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ACIDIC ISOMERIZATION OF ALANTOLACTONE DERIVATIVES

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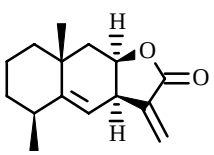
*A series of derivatives of the natural sesquiterpene lactones alantolactone (**1**) and isoalantolactone (**2**) was prepared. The α-methylene-γ-lactone moiety was retained in the structures of these for further modifications using reactions that affected exclusively the nonconjugated double bonds of the decalin ring.*

Key words: sesquiterpene lactones, alantolactone, isoalantolactone, acidic isomerization, *Inula helenium* L.

The great potential biological and pharmacological activities of natural sesquiterpene lactones are responsible for the interest in developing this area of chemistry [1, 2]. The most promising direction is the chemical modification of compounds isolated from natural sources in order to prepare substances with new properties. Certain natural sesquiterpene lactones have been used as effective medicinal preparations (for example, the antitumor preparation Arglabin [3]).

The goal of the present work was to prepare a series of derivatives based on the natural sesquiterpene lactones alantolactone (**1**) and isoalantolactone (**2**) in the structures of which the α-methylene-γ-lactone moiety was retained for further modifications. This was achieved using reactions that affected exclusively the nonconjugated double bonds of the decalin ring.



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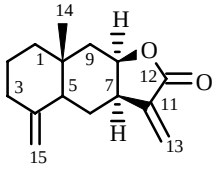

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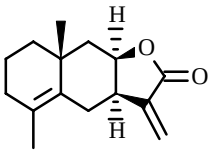

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A mixture of lactones **1** and **2** (~1:1 ratio) was isolated from roots of *Inula helenium* L. (Asteraceae) by a method consisting of extraction of the ground raw material with $CHCl_3$ and subsequent chromatography over a column of SiO_2. Fractions containing this mixture were evaporated and crystallized (2-3 times) from aqueous CH_3OH (70%) to afford about 25% (of the total content of the extract) of pure **2**. The isomers were further separated over a column of SiO_2 impregnated with $AgNO_3$ (5%) with gradient elution by benzene in light petroleum ether. The compounds isolated by chromatography over the column impregnated with Ag contained an impurity of Ag (2-5% according to elemental analysis) that was removed by passing their benzene solution over a layer of neutral Al_2O_3 (activity I). The resulting compounds were identical to those in the literature [4].

It is well known that olefins can undergo acidic isomerization to form intermediates and transition-state carbonium ions in which prototropic and skeletal rearrangements are observed. Therefore, we investigated the reactions of the alantolactone derivatives with acids.

Alantolactone (**1**) is stable to acids (under drastic conditions the reaction mixture polymerizes) according to the literature [5] and our data.

Shifts of the exocyclic double bond in the decalin ring of **2** that occur in the presence of acids have been reported [6]. This formed a mixture of the thermodynamically more favorable isomeric trisubstituted olefins that contain an endocyclic double bond between C-4 and C-5 (**3**) or C-3 and C-4. The ratio of products depends on the acid used (2:1 for methanesulfonic acid in trifluoroethanol [5] and 1:3 in formic acid [7]). We found the conditions for selective isomerization of **2** into **3**. The PMR spectrum of **3** contained a singlet for the methyl on the double bond (1.60 ppm) instead of signals for the exomethylene protons on C-15. The ^{13}C NMR exhibited signals for C-15 at 26.6 ppm and showed shifts for C-4 and C-5 from 148.34 to 126.52 ppm

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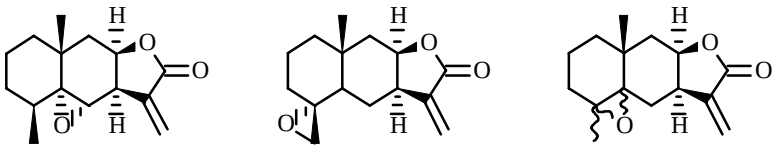
and from 45.55 to 130.56 ppm, respectively. The spectral data as a whole defined the compound as alloalantolactone, which was isolated previously from another plant of this genus, *I. racemosa* [8].

Isoalantolactone (**2**) also isomerized if trifluoroacetic acid (in $CHCl_3$) or H_2SO_4 (in acetic acid) were used at room temperature. The yield was highest (81%) for the reaction with a 5-fold excess of trifluoroacetic acid. The product was purified by chromatography. In contrast with **1** and **2**, it turned out to be quite labile and gradually polymerized upon storage under normal conditions.

Lactones **1**-**3** were epoxidized by peracid at the nonconjugated double bond using the literature method [9]. The conversion occurred at room temperature during 1-7 days depending on the structure of the starting compound (**1** was the most reactive). In all instances, the epoxy derivatives **4**-**6** were obtained in quantitative yields.



4 **5** **6a, b**

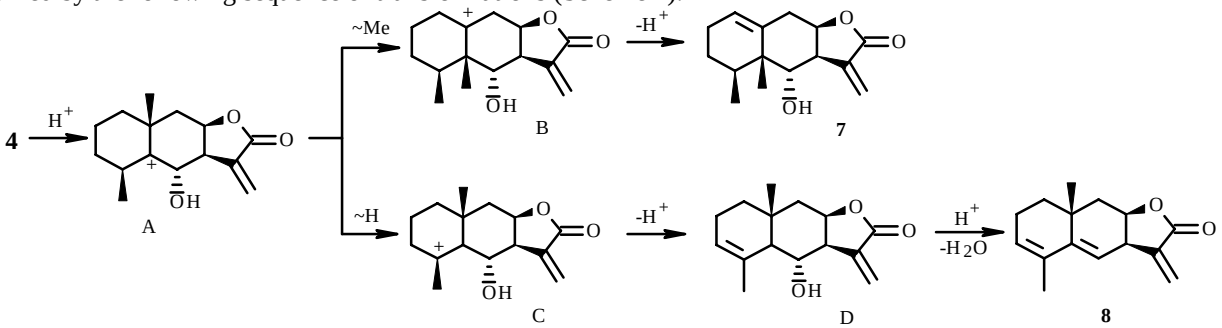
The epoxidation of **1** and **2** by peracetic acid was reported to be stereospecific, i.e., one structural isomer formed in which the epoxide oxygen had the α-orientation according to an x-ray crystal structure (XCS) [9]. This was confirmed by our investigations. Tables 1 and 2 give the NMR spectra of the starting compounds and the resulting products.

The PMR spectrum of epoxyalantolactone **4** lacked a signal for a C-6 olefinic proton. Instead, a doublet appeared at 2.89 ppm that corresponded to the proton on the epoxide C atom (signals for C-5 and C-6 appeared at 66.77 and 60.43 ppm, respectively, in the ^{13}C NMR spectrum). The PMR spectrum of epoxyisoalantolactone **5** also had signals for protons of the oxirane ring at 2.63 (dd, 1H) and 2.50 ppm (d, 1H) instead of a signal for the exomethylene protons. Corresponding changes were observed also in the ^{13}C NMR spectrum (Table 2). Signals for the epoxide C atoms shifted to strong field (from 106.02 to 50.23 ppm for C-15 and from 148.34 to 57.99 ppm for C-4). Our spectral results agreed with those in the literature [9] and confirmed the structures of **4** and **5** and the orientation of the epoxide O atom.

Epoxidation of **3** produced a mixture of isomers in a 3:2 ratio. The PMR and ^{13}C NMR spectra of **6a** and **6b** were very similar (Tables 1 and 2). Epoxidation of the lactone telekin, which has a similar structure, is known to form the α-epoxide as the main product and the β-epoxide as the minor one [10]. The chemical shift (CS) of the angular methyl on C-10 of the major component of **6** was 1.03 ppm whereas that of the minor one shifted to weaker field to 1.16 ppm. This is comparable with data for α- and β-epoxyisotelekin [10]. Thus, the major component was assumed to have the α-orientation of the oxirane O atom; the minor, the β-orientation, based on the literature data and the NMR spectra. Pure epimers **6a** and **6b** were obtained by repeated recrystallization from CH_3OH.

Attempts were made to open the epoxide ring in **4**-**6**. Lactones containing an epoxide are known to convert usually into diols under acid-catalysis conditions [11]. However, we showed that **4** formed alcohol **7** as the main product under various acidic conditions (boiling in aqueous oxalic acid; stirring at room temperature in aqueous acetone with trifluoroacetic, sulfuric, or perchloric acids). The ester (formate) of this alcohol was prepared by treating **4** with formic acid in acetone [12]. This reaction is an example of the transformation of the eudesmane lactone skeleton into that of eremophilane.

The best yield (~50%) of **7** was obtained after boiling for 5 h in a 3-fold excess of oxalic acid. Work up of the reaction mixture isolated **7** as large transparent crystals (from benzene with hexane). Column chromatography over Silpearl (benzene eluent) detected a side product of this reaction (13% yield), conjugated diene lactone **8**. The formation of **7** and **8** can be explained by the following sequence of transformations (Scheme 1).



Scheme 1

TABLE 1. Chemical Shifts (δ, ppm) and Spin—Spin Coupling Constants (J/Hz) of Protons in PMR Spectra of Alantolactone Derivatives (in $CDCl_3$)

Compound	Signal of proton on C atoms										
	C-1	C-2	C-3	C-4	C-6	C-7	C-8	C-9	C-13	C-14	C-15
1		1.3-1.7 (6H)		2.43 m	5.12 d, J = 4.1	3.56 m, J_1 = 1.8, J_2 = 3.3, J_3 = 4.1, J_4 = 10.9	4.79 m, $J_1 = J_2$ =3.3, J_3 = 7.0	2.09 dd, J_1 = 3.3, J_2 = 14.9; 1.52 dd, J_1 = 3.3, J_2 = 14.9	6.18 d, J = 1.9; 5.59 d, J = 1.8	1.17 s, (3H)	1.07 d, J = 7.5 (3H)
2	1.96-2.29 (2H)	1.4-1.6 (2H)	1.34-1.81 (2H)	-	1.68 ddd, J_1 = 2.7, J_2 = 7.0, J_3 = 14.1; 1.42 d J = 12.0	2.94 m, J_1 = 5.1, J_2 = 7.0, J_3 = 11.9	4.46 dt, $J_1 = J_2$ = 1.8, J_3 = 4.9	2.15 dd, J_1 = 1.4, J_2 = 15.5; 1.45 d, J = 15.5	6.08 d, J = 0.8; 5.56 d, J = 0.7	0.78 s (3H)	4.73 d, J = 1.4; 4.39 d, J = 1.2
3	1.42 dd, J_1 = 4.3, J_2 = 7.2 (2H)	1.51-1.64 (2H)	1.81-2.00 (2H)	-	2.75 dd, J_1 = 7.6, J_2 = 13.5; 1.81-2.00	3.01 m	4.45 dt, $J_1 = J_2$ = 7.24, J_3 = 6.5	1.69 d, J = 6.5 (2H)	6.19 d, J = 2.7; 5.57 d, J = 2.4	1.03 s (3H)	1.60 s (3H)
4			1.3-2.0 (7H)		2.89 d, J = 2.54	3.66 ddd, $J_1 = J_2$ = 2.54, J_3 = 8.8	4.66 ddd, J_1 = 1.4, J_2 = 4.3, J_3 = 8.8	1.91 dd, J_1 = 4.3, J_2 = 15.2; 1.55 dd, J_1 = 1.4, J_2 = 15.2	6.40 d, J = 2.8; 5.76 d, J = 2.54	1.10 s (3H)	1.03 d, J=7.63 (3H)
5		0.8-1.9 (6H)		-	0.9 m; 1.53 m	2.86 m, $J_1 = J_2$ = 5.3, J_3 = 10.2	4.43 dt, J_1 = 1.5, $J_2 = J_3$ = 4.8	2.12 dd, J_1 = 1.5, J_2 = 15.5; 1.48 dd, J_1 = 4.8, J_2 = 15.5	6.05 d, J = 1.0; 5.50 d, J= 0.8	0.92 s (3H)	2.63 dd, J_1 = 1.96, J_2 = 4.4; 2.50 d, J = 4.4
6a		1.1-1.9 (6H)		-	1.1-1.9 (2H)	3.22 m	3.22 m	1.1-1.9 (2H)	6.29 d, J = 2.9; 5.58 d, J = 2.5	1.03 s (3H)	1.35 s (3H)
6b		1.1-1.9 (6H)		-	1.6 dd, J_1 = 7.4, J_2 = 14.5; 1.8 dd, J_1 = 12.0, J_2 = 14.5	3.19 m J_1 = 5.2, J_2 = 7.4, J_3 = 12.0	4.54 ddd, J_1 = 2.0, J_2 = 4.7, J_3 = 5.2	2.05 dd, J_1 = 2.0, J_2 = 15.5; 1.74 dd, J_1 = 4.7, J_2 = 15.5	6.11 d, J = 1.2; 5.55 d, J = 1.1	1.16 s (3H)	1.27 s (3H)
7	5.62 m	1.8-2.1 (2H)	1.3-1.5 (2H)	1.8-2.1	3.98 d, J = 5.67	3.24 m	4.68 dt, J_1 = 7.2, J_2 = 8.0, J_3 = 9.6	2.62 dd, J_1 = 7.2, J_2 =14.1; 2.24 m, J_1 = 9.6, J_2 = 14.1	6.32 d, J = 3.13; 5.68 d, J = 2.8	0.98 d, J = 6.8 (3H)	0.95 s (3H)
8	2.06 (2H)	1.37 m; 2.06	5.61 m	-	5.31 d, J = 4.2	3.74 m	4.86 m	2.22 dd, J_1 = 2.3, J_2 = 15.3; 1.58 dd, J = 15.3	6.23 d, J = 1.8; 5.67 d, J = 1.4	1.01 s (3H)	1.75 s (3H)

TABLE 1. (continued)

Compound	Signal of proton on C atoms										
	C-1	C-2	C-3	C-4	C-6	C-7	C-8	C-9	C-13	C-14	C-15
9	1.24-1.42 (2H)	1.24-1.42; 1.50-1.72	2.47 dt, $J_1 = J_2 = 7.0$, $J_3 = 13.0$; 1.50-1.72	-	2.94 dd, $J_1 = 11.2$, $J_2 = 12.5$; 2.33 dd, $J_1 = 4.7$, $J_2 = 11.2$	3.25 m	4.7 dt, $J_1 = 6.8$, $J_2 = J_3 = 8.8$	2.01 m (2H)	6.31 d, J = 2.9; 5.65 d, J = 2.7	1.00 s (3H)	1.14 s (3H)
10[a]		1.1-1.9 (6H)		-	1.70 m $J_1 = 9.0$, $J_2 = 15.0$; 1.85 m	3.24 m, $J_1 = 6.0$, $J_2 = 9.0$, $J_3 = 11.0$	4.51 dt, $J_1 = J_2 = 5.1$, $J_3 = 6.0$	2.00 dd, $J_1 = 5.1$, $J_2 = 15.5$; 1.68 m	6.09 d, J = 1.2; 5.52 d, J = 1.0	1.09 s (3H)	1.21 s (3H)

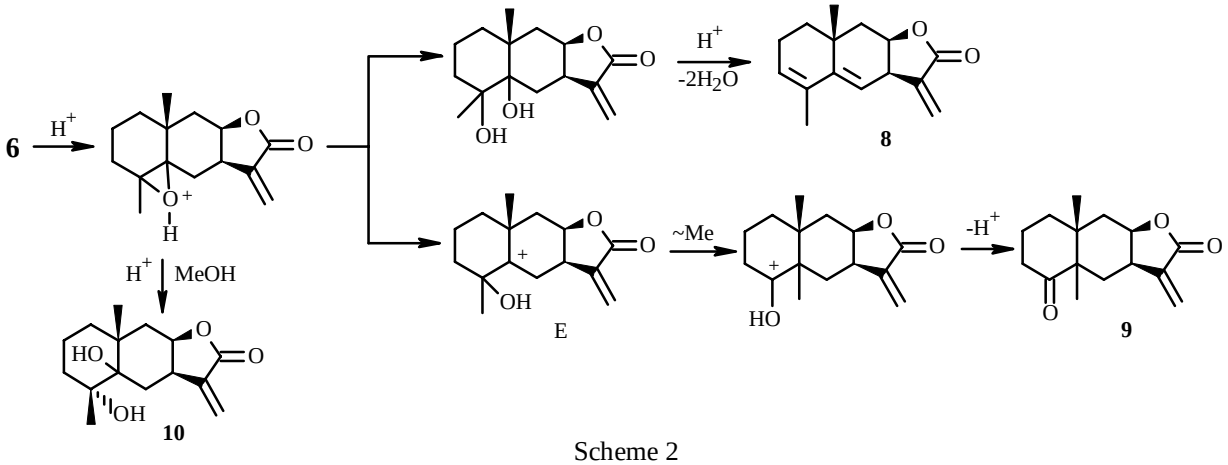
[a]Methoxy proton signals observed at 3.07 ppm (s, 3H).

It can be assumed that protonation of **4** opens the oxirane ring to form cation A, which can rearrange by two pathways. In the first, the methyl migrates from the 10-position to the 5-position by the known Wagner—Meerwein rearrangement. Cation B is stabilized by loss of a proton from the 1-position and forms a double bond between C-1 and C-10 (**7**). Loss of a proton from the 9-position does not occur apparently because of the presence of the C-8 oxygen and the increased CH acidity of the 9-CH_2 group due to this. The structure of **7** was established using NMR spectra.

The PMR spectrum exhibited signals for the exomethylene of the lactone ring (doublets at 6.32 and 5.68 ppm), the olefinic proton (multiplet at 5.62 ppm), lactone protons H-8 (doublet of triplets at 4.68 ppm), and H-7 (multiplet at 3.24 ppm). The SSCC of these protons corresponded with *cis*-fusion of the lactone ring. A doublet at 3.98 ppm was assigned to proton H-6, which is conjugated to the hydroxyl. The ^{13}C NMR spectrum contained signals for C atoms of the double bond C-1 (127.70 ppm) and C-10 (quaternary signal at 136.28 ppm), C-6 with the hydroxyl (73.79 ppm), and methyls shifted to weak field owing to the effect of the OH oxygen. The structure of **7** was confirmed by an XCS (performed by V. A. Tofienko at the Chemistry Department of Moscow State University, to be reported separately).

A hydride ion can also migrate from C-4 in cation A to give cation C (Scheme 1). Deprotonation of cation C forms intermediate alcohol D (identified in the reaction mixture using PMR spectroscopy) that then dehydrates to conjugated diene **8**.

Diene **8** is more conveniently prepared in preparative amounts from another epoxy derivative. It is the main product (56% yield) from opening of the epoxide ring in **6** under analogous conditions. Apparently the epoxide is hydrolyzed and a double dehydration of the resulting diol occurs during the transformation. Like for **4**, the reaction is not selective. Epoxide **6** isomerized in parallel to ketone **9** (24% yield). The formation of **9** is explained by migration of methyl into the 5-position from intermediate carbonium ion E with loss of a proton from the protonated O atom of the carbonyl (Scheme 2).



Scheme 2

TABLE 2. ^{13}C NMR Spectra (δ, ppm) of Alantolactone Derivatives (in $CDCl_3$)

Compound	C atom														
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15
1	41.15	16.23	32.14	37.01	139.28	118.19	38.92	75.88	42.05	32.04	148.58	169.99	121.14	28.05	22.05
2	41.57	22.14	36.24	148.34	45.55	26.91	39.91	76.22	40.75	33.68	141.56	170.05	119.49	17.11	106.02
3	42.29	18.35	31.63	126.52	130.56	27.61	40.93	75.94	36.77	33.28	139.69	170.20	121.03	19.06	26.60
4	38.78	15.71	28.78	36.30	66.77	60.43	36.63	74.43	36.93	31.81	135.93	168.94	123.09	23.23	17.34
5	41.26	19.84	34.75	57.99	43.63	22.58	39.87	75.96	40.84	33.75	141.28	170.01	120.15	18.04	50.23
6a	33.99	15.23	37.81	69.44	65.26	26.75	38.25	76.18	28.65	31.66	142.63	172.63	121.97	22.78	20.90
6b	31.87	16.30	43.44	66.41	63.84	29.86	37.41	74.65	34.81	31.59	140.44	171.50	125.27	22.99	19.86
7	127.70	25.38	27.15	32.25	42.60	73.79	46.16	75.68	36.10	136.28	134.78	172.55	123.40	19.28	17.20
8	39.70	36.93	126.93	140.77	142.72	119.77	39.49	76.18	22.04	30.54	130.21	172.78	122.93	36.23	22.04
9	37.86	31.77	38.72	212.80	61.57	34.72	38.17	76.57	19.51	44.05	140.82	171.31	125.24	25.72	18.47
10[a]	35.88	16.63	29.81	75.16	78.41	28.75	36.97	76.32	39.22	34.89	143.06	171.24	121.09	18.47	24.12

*Methoxy signals appeared at 48.91 ppm.

TABLE 3. Mass and IR Spectral Data of Alantolactone Derivatives **6-10**

Compound	Diagnostic ion, *m/z* (I_{rel}, %)	IR spectrum (ν, cm^{-1})
6a	248 (M^+, 17), 233 (7), 230 (8), 217 (3), 215 (7), 205 (38), 190 (65), 178 (100), 163 (20), 145 (34), 137 (45), 119 (33), 109 (51), 95 (56), 78 (77), 71 (45), 55 (49), 43 (27)	1758, 1232, 1127, 1028, 990
6b	248 (M^+, 10), 233 (4), 230 (8), 217 (3), 215 (7), 205 (35), 190 (47), 178 (100), 163 (24), 145 (37), 137 (40), 119 (34), 109 (52), 95 (51), 78 (100), 71 (44), 55 (78), 43 (30)	1758, 1261, 1138, 1000, 937
7	248 (M^+, 14), 230 (100), 219 (14), 215 (48), 201 (47), 188 (28), 173 (20), 163 (22), 152 (21), 145 (41), 134 (44), 123 (70), 107 (77), 91 (69), 80 (54), 69 (77), 55 (63), 34 (27)	3453, 1753, 1293, 1106, 1000, 973
8	230 (M^+, 54), 215 (11), 197 (12), 187 (6), 169 (23), 143 (25), 128 (27), 121 (100), 105 (33), 91 (48), 76 (28), 65 (24), 55 (29), 43 (28)	1720, 1640, 1267, 1147, 1120, 1000, 960, 894
9	248 (M^+, 6), 233 (3), 230 (16), 207 (54), 179 (11), 139 (16), 121 (23), 111 (24), 95 (100), 80 (57), 55 (51), 43 (34)	1753, 1691, 1278, 1152, 998, 944
10	280 (M^+, 20), 265 (23), 248 (64), 237 (27), 230 (15), 205 (17), 187 (15), 180 (47), 161 (24), 133 (18), 125 (64), 98 (79), 84 (100), 72 (84), 59 (78), 55 (72), 43 (28)	3545, 1748, 1266, 1165, 1081, 968

Compound **8** was assigned the structure 5,8a-dimethyl-3-methylene-3a,7,8,8a,9,9a-hexahydro-3*H*-naphtho[2,3-*b*]furan-2-one based on NMR spectra. The PMR spectrum contained signals for protons of the lactone exomethylene (doublets at 6.23 and 5.67 ppm), olefinic H-3 protons (multiplet at 5.61 ppm), and H-6 (doublet at 5.31 ppm) in addition to a signal for the C-15 methyl protons shifted to weak field at 1.75 ppm. The ^{13}C NMR spectrum confirmed the proposed structure (Table 2). Signals were observed for C atoms of the double bonds C-3 (126.93 ppm) and C-4 (140.77 ppm, quaternary) and C-5 (142.72 ppm, quaternary) and C-6 (119.77 ppm). The CS of C-5 and C-6 were close to those for **1** (Table 2).

The structure 4a,8a-dimethyl-3-methylenedecahydronaphtho[2,3-*b*]furan-2,5-dione was proposed for **9** based on spectral data. Thus, the PMR of **9** contained signals for protons of the lactone exomethylene (doublets at 6.31 and 5.65 ppm) and one of the H-3 protons (doublet of triplets at 2.47 ppm). The presence of the carbonyl was confirmed by a signal in the ^{13}C NMR spectrum for quaternary C-4 at 212.80 ppm.

Epoxyisoalantolactone **5** formed immediately a complicated mixture of compounds in the presence of acids (even under mild conditions). Derivatives with an aldehyde (according to PMR spectra) and polymers dominated the products.

We demonstrated the capability for acid-catalyzed nucleophilic opening of the oxirane ring by aliphatic alcohols (using CH_3OH as an example) using the mixture of **6a** and **6b** as an example. The structure of the product **10** was established using

NMR spectroscopy. Thus, the PMR spectrum contained signals for the exomethylene protons as doublets at 6.09 and 5.52 ppm and a well resolved signal for the methoxy as a singlet at 3.07 ppm. The ^{13}C NMR spectrum exhibited signals for C atoms conjugated to O for quaternary C-4 (75.16 ppm) and C-5 (78.41 ppm) that were shifted to weak field compared with **6**, for methoxy (48.91 ppm), and for methyls on C-14 (18.47 ppm) and C-15 (24.12 ppm).

Thus, acid-catalyzed transformations of **1-3** and their epoxide derivatives **4-6** occur with retention of the lactone ring. The products contain an exomethylene conjugated to the lactone carbonyl and make it possible to prepared from these compounds a large set of lactones substituted with various functionalities that possess higher biological activity, are water soluble, and can be transported.

EXPERIMENTAL

NMR spectra were recorded on a Bruker DPX-200 spectrometer at working frequency 200 MHz (data given in Tables 1 and 2). Mass spectra were recorded in a Finnigan 4021 GC—MS at 70 eV ionization energy. IR spectra (KBr disks) were obtained on a Bruker ZFS-113v instrument (Table 3).

The course of reactions and purity of products were monitored using TLC on Silufol plates using benzene:ethylacetate (3:2) and GC (Chrom-5 chromatograph, 3.6 m × 3 mm column packed with Inerton Super 0.125-0.160 mm with 5% XE-60, flame-ionization detector, detector and vaporizer temperature 250°C, thermostat 75°C). Elemental analyses of all initially prepared compounds agreed with those calculated.

Alloalantolactone (5,8a-dimethyl-3-methylene-3a,4,6,7,8,8a,9,9a-octahydro-3*H*-naphtho[2,3-*b*]furan-2-one, 3). A solution of **1** (1.16 g, 5 mmol) in $CHCl_3$ (20 mL) was stirred, treated with trifluoroacetic acid (4.5 mL), and left at room temperature. After the starting lactone disappeared (course of reaction monitored using PMR spectroscopy), the mixture was poured into water, neutralized with saturated Na_2CO_3 solution, and extracted with $CHCl_3$ (3 × 20 mL). The extracts were washed and dried. Solvent was evaporated. The solid was passed over a layer of SiO_2 (benzene eluent) to afford a colorless oil (0.94 g, 81%).

Epoxyalloalantolactones 6a and 6b were prepared by cooling (ice) a solution of peracetic acid (acetic anhydride, 5 mL; H_2O_2, 1.1 mL, 30%; H_2SO_4, one drop) and adding solid sodium acetate until the pH was ~5-6 and a solution of alloalantolactone (**3**, 2.32 g, 10 mmol) in CH_2Cl_2 (5 mL). The mixture was left at room temperature. The formation of products was monitored using TLC. After the starting lactone disappeared (1-2 d), the mixture was poured into water, neutralized with $NaHCO_3$ solution, and extracted with $CHCl_3$ (3 × 10 mL). Solvent was evaporated. The solid was passed over a column of neutral Al_2O_3 in benzene to remove traces of acetic anhydride and afforded **6a** and **6b** (2.1 g, 85%). Repeated crystallization from CH_3OH (PMR monitoring) isolated pure **6a** (mp 103-104°C) and **6b** (mp 136-139°C).

4-Hydroxy-4a,5-dimethyl-3-methylene-3a,4,4a,5,6,7,9,9a-octahydro-3*H*-naphtho[2,3-*b*]furan-2-one (7) and 5,8a-dimethyl-3-methylene-3a,7,8,8a,9,9a-hexahydro-3*H*-naphtho[2,3-*b*]furan-2-one (8). Epoxyalantolactone (**4**, 2.48 g, 10 mmol) in aqueous oxalic acid (5 g in 50 mL water) was boiled for 5 h, cooled, neutralized with $NaHCO_3$ solution (5%), and extracted with $CHCl_3$ (3 × 30 mL). Solvent was evaporated to afford a yellow oil, crystallization of which from benzene:hexane (3:1) afforded **7** (1.2 g, 48%). The mother liquor was evaporated and passed over a column of SiO_2 (Silpearl) with elution by benzene to afford **8** (0.3 g, 13%), mp 93-95°C (hexane). Addition to the eluent of ethylacetate (5%) isolated **7** (0.28 g), mp 101-102°C. Overall yield of **7**, 61%.

4a,8a-Dimethyl-3-methylenedecahydronaphtho[2,3-*b*]furan-2,5-dione (9). A mixture of **6a** and **6b** (2.48 g, 10 mmol) in aqueous oxalic acid (4 g in 50 mL water) was boiled for 3 h, neutralized with $NaHCO_3$ (6 g in 100 mL water), and extracted with $CHCl_3$ (3 × 30 mL). The solid left after evaporation of solvent was passed over a column of SiO_2 (Silpearl) with elution by benzene to isolate two compounds **8** (1.3 g, 56%) and **9** (0.6 g, 24%), mp 170-171°C (CH_3OH).

4a-Hydroxy-5-methoxy-5,8a-dimethyl-3-methylenedecahydronaphtho[2,3-*b*]furan-2-one (10). Epoxyalloalantolactones **6a** and **6b** (1.24 g, 5 mmol) in CH_3OH (100 mL) were treated with KU-2 ion-exchanger in the H-form (1 g) and stirred at room temperature until the starting material disappeared. The resin was filtered off. CH_3OH was evaporated. The solid was passed over a column of SiO_2 (Silpearl) with elution by benzene. A fraction with R_f 0.5 was collected. Recrystallization from benzene:hexane afforded **10** (0.7 g, 51%), mp 115-116°C.

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