH_2 system in the molecule[4-6] is directly responsible for the cytotoxic activities of observed compounds.

The physiological activity of a lactone increases with the presence of more than one unsaturated ester or epoxide group in the five-membered and six-membered ring molecule. It has also been demonstrated that synthetic α-methylene butyrolactone derivatives containing no other reactive functional group can have growth inhibition activity comparable to that of multifunctional products.[7-10]

The results published in this field, to date, have opened the way to the formulation of new synthetic methods for obtaining lactone, α-methylene butyrolactone and similar functional compounds which exhibit some therapeutic effects as growth inhibitors in cultures of CCRF-CEM human lymphoblastic leukemia cells.[11,12]

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Our investigations of the biotransformation of lactones was started with microorganisms because of several favorable aspects: the short vegetation period, the ability of the enzyme system to adapt to altered development conditions and the possibility of developing selective methods for obtaining new active compounds or for the synthesis of precursors of new biologically active compounds.

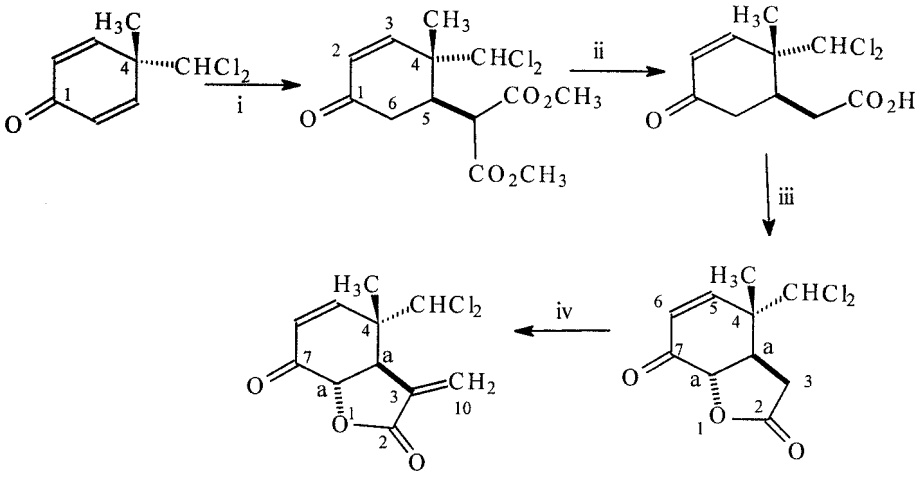
The microorganisms developed in the nutrient substrate inter alia containing lactone as well as in substrates in which lactone was used as the source of organic carbon.

The investigation of extracellular samples demonstrated the ability of the tested fungi and bacteria to biotransform synthetic lactones, and depending on the chemical structure of biotransformation products, evidenced the biodegradation mechanisms of the lacones.[13]

Chemical Assay

In our laboratory the chemical synthesis of a biologically active benzofuran type lactone with a new structure, an a-methylene butyrolactone, was achieved. The chemical transformation of 4-dichloromethyl-4-methyl-5-(dimethoxycarbonyl) methylene-2-cyclohexenone (**1**) in the synthesis of several polyfunctional products with the g-lactone ring was also reported.

The most direct route to a g-lactone seems to be acetoxylation,[15] oxidation[14] and cyclisation of 4-dichloromethyl-4-methyl-5-methylenecarboxy-1-cyclohexenone (**2**) (Scheme 1) with lead(IV) acetate which results in a white crystalline product,



i. CH_2 $(COOCH_3)_2$ CH_3OH, NA
ii. HCl 1:1
iii. $Pb(OAc)_4$ BF_3-Et_2O
iv. HCOOEt, NaH, HCHo

Scheme 1

containing only the g-lactone *trans*-3H, 3aH, 7aH-4-methyl-4-dichloromethyl-2,7-benzofuranione (**3**) in a yield of 75–80%.

The g-lactone derivative[16,17] **3** was formylated by the standard technique to give the sodium salt of the a-formyl g-lactone (not-isolated) in 65.5% yield. Subsequent refluxing with formaldehyde gave white crystals in 56% yield.

The structure of the obtained compounds were characterized by their physical and chemical constants, ^{1}H-NMR and IR spectra.

Bioassay

The investigation encompassed the biotransformation reactions of the lactones when the lactone was used as a component in the nutrient substrate in the concentration of 2 mg on 10 mL of fermentation solution with the following microorganisms: *B. mycoides, A. tumefaciens, A. niger* and *S. cerevisiae.*

The microorganisms *B. mycoides, A. tumefaciens, P. glicinea* and *P. fluorescens* were used to investigate the lactone biotransformation mechanisms when the lactone was used as a source of organic carbon, which was achieved by exchanging the standard nutrient substrate with a mineral substrate.

RESULTS AND DISCUSSION

The ability of *A. niger* and *S. cerevisiae* fungi as well as *A. tumefaciens* and *B. mycoides* to transform the lactone, when it was used as a constituent element of nutrient substrate, was investigated in the first series of experiments.

The investigations were performed over 5 days according to the microorganism inoculation and the obtained results pertaining to the extracellular part of the investigation for the individual microbiological species are presented in Table I.

TABLE I. Comparative values for the starting lactone and valuable lactone products in investigated samples

Culture	R_f value of the starting lactone	R_f values of the biotransformation products	Total amount of lactone [mg]
A. niger	0.24	0.09, 0.36, 0.43	200
S. cerevisiae	0.24	–	200
B. mycoides	0.24	0.09, 0.42	200
A. tumefaciens	0.24	–	200

S. cerevisiae completely degrades the lactone to organic compounds with small biomass and includes them in their metabolic process. The *A. niger* fungi degrade the lactone at a slower rate, which enabled the identification of three transformation products $R_f = 0.09$ $R_f = 0.36$ and $R_f = 0.42$.

The result obtained for the metabolic parameters of the tested samples, with bacteria cultivation, compared with those registered for standards, enabled the

following conclusions to be drawn: *B. mycoides* degrade the lactone at a slow rate, which enabled the identification of two transformation products $R_f = 0.09$, and $R_f = 0.42$.

Within five days, *A. tumefaciens* bacteria completely degraded the lactone, but no lactone and no products of its biotransformation could be identified.

The obtained experimental results demonstrate the essential influence of the lactone on the metabolism of the bacteria. In addition to the investigation *of A. tumefaciens* and with lactone as the source of organic carbon, two more microorganisms *Pseudomonas glicinea* and *Pseudomonas fluorescens* were introduced into the second series of experiments.

The lactone was added to the mineral nutrient substrate in concentrations of 1 mg/mL and 7 mg/mL. The development of microorganisms was interrupted after five days, and the samples thus obtained were treated in the same way as in the first series of investigations. The results obtained are presented in Table II.

TABLE II. Lactone degradation products in the samples in which the lactone was used as a source of carbon

Culture	Lactone [C]/mg	R_f value of the starting lactone	R_f values of the degradation products	Total amount of lactone [mg]
A. tumefaciens	1/7	0.24	0.43	200
B. mycoides	1/7	0.24	0.10, 0.44	200
P. glicinea	1	0.24	0.17, 0.45, 0.83, 0.86	200
	7		0.17, 0.44, 0.78, 0.87, 0.92	200
P. fluorescens	1/7	0.24	-0.17, 0.45	200

Finally, based on the presented results, is can be concluded:

Both species *S. cerevisiae and A. niger* degrade the lactone but at different rates, the degradation being slower in the case of *A. niger*.

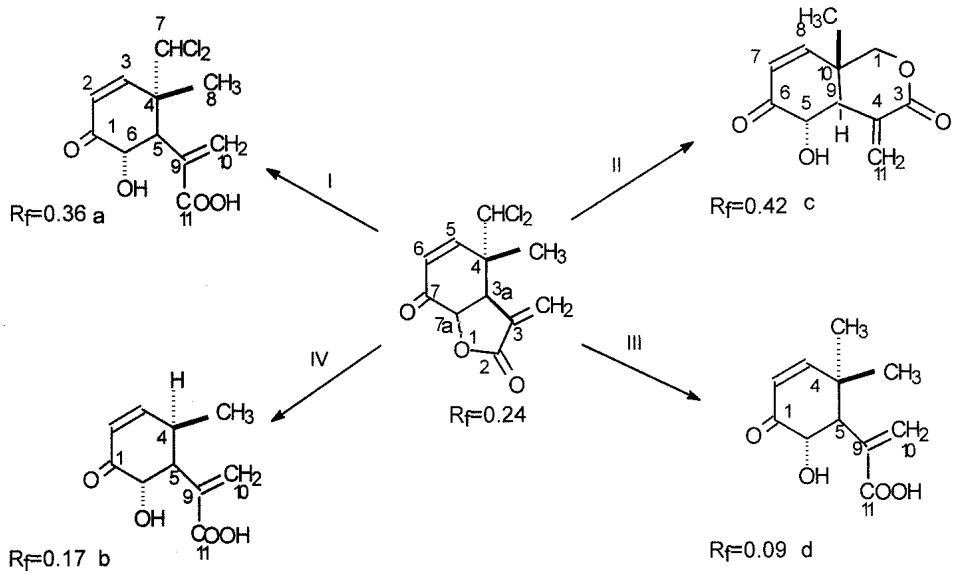
The investigation using the lactone as a source of organic carbon for the *P. glicinea, A. tumefaciens, B. mycoides* and *P. fluorescens* bacteria yielded the following conclusion. All four species use lactone as a source of organic carbon but the rate and the effect of the degradation depend on the structure of the group and on the lactone concentration.

The lactone biotransformation mechanism also depends on the microbiological species being almost identical for *A. tumefaciens s, B. mycoides* and *P. fluorescens* but different for *P. glicinea.* (Scheme 2).

EXPERIMENTAL

General

Melting points were recorded on a Kofler-hot stage apparatus and are uncorrected. Microanalysis of carbon and hydrogen was carried out with a Carlo Erba 1106 microanalyser. The IR spectra were run on a Perkin-Elmer Grating Spectrophotometer either Model 137 or Model 197. The NMR



I= *A.niger. P.glicinea*
II= *A.niger. B.mycoides P.tumefacions. P.fluorescens*
III= *A.niger. B.mycoides P.fluorescens*
IV= *P.glicinea.*

Scheme 2. Biotransformation of lactone

spectra were recorded on a VARIAN FT 80A a 200 "Gemini" Spectrometer (^{1}H at 80 and 200 MHz, ^{13}C at 25 MHz and 80 MHz); $CDCl_3$, using TMS as the internal standard. Chemical shifts are given in δ (ppm), coupling constants *J* in Hz. Abbreviations: *s*-singlet, *d*-doublet, *t*-triplet, *q*-quartet, *m*-multiplets and *b*-broad. The Mass spectroscopic analyses were carried out on a Finnigen MAT 8230 spectrometer. Abbreviations used: LTA - Lead tetraacetate, TLC-thin layer chromatography, THF-tetrahydrofuran. The preparative layer chromatography was carried out using Merck Kieselgel 60 $PF_{254+366}$.

*4-Dichloromethyl-4-methyl-5-(dimethoxycarbonyl)methylene-2-cyclohexenone (***1***)*

A solution of 945 mg of the ketone 4-dichloromethyl-4-methyl-2,5-cyclohexa-dienone, 660 mg dimethyl malonate, and sodium methoxide (from 115 mg of sodium in 15 mL methanol) was kept under nitrogen at room temperature for 2 h. The yellow solution was evaporated under vacuum and ether was added. The resultant suspension was filtered and the precipitate was washed with ether. Evaporation of the combined filtrate and washing and crystallization of the solid residue yielded 350 mg of starting ketone. The precipitate was dissolved in the minimal amount of water, saturated with carbon dioxide and the solution was extracted with chloroform. The extract was dried over anhydrous sodium sulfate and evaporated. Crystallization of the solid residue, 540 mg, (34.5%), from ether gave the ester, m.p. 108–109 °C. Spectral data according to the literature.[19,20]

*4-Methyl-4-dichloromethyl-5-methylenecarboxy-2-cyclohexenone (***2***)*

A mixture of 100 mg of ester and 5 mL of 50% hydrochloric acid was refluxed for 4h. The cooled suspension was filtered. The filrate was extracted with chloroform, and the extract was dried and evaporated. Crystalliziation from ether of the combined residue and the previous precipitate yielded a total of 65 mg (96%) of **2** m.p. 185 °C.

IR (KBr): ν(cm^{-1}) 3450–2570 (OH), 1725 (C=O acid), 1705 (C=O, enone). ^{1}H-NMR ($CDCl_3$. δ) 1.35 (*s*, 3H, CH_3), 6.51 (*s*, H, CHCl), 6.05 (*d*, H, *J* = 10.2 Hz), 7.04 (*d*, H, *J* = 10.2 Hz), m.p. 185 – 186 °C, yield 96%. Anal. calc. for $C_{10}H_{12}O_3Cl_2$ (251.109): C, 47.81; H, 4.82. Required: C, 47.96; H, 4.85

*trans-3H,3aH, 7aH-4-Dichloromethyl-4-methyl-2,7-benzofurandione (**3**)*

To a suspension of LTA (1.2 mmol) in cold benzene (20 mL) and borontriforide etherate (5 cm), a solution of compound 1 (590 mg, 1.2 mmol) in benzene was added over 5 h at room temperature. The reaction mixture was then poured into cold water (150 mL) and the solution obtained was filtered over cellite 577. The organic layer was separated from the aqueous layer, extracted with a saturated solution of sodium bicarbonate and sodium chloride, and then dried with anhydrous sodium sulfate. Evaporation of the solvent afforded an oil, which crystallized out from ether.

IR (KBr), ν(cm^{-1}): 1785 (C=O), lactone), 1695 (C=C–C=O), 1180 (C–O), 810, 790, (C–Cl). ^{1}H-NMR ($CDCl_3$, δ): 1.41 (*s*, 3H, CH_3), 2.51 (AB*q*. 2H, C-3, ^2J = 14.71 Hz, ^3J=8.06 Hz, ^3J=12.54 Hz), 3.51 (*m*, H, C-3a, ^3J=8.06 Hz, ^3J=12.54 Hz, ^3J=7.73 Hz, ^4J=1.79 Hz), 5.14 (*d*, 1H, C-7a, ^3J=7.73 Hz), 5.79 (*s*, 1H, $CHCl_2$), 6.31 (*d*, H, C-6, ^3J=10.31 Hz), 6.75 (*dd* 1H, C-5, ^3J=10.31 Hz, ^4J=1.79 Hz). ^{13}C-NMR, ppm: 173.54 (C-2), 43.27 (C-3), 29.67 (C-3a), 44.38 (C-4), 150.29 (C-5), 129.8 (C-6), 195.54 (C-7), 80.33 (C-7a), 18.98 (CH_3), 79.76 ($CHCl_2$); m.p. 118 °C, yield 71%. Anal. calc. for $C_{10}H_{10}O_3Cl_2$ (249.092): C, 48.19; H, 4.02. Required: C, 48.56; H, 4.07.

*trans-3H,3aH, 7aH-4-Dichloromethyl-4-methyl-3-methylyliden-2,7-benzofurandione (**4**)*

A sodium hydride dispersion in mineral oil (57%, 4.4 g 0.105 mol) was placed in a dry 250 mL three-necked flask to which an additional funnel and mechanical stirrer were attached and washed three times with dry hexane and then suspended in diethyl ether (100 mL, freshly distilled from $LiAlH_4$) under nitrogen. A mixture of the γ-lactone (2.5 g. 0.01 mol) and ethyl formate (0.74 g. 0.01 mol dried over K_2CO_3 and distilled from P_2O_5) was slowly added to the stirred suspension, immediately following the addition of absolute ethanol (0.5 mL), at a rate that maintained a gentle reflux of the reaction solvent. After stirring overnight the reaction mixture was rapidly filtered by suction and the resulting solid was washed well with dry diethyl ether and dried under vacuum, which produced the sodium salt of the α-formyl γ-lactone in the form of a light tan powder (1.95 g, 65.5%). The sodium salt of the formyl γ-lactone (1.45 g, 0.05 mol) and formaldehyde (200 mg, 0.085 mol) were refluxed in THF as solvent, the latter had been refluxed under nitrogen for a period of 4 h. The suspension containing the α-methylene γ-lactone was filtered through a large media frit, and the solvent was removed under reduced pressure. The crude reaction products were purified by passage through a 20.0 cm. Silica gel pad using dichloromethane as the solvent. The substituted methylene lactone was repurified by removal of the solvent under reduced pressure, the addition of 10 mL of 6 M hydrochloric acid, and by extraction three times with 15 mL ethyl ether. The combined previously obtained organic phases were washed with a saturated sodium chloride solution, dried with anhydrous sodium sulfate (Na_2SO_4 anh.), and the solvent removed under vacuum. The α-methylene-γ-lactone crystallized out from petrolether (yield of 730 mg, 56%).

IR (KBr): ν(cm^{-1}) 1765 (C=O, γ-lact), 1705 (conj.), 1668, 1649 (C=CH_2) (C–O), 835 (=CH_2), 800, 780 (C–Cl). ^{1}H-NMR ($CDCl_3$, δ): 1.35 (*s*, 3H, CH_3), 3.95 (*bd*, H, C-3a, ^3J=8.82 Hz, ^4J=2.02 Hz, ^4J=3.03 Hz), 5.03 (*d*, H, C-7a, ^3J=8.82 Hz), 5.75 (*dd*. H, C-10 *trans*, ^2J=2.48 Hz, ^4J=3.03 Hz), 5.85 (*s*, 1H, $CHCl_2$) 6.30 (*dd*, H, C-10 *cis*, ^2J=2.48 Hz, ^4J=2.02 Hz), 6.15 (*d*, H, C-5, ^3J=11.26 Hz), 6.51 (*d*, H, C-6 ^{3}J=11.26 Hz). ^{13}C-NMR ppm: 171.7 (C-2), 126.7 (C-3), 24.5 (C-3a), 44.3 (C-4), 150.2 (C-5), 129.8 (C-6), 195.6 (C-7), 80.3 (C-7a), 18.9 (CH_3), 78.8 ($CHCl_2$), 137.33, (C-10). MS, M^+, 260.000, m.p. 128–130 °C, yield 56%. Anal. calc. for $C_{11}H_{10}O_3Cl_2$(260.005): C, 50.77; H, 3.88. Required: C, 50.25; H, 4.01.

Microorganisms

The strains *Bacillus mycoides, Pseudomonas glicinea, Aspergillus niger, Agrobacterium tumefaciens, Saccharomyces cerevisiae*, and *Pseudomonas fluorescens* were from the collection of microorganisms of the Faculty of Science, Department of Biology, University of Kragujevac.

Fermentation. The *A. niger* and *S. cerevisiae* fungi were inoculated in a medium of the following composition: peptone 1 (15.0 g), yeast extracts (5.0 g), dextrose (10.0 g), NaCl (10.0 g) and distilled water

(1000 mL). A 1 mL suspension of the culture was put into 10-mL of aqueous substrate to which 2 mg of lactone had been added (*ca.* 200 mg). This was incubated for five days at a temperature of 22 °C.

The *B. mycoides* and *A. tumefaciens* bacteria were inoculated into a substrate consisting of a mixture of peptone 1 greasy extract, NaCl, K_2HPO_4 total weight of 23.3 g dissolved in 1000 mL of distilled water. The culture was obtained by adding 1 mL of medium suspension to 10 mL of substrate containing 2 mg of the lactone (*ca.* 200 mg) and incubated for five days at a temperature of 22 °C.

In the second series of the present investigation, in which the lactone served as a source of organic carbon, a modified nutrient substrate was used. Hence, *B. mycoides, A. tumefaciens, P. glicinea* and *P. fluorescens* were cultivated on a mineral substrate of the following composition: agar-agar (20.0 g), KNO_3 (2.0 g), $MgSO_4 \cdot 7H_2O$ (0.8 g), $FeSO_4 \cdot 7H_2O$ (0.1 g), $NH_4H_2PO_4$ (1.0 g), dissolved in 1000 mL of distilled water (pH 7.0–7.2).

The lactone was added to the nutrient substrate in two different concentrations. The first series of samples had 1 mg of lactone in 10 mL of substrate (*cca.* 200 mg), whereas the second one had 7 mg of lactone in 10 mL of substrate (*ca.* 200 mg).

Determination of the products

Following the separation of mycelium, the sample, of 1000-mL volume, was extracted with the same volume of CH_2Cl_2 in order to identify the starting lactone, the number and the chemical structure of transformed lactone products.

The extract thus obtained was dried with anhydrous Na_2SO_4, filtered, concentrated, and analyzed by thin-layer chromatography (TLC) on silica-gel using hexane:acetone = 6:4 as the solvent. The R_f values were determined relative to the standard, starting lactone.

The identification of the extracellular degradation products of the synthetic lactone was performed by preparative TLC on silica gel, using hexane:acetone = 6:4 as the solvent system. The spot fronts of the unkown compounds were marked by comparison wih a chromatogram obtained under the same conditions when the spots were visible after developing the chromatogram with H_2SO_4 or UV irradiation. The crude metabolic compounds were analyzed by IR. ^{13}C-and ^{1}H-NMR spectreoscopic analysis, and compared to literature data.[22]

Compound *(a):2-(4-dichloromethyl-6-hydroxy-4-methyl-2-cyclohex-2-en-1-one) acrylic acid.* R_f=0.36. IR (KBr), ν(cm^{-1}) 3450-2570 (OH), 1755 (C=O), 1705 (C=O conj.), 1668, 1649 (C=CH_2), 1238, 1180 (C–O), 855 (=CH_2), 800, 780, (C–Cl). ^{1}H-NMR ($CDCl_3$, δ): 1.35 (*s*, 3H, CH_3), 3.85 (*bd*, H, C-5, ^3J=9.56 Hz), 5.03 (*d*, H, C-6, ^3J=9.56 Hz), 5.41 (*bd*, H, C-10, ^2J=1.75 Hz), 5.75 (*bd*, H, C-10, ^2J=1.75 Hz), 5.85 (*s*, 1H, $CHCl_2$), 6.15 (*d*, H, C-2, ^3J=11.26 Hz), 6.51 (*d*,H, C-3, ^3J=11.26 Hz), 8.67 (*bs*. H, COO*H*). ^{13}C-NMR ppm: 166.7 (C=O, C-11), 145.7 (C-9), 120.2 (C-10), 35.57 (C-5), 46.38 (C-4), 148.29 (C-3), 129.8 (C-2), 195.6 (C-1), 77.6 (C-6), 18.98 (C-8), 79.76 (C-7). m.p. 155–157 °C, yield. 42 mg. 19.7%. Anal. calc. for $C_{11}H_{12}O_4Cl_2$(278.0114): C, 47.33; H, 4.35. Required: C, 47.84; H, 4.21.

Compound (b): 2-(6-hydroxy-4-methyl-2-cyclohex-2-en-1-one) acrylic acid. R_f=0.17. IR (KBr), ν(cm^{-1}) 3450–2570 (OH), 1765 (C=O), 1705 (C=O, conj.), 1668, 1649, (C=CH_2), 1180 (C–O), 845 (=CH_2). ^{1}H-NMR ($CDCl_3$, δ): 1.23 (*d*, 3H, CH_3, ^3J=9.2 Hz), 2.05 (*m*, H, C-4, ^3J=9.2 Hz), 3.34 (*m*, H, C-5, ^3J=8.75 Hz), 5.09 (*d*, H, C-6. ^3J=8.75 Hz), 5.37 (*bd*, H, C-9, ^2J=1.7 Hz), 5.73 (*bd*, H, C-9, ^2J=1.7 Hz), 6.15 (*d*, H, C-5, ^3J=10.33 Hz), 6.51 (*d*,H, C-6, ^3J=10.33 Hz), 8.61 (*bs*,H. COO*H*). ^{13}C-NMR, ppm: 168.3 (C=O,C-10), 149.6 (C-8), 123.8 (C-9), 36.67 (C-5), 40.72 (C-4), 149.19 (C-3), 127.6 (C-2), 194.4 (C-1), 74.2 (C-6), 16.8 (C-7), oil, yield, 32 mg. 21%. Anal. calc. for $C_{10}H_{12}O_4$; (196.0735); C, 61.20; H, 6.17. Required: C, 61.78; H, 6.21.

Compound (c): 10-methyl-4-methyliden-5-hydroxy-perhydroisochrom-7-en-3,6-dione: R_f=0.44. IR (KBr), ν(cm^{-1}): 3560-3360 (OH), 1740 (C=O, δ-lact), 1705 (C=O, conj.), 1685 1649 (C=CH_2), 1250 (C–O), 855 (=CH_2). ^{1}H-NMR ($CDCl_3$, δ): 1.25 (*s*, 3H, CH_3), 4.15 (AB*q*., 2H, Δν=32.6 Hz), 5.23 (*d*, H, C-5, ^3J=7.9Hz), 2.90 (*bd*, H,C-9, ^3J=7.9 Hz, ^4J=0.8 Hz), 5.14 (*bd*. H,C-10, ^2J=1.75 Hz, ^4J=0.6 Hz), 5.72 (*bd*, H, C-10, ^2J=1.75 Hz, ^4J=0.8 Hz), 6.15, (*d*, H, C-5, ^3J= 11.2 Hz) 6.51 (*d*,H,C-6, ^3J=11.2 Hz). ^{13}C-NMR (ppm):

167.7 (C=O,C-3), 149.3 (C-4), 110.2 (C-11), 33.47 (C-9), 36.38 (C-10), 150.23 (C-8), 129.0 (C-7), 196.54 (C-6), 73.31 (C-5), 14.38 CH_3. M.p. 139–141 °C, yield, 36 mg, 22.7%. Anal. calc. for $C_{11}H_{10}O_4$ (206.0579): C, 64.06; H, 4.89. Required: C, 64.67; H, 4.25.

Compound (d): 2-(4-dimethyl-6-hydroxy-2-cyclohex-2-en-1-one)acrylic acid R_f = 0.09. IR (film), ν(cm^{-1}): 3450-2570 (OH), 1755 (C=O), 1705 (C=O conj.), 1668, 1649 (C=CH_2), 1170 (C–O), 845 (=CH_2). ^{1}H-NMR ($CDCl_3$, δ): 1.23 (*s*, 2H, CH_3), 1.34 (*s*, 3H, CH_3), 3.21 (*m*, H, C-5, ^3J=9.25 Hz), 5.19 (*d*, H, C-6, ^3J=9.25 Hz), 5.37 (*bd*. H, C-9, ^2J=1.8 Hz), 5.69 (*bd*, H, C-9, ^2J=1.8 Hz), 6.10 (*d*, H, C-5, ^3J=10.75Hz), 6.28 (*d*, H, C-6, ^3J=10.75 Hz). Oil, yield 19 mg, 11.8%. $C_{11}H_{14}O_4$: MS, M^+ (210.089) 11, 192 (M^+–18) 21, 195 (M^+–15) 14, 177 (M^+–18–15) 24.

И З В О Д

МИКРОБИОЛОШКА ТРАНСФОРМАЦИЈА СИНТЕТИЧКОГ ЛАКТОНА БЕНЗОФУРАНСКОГ ТИПА

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Циљ овог рада је испитивање могућности биотрансформације бензофуранског деривата, са α-метилен-γ-бутиролактонском структурном јединицом, са различитим сојевима микроорганизама: *Aspergillus niger, Saccharomyces cerrevisiae, Bacillus mycoides, Agrobacterium tumefaciens, Pseudomonas glicinea* и *Pseudomonas fluorescens* у циљу добивања нових једињења са специфичнијом антимикробном активношћу. Такође изоловани и идентификовани производи су указали и потврдили основне биодеградационе путеве испитиваног лактона.

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